Exploration of Drug Science

Open Exploration

Open Access Original Article

A gas chromatographic and spectrophotometric-based assessment of an oral preparation from a traditional exhilarating formulation; linking Persian medicine to the modern phytopharmaceuticals

Ali Sahragard[1,2], Aida Alipour[1,2], Mohammad M. Zarshenas[1,2*]

[1]Medicinal Plants Processing Research Center, Shiraz University of Medical Sciences, Shiraz 7474133858, Iran
[2]Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz 7146864685, Iran

***Correspondence:** Mohammad M. Zarshenas, Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz 7146864685, Iran. zarm@sums.ac.ir
Academic Editor: Rangasamy Jayakumar, Amrita Vishwa Vidyapeetham University, India
Received: January 10, 2025 **Accepted:** May 25, 2025 **Published:** July 22, 2025

Cite this article: Sahragard A, Alipour A, Zarshenas MM. A gas chromatographic and spectrophotometric-based assessment of an oral preparation from a traditional exhilarating formulation; linking Persian medicine to the modern phytopharmaceuticals. Explor Drug Sci. 2025;3:1008120. https://doi.org/10.37349/eds.2025.1008120

Abstract

Aim: Depression is one of the most important mental diseases. Different pharmacological and non-pharmacological methods are used to treat depression. Traditional and complementary medicine also have a special role in the treatment of depression. Among the specific medicinal formulations mentioned in Traditional Persian Medicine (TPM), an important and widely used form is "*Mufarrah*" (exhilarating), which indirectly refers to the mood-stabilizing group. In this work, a related traditional formulation has been reformulated and standardized as a conventional tablet.

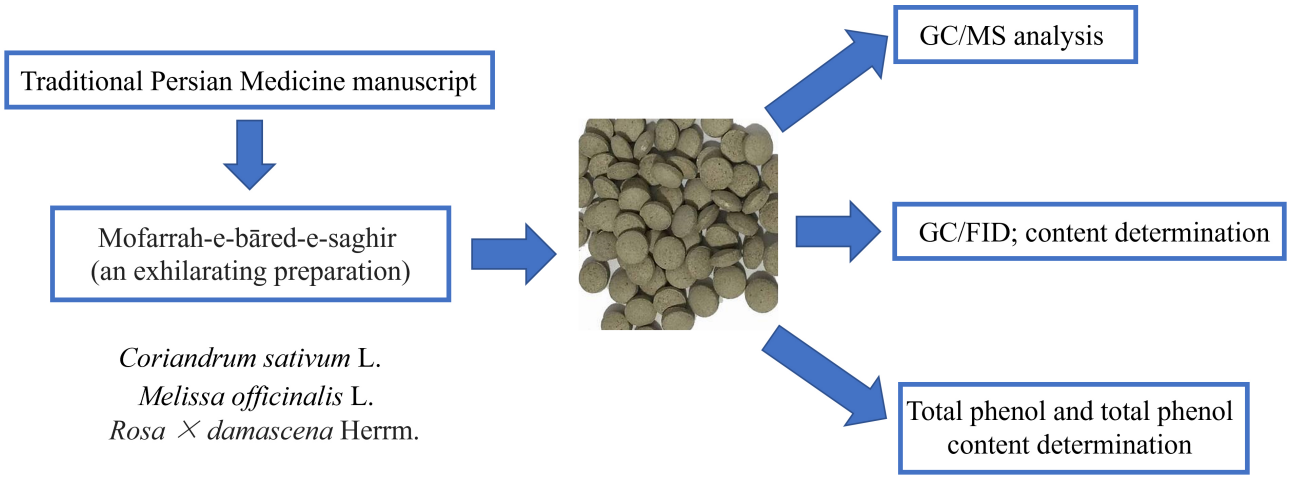
Methods: A simple and famous example among this group is "Mufarrah-e-Bared-e-Saghir", containing *Rosa* × *damascena* Herrm., *Coriandrum sativum* L., *Melissa Officinalis* L. Following tablet preparation of the mentioned remedy, total phenolic and flavonoid content was determined using the spectrophotometric method. Volatile constituent analysis and quantification of linalool as the main component were carried out via gas chromatography (GC) [GC/MS (mass spectrometry) and GC/FID (flame ionization detector)].

Results: According to the results, the main compound of the final product was linalool (54.6%). Linalool, total phenol, and total flavonoid amounts have been calculated, respectively, 2,379.65 ± 262.13 μg/mL of the extracted essential oil, 163.23 ± 0.61, and 41.41 ± 2.3 mg/g extract.

Conclusions: Prepared tablets as a reformulated traditional medicine product with rich total phenols and flavonoids, as well as the presence of linalool as a considerable icon with antidepressant activities, can be introduced to the Persian medicinal plants market to control depression.

Keywords

Mufarrah, standardization, *Rosa* × *damascena* Herrm., *Coriandrum sativum* L., *Melissa Officinalis* L.



Graphical abstract. A concise view of the study design, formulation, and content determination. GC/MS: gas chromatography/mass spectrometry; FID: flame ionization detector

Introduction

Mood disorders are the most prevalent and disabling diseases among neuropathic disorders [1, 2]. One of the most important diseases in this category is depression. Currently, 17% of people in the world are suffering from this disease. Depression is increasing worldwide, which makes global society concerned [3, 4]. Annually, 351 million people suffer from depression [2].

It is reported that females are twice as likely as males to be depressed [5, 6]. The most important intervention factors are genetic and environmental [7, 8]. The main feature is feeling depressed for at least two weeks in different situations. Besides, it is usually accompanied by sleep and eating disorders, fatigue, weakness, pain, and lack of self-confidence [9, 10].

Different pharmacological and non-pharmacological methods are used to treat depression. Pharmacological treatment includes tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) [11, 12]. Various non-pharmacological therapies have been studied to relieve a patient's depression, including complementary medicine, massage therapy, exercise, acupuncture and acupressure, music therapy, and yoga [13, 14]. Other non-pharmacological interventions, such as transcranial direct current stimulation (TDCS) and electroshock therapy, have also been reported [15, 16].

Along with common medicines, medicinal plants have been widely considered as alternative or complementary remedies for depression. Complementary documents are a valuable resource for discovering new medicines. Traditional Persian Medicine (TPM), consisting of many medical and pharmaceutical manuscripts, has introduced numerous herbal medicines to manage different diseases [17–19]. As mood-elevating supplements, TPM has reported a class, namely Mufarrah (exhilarators). These medicines regulate mood disorders and simultaneously enhance memory and thinking [20, 21].

Reported in Qarabadin-e-Salehi, one of the most famous formulary textbooks in TPM, Mufarrah-e-Bared-e-Saghir (simple cold exhilarator) is an effective multi-ingredient traditional formulation consisting of *Coriandrum sativum* L. (*C. sativum*) (2 parts), *Rosa* × *damascena* Herrm (*R. damascena*) (1 part), and *Melissa officinalis* L. (*M. officinalis*) (0.6 part) [22].

R. damascena (Rosaceae) is traditionally used for headaches, exhilaration, and improving the heart function, lungs, stomach, and liver [21]. It is effective in the treatment of depression [21, 23], convulsions [23, 24], dementia and nervous stress [23, 25], and insomnia [26, 27]. It also has anti-nociceptive effects [28] and antioxidant activity [29, 30]. *M. officinalis* (Lamiaceae) is also used for exhilaration, toothache, enhancement of memory, and brain function [21, 30]. It is revealed to be effective in insomnia, reducing stress, and enhancing memory, convulsion, Alzheimer's, depression, and anxiety [31–34]. This plant has been observed to have considerable antioxidant, anti-inflammatory, and anti-nociceptive effects [35, 36]. *C.*

sativum (Apiaceae) is traditionally used for exhilarating, insomnia, preventing smallpox and jaundice, relieving dental pain, and suppressing cough [21, 37]. Different pharmacological effects have been reported for *C. sativum*, including effects on insomnia, anticonvulsive activity, enhancing memory, anti-Alzheimer effects, antidepressant effects, and reducing anxiety [38–41]. Besides, it has analgesic, antioxidant, and anti-inflammatory activities [40, 42].

This study aimed to introduce, formulate, and determine the related phytochemicals in the prepared product via chromatographic and spectrophotometric methods.

Materials and methods

Purchased samples of each plant were authenticated by a botanist from the Department of Phytopharmaceuticals, Shiraz School of Pharmacy, with a voucher number (*R. damascena*: PM1329; *M. officinalis*: PM1318; *C. sativum*: PM1248). Polyvinylpyrrolidone was from Sigma-Aldrich (CAS 9003-39-8), magnesium stearate from Merck (415057), ethanol from Taghtir Khorasan Co. (Iran), methanol (Merck: 39302), linalool (Sigma-Aldrich: C39288), gallic acid (Sigma-Aldrich: G7384), quercetin (Sigma-Aldrich, CAS 117-39-5), aluminum chloride (Merck: 206911), Folin-Ciocalteu (Sigma-Aldrich: F9295), and sodium carbonate (Supelco: 1.06329).

Tablet preparation and extraction of the product's essential oil

After related pharmaceutical evaluations, a compressed tablet (700 mg) containing 420 mg of herbal mixed powder (4 times daily), polyvinylpyrrolidone, starch, and magnesium stearate (280 mg overall) was prepared, granulated (wet). The content of the herbal mixed powder was according to the related manuscript mentioned in the TPM text (nearly 1,700 mg daily). According to the instructions in the British Pharmacopeia, prepared tablets were assessed based on some of the main pharmaceutical evaluations, such as hardness, friability, disintegration, weight variation, and flowability (mixed powder for tablet preparation).

The prepared tablets were subjected to the hydrodistillation method using a Clevenger apparatus. The yielded essential oil (EO) was kept in a freezer (–20°C) for further steps.

Preparation of the extract

The tablets' hydroalcoholic extract was prepared using 70% ethanol via an ultrasonic bath at 40°C for 20 minutes. The extract is concentrated and dried for the next step.

GC/MS and GC/FID analysis of the essential oil

GC/MS (gas chromatography/mass spectrometry) analysis was performed on an Agilent 7789A GC equipped with an HP-5 column and connected to a mass spectrometer operating at a mass range of 30 to 600 m/z and 70 eV ionization energy. Helium was selected as the carrier gas, the flow rate was 1 mL/min, and the split ratio was 1:30. The injector temperature was 250°C, the detector temperature was 280°C, and the column temperature was programmed linearly from 60° to 250°C (at a rate of 5°C/min) and then held at 250°C for 10 minutes. The EO sample in dichloromethane (approximately 1%) was injected. The same analytical methods and conditions were used for GC/FID (flame ionization detector) analysis. Identification and quantification of the components were based on comparing their mass spectra with Wiley (n17) and Adams library spectra, as well as mass spectra reported in various literature [43].

Stock solution and linalool (major essential oil constituent) concentration series

Although there are valuable volatile compounds for quantification, linalool, with an area of 54% from the data of GC/MS, was considered the main marker for further steps. Various concentrations of linalool in methanol (345, 690, 1,380, 2,760, and 5,520 µg/mL) were prepared and injected into the GC/FID to determine the quantitative values (Table 1). To check repeatability, three injections were performed for each standard, and the standard curve was drawn via the mean value of the three injections. For the EO sample of the product as well, the mean value of at least three injections was considered as the concentration of the sample.

Table 1. Standard linalool calibration

Concentration (µg/mL)	Mean ± SD	RSD%
345	64.06 ± 3.35	5.22
690	118.13 ± 4.94	4.18
1,380	286.17 ± 7.38	2.57
2,760	623.13 ± 19.11	3.06
5,520	1,146.37 ± 39.33	3.43

RSD: relative standard deviation; SD: standard deviation

Also, for method validation, a linalool marker with a concentration of 345 µg/mL was injected into the device on three different days and three times each day so that intraday and interday differences, as well as RSD (relative standard deviation), would be calculated. Limit of detection (LOD) and limit of quantification (LOQ) were measured for the concerned marker. To specify the amount of the concerned marker in the product sample, the EO was injected into the GC/FID, and the value was specified using the line equation and area under the curve.

Determination of the total phenolic content of extracts

Phenolic and polyphenolic compounds are the main group of natural antioxidants available in plants [44, 45], and they would be measured using the Folin-Ciocalteu reagent and colorimetric method via a UV spectrophotometer [46]. In this method, metal oxides will be reduced by polyphenolic antioxidants such as gallic acid and catechin, and a blue-colored solution will be created [44, 47].

In this test, gallic acid was used as the standard, and total phenolic content was reported based on gallic acid (mg/g). Firstly, gallic acid stock solutions (6.25, 12.5, 25, 50, 100, and 200 mg/mL) were prepared by dissolving them in methanol, and 60 mg of the product was then dissolved in 20 mL of methanol and passed through a filter paper (Table 2). Afterward, 0.5 mL of various concentrations of gallic acid was diluted by 2.5 mL of Folin-Ciocalteu and mixed with 2 mL sodium carbonate (75 g/L) and kept in the dark at room temperature. The absorbance was measured at 765 nm using a UV spectrophotometer (methanol as the blank). This test was performed three times for every concentration of gallic acid stock solutions. Then the graph of absorbance versus concentration was drawn, and the line equation was calculated (Figure 1) [4].

Table 2. Standard phenolic content calibration

Standard	Conc. mg/mL	Abs.
Gallic acid	6.25	0.037
Gallic acid	12.5	0.059
Gallic acid	25	0.134
Gallic acid	50	0.242
Gallic acid	100	0.468
Gallic acid	200	0.948

Abs.: absorbance; Conc.: concentration

Determination of the flavonoid content of the prepared tablet

The Dowd method was applied [48], and 2 mL of the extract was mixed with 2 mL of aluminum chloride (2%); it was kept in the dark for 10 minutes at room temperature. The UV absorption range was measured via a UV spectrophotometer (415 nm). Flavonoid content in the dried plant (mg/g) was calculated based on quercetin, and the calibration curve was drawn. Various concentrations of quercetin (3.125, 6.25, 12.5, 25, and 50 mg/mL) were prepared in methanol (Table 3) and used as the standard to draw the calibration curve so that flavonoid content would be measured (Figure 2). The injection volume was 1 microliter in all cases.

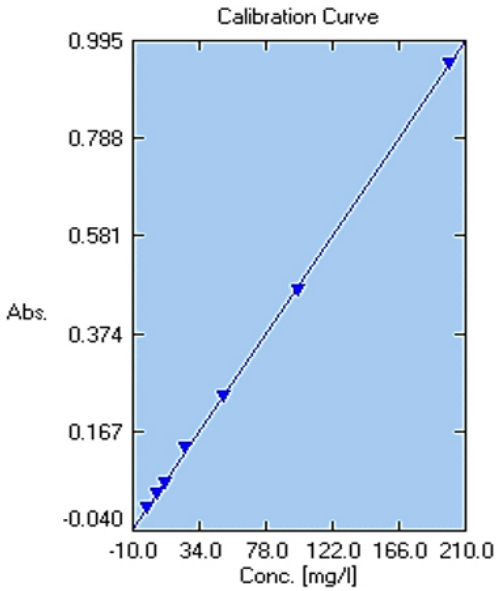


Figure 1. A gallic acid standard curve. Abs.: absorbance; Conc.: concentration

Table 3. Standard flavonoid calibration

Standard	Conc. mg/mL	Abs.
Quercetin	3.125	0.091
Quercetin	6.25	0.172
Quercetin	12.5	0.357
Quercetin	25	0.703
Quercetin	50	1.46

Abs.: absorbance; Conc.: concentration

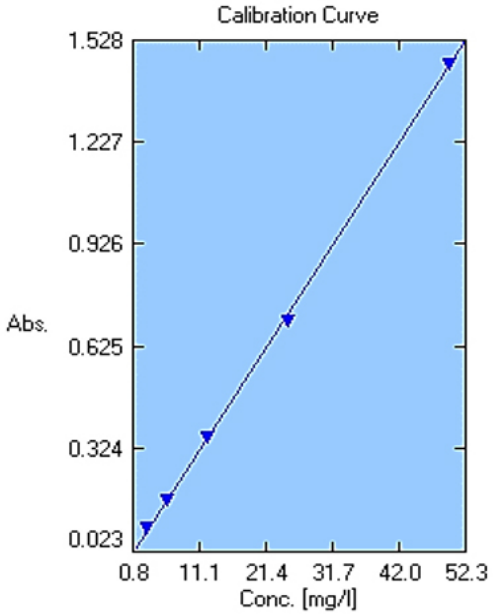


Figure 2. Quercetin standard curve. Abs.: absorbance; Conc.: concentration

Results

Analysis of the essential oil compositions in the final formulation

According to the data from GC/MS (Figure 3), EO ingredients were identified, and linalool was considered the main constituent (Table 4).

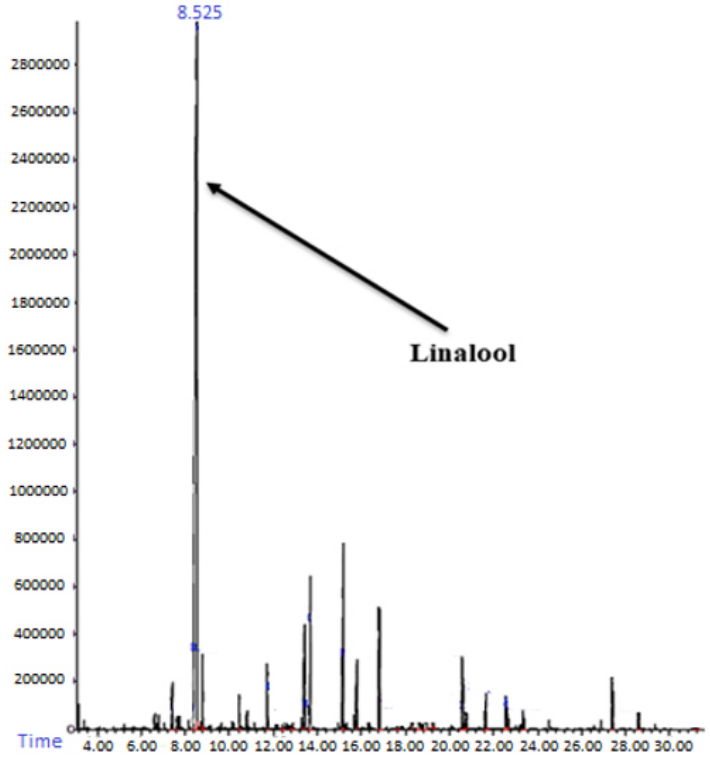


Figure 3. GC/MS spectrum of the final product. GC/MS: gas chromatography/mass spectrometry

Table 4. Essential oil compositions. (KI indices were calculated based on the reference, Adams RP [49]. Identification of essential oil components by gas chromatography/quadrupole mass spectroscopy: Allured, Carol Stream, IL 60188, USA.)

Number	Component	Retention time (min)	Area (%)	KI (calculated)	KI (reference)
1	γ-Terpinene	7.406	1.21	1,058.309	1,060
2	n-Octanol	7.639	0.58	1,068.062	1,070
3	Linalool	8.525	54.60	1,104.720	1,101
4	Phenethyl alcohol	8.793	2.06	1,115.004	1,114
5	4-Terpineol	10.454	1.01	1,178.741	1,180
6	β-Citronellol	11.725	2.02	1,227.221	1,228
7	Geraniol	12.424	1.14	1,253.759	1,255
8	Thymol	13.409	3.79	1,291.154	1,292
9	Carvacrol	13.677	5.01	1,301.365	1,300
10	Eugenol	15.170	7.11	1,359.571	1,362
11	Geranyl acetate	15.782	2.11	1,383.431	1,386
12	trans-Caryophyllene	16.802	4.22	1,424.128	1,420
13	α-Humulene	17.623	0.72	1,457.421	1,456
14	Curcumene	18.288	0.70	1,484.388	1,483
15	Zingiberene	18.591	1.15	1,496.675	1,495
16	β-Sesquiphellandrene	19.285	0.99	1,526.065	1,525
17	Caryophyllene oxide	20.748	0.59	1,588.373	1,589
18	Dillapiole	21.634	1.13	1,627.378	1,625
19	Turmerone	22.630	0.69	1,671.862	1,672
20	n-Nonadecane	27.381	1.75	1,898.033	1,899
21	Palmitic acid	28.575	0.68	1,959.454	1,960
22	Oleic acid	31.909	0.59	2,137.075	2,141
-	Identification (%)	93.85			

KI: Kovats index

After injecting the EO and the linalool at a similar temperature and comparing the linalool peak in the spectrum generated by the EO, the similarity of both peaks and their locations in both spectra was ensured (Figure 4), and the calibration curve was drawn (Figure 5). Three injections were performed for each standard, and the standard curve was plotted via the mean value of the three injections (Table 5). Considering the point that the density of the obtained EO was estimated as 1, the linalool sample concentration was calculated at 2,379.65 ± 262.13 µg/mL (LOD: 0.06 mg/mL, LOQ: 0.18 mg/mL) in 1 mL injection of the EO (Figure 6).

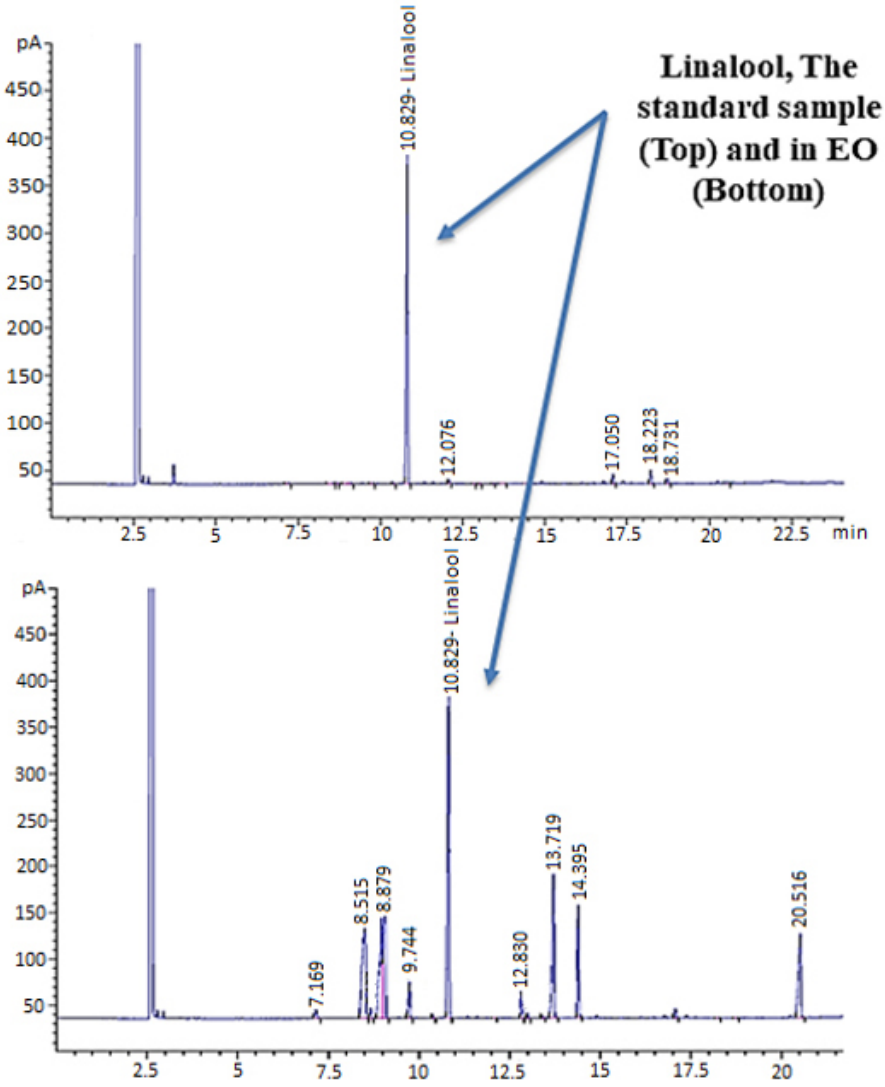


Figure 4. Comparison of the appearance of standard linalool and the same marker in the EO. EO: essential oil

Table 5. The intra-day and inter-day values

Days	Area (%)			Mean SD (intra-day)	RSD% (intra-day)	RSD% (inter-day)
	A_1	A_2	A_3			
1	1,117.2	1,191.1	1,130.8	1,146.37 ± 39.33	3.43	3.20
2	1,129.9	1,180.5	1,198.5	1,169.63 ± 35.57	3.04	
3	1,138.5	1,202.2	1,110.7	1,150.5 ± 46.90	4.08	

RSD: relative standard deviation; SD: standard deviation

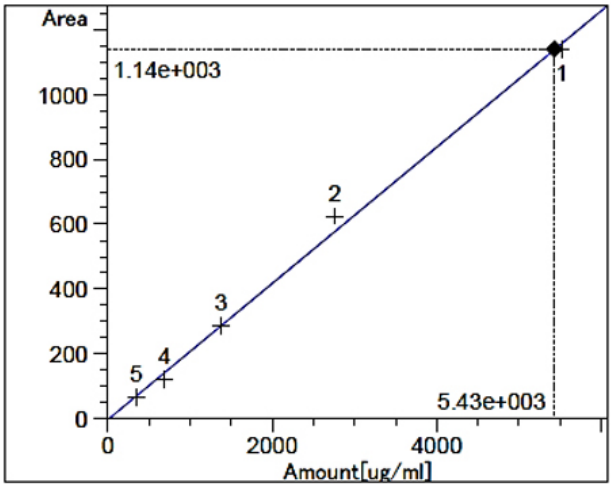


Figure 5. The standard curve of linalool

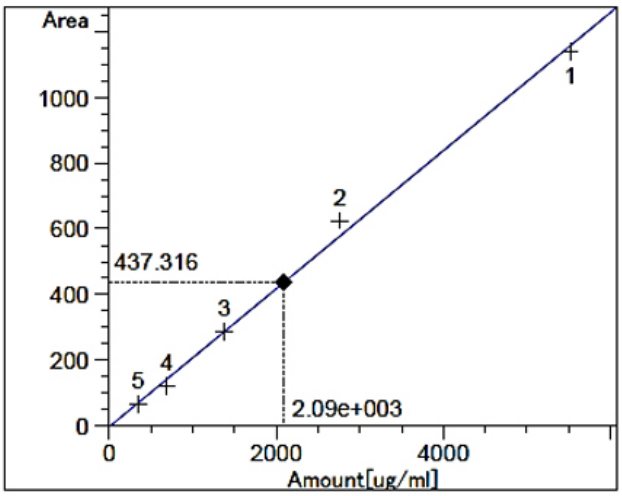


Figure 6. Determination of linalool on the calibration curve of standard linalool

The yield of the hydroalcoholic extract

The yield was calculated to be 5.9% v/w.

Determination of the flavonoid content

According to Table 6, the total flavonoid content in one gram of extract is 41.41 ± 2.3 mg/g extract (based on quercetin).

Table 6. The total flavonoid in the extract is based on quercetin

Stock Conc. (mg/mL)	Total flavonoid in stock (mg/mL)			Total flavonoid in extract (mg/g)			AV ± SD (mg/g)
	Repetition 1	Repetition 2	Repetition 3				
1,000	44.09	40.05	40.09	44.09	40.05	40.09	41.41 ± 2.3

AV ± SD: average ± standard deviation; Conc.: concentration

Determination of the total phenolic content

According to Table 7, the total phenol content in one g of the extract was 163.23 ± 0.61 mg/g (based on gallic acid).

Table 7. Total phenolic content in the extract is based on gallic acid

Stock Conc. (mg/mL)	Total phenol in stock (mg/mL)			Total phenol in extract (mg/g)			AV ± SD (mg/g)
	Repetition 1	Repetition 2	Repetition 3				
1,000	162.52	163.59	163.59	162.52	163.59	163.59	163.23 ± 0.61

AV ± SD: average ± standard deviation; Conc.: concentration

Discussion

Considering the high prevalence of depression among people of different ages, its increasing prevalence can be attributed to economic and social reasons, etc. [50, 51]. Accordingly, it is important to provide a variety of medicines to control this complication. This research aimed to introduce a reformulated natural medicine, Mufarrah-e-Bared-e-Saghir, from TPM to improve social and public welfare and introduce a related product.

Similar effects have been reported in modern medicine for the herbal ingredients used in this formulation. Herein, some of them are referred to. In a study, the aqueous extract of *C. sativum* seed at 100 mg/kg showed an anxiolytic effect in male albino mice compared to the control group in performing the elevated plus-maze (EPM) test as an animal model of anxiety [52, 53].

Another study evaluated the antidepressant and anti-anxiety effects of the ethanol extract of *C. sativum* seed in Albino mice. Compared with the standard treatment group, the evaluation of the antidepressant activity of 200 mg/kg ethanol extract of *C. sativum* seed showed a significant reduction in immobility time, while 200 mg/kg of it would result in a significant reduction of locomotion as a criterion for anxiety [54].

Animal studies have shown that *M. officinalis* at a dose of 25 to 300 mg/kg has antidepressant effects [55]. In another study, it was observed that the ethanol extract of *M. officinalis* would increase the neurotransmission of norepinephrine, which in turn produced antidepressant effects in the forced swimming test [56]. An animal study on mice showed that an aqueous extract of *M. officinalis* can significantly reduce immobility and increase climbing behavior similar to that observed with imipramine. Besides, compared to the control group, the EO obtained from the plant can reduce immobility and increase climbing in mice. However, a considerable increase was observed in the forced swimming test at the highest dose (300 mg/kg) [57].

In respect of *R. damascena*, a study has been performed on rats using a forced swimming test, and the results indicate that oral rose drops with 10, 20, and 40% concentrations significantly reduce depression acutely and in a short period compared to placebo, which was similar to amphetamine. Considering this, the effect may be due to the release of presynaptic amines [58]. In another study, the aqueous extract of *R. damascena* (15 mg/kg) used in male rats caused a significant increase in swimming time and reduction of immobility duration compared to the control group, and this shows that it has an antidepressant effect [59]. Besides, *R. damascena* can lead to a reduction in neurogenic stress [60]. In some studies, the effectiveness of linalool (the main substance of this product) has been reported in the treatment of brain diseases and mood disorders, especially depression and anxiety. A study conducted on Wistar male rats using a forced swimming test showed that linalool has considerable antidepressant effects [61–63].

In another study performed on mice using a forced swimming test and antagonist drugs to receptors related to the depression process, such as 5-HT1A, it can be concluded that linalool has antidepressant-like effects by interacting with the monoaminergic system [64].

Linalool has also been shown to have antidepressant-like activity in the tail suspension test in male mice [65]. Besides, some other pharmacological properties have been reported for linalool, such as antiepileptic effect, sedative activity, mood-stabilizing, anti-nociceptive, and anti-inflammatory activity [38, 66], as well as competitive NMDA receptor inhibition, which has resulted in antidepressant and anti-anxiety properties in pre-clinical studies [61, 67].

In this study, Mufarrah-e-Bared-e-Saghir was prepared based on the citations found in TPM texts. Subsequently, phytochemical research and standardization were conducted. Standardization is defined as the optimal technical application of shared knowledge, which includes processes for selection that facilitate appropriate choices for approval, along with consistent decisions to maintain established standards [19].

Subsequently, GC studies were conducted on the EO and extract of the final product, determining the EO components as well as the total phenols and flavonoid content in the extract. Overall, this formulation could be utilized in clinical and industrial settings to address anxiety and depression. The obtained spectra may also serve as a reference for evaluating market samples.

Abbreviations

EO: essential oil

FID: flame ionization detector

GC/MS: gas chromatography/mass spectrometry

LOD: limit of detection

LOQ: limit of quantification

TPM: Traditional Persian Medicine

Declarations

Author contributions

AS: Methodology, Writing—original draft. AA: Writing—original draft, Investigation, Writing—review & editing. MMZ: Conceptualization, Writing—review & editing, Supervision. All authors read and approved the submitted version.

Conflicts of interest

The authors have no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

Funding

This manuscript was supported by the School of Pharmacy, Shiraz University of Medical Sciences [Project number: 16872]. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Publisher's note

References

1. Acid L. Final report on the safety assessment of oleic acid, laurie acid, palmitic acid, myristic acid, and stearic acid. J Am Coll Toxicol. 1987;6:321–401.
2. Flaherty A, NS R. In: Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry. Philadelphia: Lippincott Williams & Wilkins; 2011.
3. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. Arch Gen Psychiatry. 1994;51:8–19. [DOI] [PubMed]
4. Sharma M, Bhattarai T, Sharma P. Anxiety and Depression among Senior Citizens. J Nepal Health Res Counc. 2021;19:305–10. [DOI] [PubMed]
5. Shi P, Yang A, Zhao Q, Chen Z, Ren X, Dai Q. A Hypothesis of Gender Differences in Self-Reporting Symptom of Depression: Implications to Solve Under-Diagnosis and Under-Treatment of Depression in Males. Front Psychiatry. 2021;12:589687. [DOI] [PubMed] [PMC]
6. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Text revision. Washington DC: American Psychiatric Association; 2000.
7. Remes O, Mendes JF, Templeton P. Biological, Psychological, and Social Determinants of Depression: A Review of Recent Literature. Brain Sci. 2021;11:1633. [DOI] [PubMed] [PMC]
8. Costello EJ, Pine DS, Hammen C, March JS, Plotsky PM, Weissman MM, et al. Development and natural history of mood disorders. Biol Psychiatry. 2002;52:529–42. [DOI] [PubMed]
9. Franchini L, Barbini B, Zanardi R, Fregna L, Martini F, Manfredi E, et al. Mood Disorders. In: Fundamentals of Psychiatry for Health Care Professionals. Cham: Springer; 2022. pp. 49–84.
10. Bauer MS, Mitchner L. What is a "mood stabilizer"? An evidence-based response. Am J Psychiatry. 2004;161:3–18. [DOI] [PubMed]
11. Gupta S, Shakya MK. Novel Approaches to Depression Treatment: Integrating Pharmacological and Non-Pharmacological Strategies. Iconic Res Eng J. 2024;8:100–12.
12. Chang JP, Zamparelli A, Nettis M, Pariante C. Antidepressant drugs: mechanisms of action and side effects. In: Sala SD, editor. Encyclopedia of Behavioral Neuroscience. 2nd ed. Amsterdam: Elsevier; 2022. pp. 613–26.
13. Khowaja B, Rind K. Efficacy of complementary and alternative medicine in treatment of postpartum depression: A situation analysis. Glob J Public Health Med. 2021;3:386–95. [DOI]
14. Guerra-Martín MD, Tejedor-Bueno MS, Correa-Casado M. Effectiveness of Complementary Therapies in Cancer Patients: A Systematic Review. Int J Environ Res Public Health. 2021;18:1017. [DOI] [PubMed] [PMC]
15. Tamminga CA, Nemeroff CB, Blakely RD, Brady L, Carter CS, Davis KL, et al. Developing novel treatments for mood disorders: accelerating discovery. Biol Psychiatry. 2002;52:589–609. [DOI] [PubMed]
16. Anand S, Hotson J. Transcranial magnetic stimulation: neurophysiological applications and safety. Brain Cogn. 2002;50:366–86. [DOI] [PubMed]
17. Norouzi M, Haghdoost AA, Karimiafshar M, Setayesh M. Comparability of Traditional Persian Medicine with the New Concepts of Personal and Precision Medicine: A Qualitative Study. Tradit Integr Med. 2024;9:128–35. [DOI]

18. Karami S, Shamshiri S, Abdollahi M, Rahimi R. An Evidence-based Review of Medicinal Plants used in Traditional Persian Medicine for Treatment of Osteoarthritis. Curr Drug Discov Technol. 2021;18: 244–71. [DOI] [PubMed]
19. Larijani B, Esfahani MM, Moghimi M, Ardakani MRS, Keshavarz M, Kordafshari G, et al. Prevention and Treatment of Flatulence From a Traditional Persian Medicine Perspective. Iran Red Crescent Med J. 2016;18:e23664. [DOI] [PubMed] [PMC]
20. Soltani M, Shams J, Ghaffari F, Alijaniha F, Naseri M. Effects Of Saffron (Crocus Sativus Linn) Supplementation On Happiness And Quality Of Life In Healthy Adults: A Randomized Double Blind Clinical Trial. J Pharm Negat Results. 2023;14:2849–55. [DOI]
21. Aghili Khorasani M, editor. Makhzanol-Advieh. Tehran: Tehran University of Medical Sciences; 1992.
22. Heravi M, editor. Qarabadin-e-salehi. Tehran: Dar-ol-khalafeh; 1765.
23. Beheshti F, Ahmadabady S, Baghcheghi Y, Anaeigoudari A, Hosseini M. A mini review of neuropharmacological effects of Rosa damascena Herrm. Pharm Sci. 2021;28:232–8. [DOI]
24. Kheirabadi M, Moghimi A, Rakhshande H, Rassouli M. Evaluation of the anticonvulsant activities of *Rosa damascena* on the PTZ induced seizures in wistar rats. J Biol Sci. 2008;8:426–30. [DOI]
25. Rasooli T, Nasiri M, Aliabadi ZK, Rajabi MR, Feizi S, Torkaman M, et al. *Rosa Damascena mill* for treating adults' anxiety, depression, and stress: A systematic review and dose-response meta-analysis of randomized controlled trials. Phytother Res. 2021;35:6585–606. [DOI] [PubMed]
26. Erarslan ZB. THE GENUS ROSA. In: KOÇYİĞİT M, ARICAN YE, HASPOLAT YK, editors. ROSA. Ankara: Kadim Publication; 2023.
27. Abolhassanzadeh Z. Rosa damascena Herrm. In: Therapeutic Medicinal Plants in Traditional Persian Medicine. Boca Raton: CRC Press; 2023.
28. Hajhashemi V, Ghannadi A, Hajiloo M. Analgesic and Anti-inflammatory Effects of Rosa damascena Hydroalcoholic Extract and its Essential Oil in Animal Models. Iran J Pharm Res. 2010;9:163–8. [PubMed] [PMC]
29. Dadkhah A, Fatemi F, Mohammadi Malayeri MR, Karvin Ashtiani MH, Mosavi Z, Naij S, et al. The anti-inflammatory and antioxidant effects of *Rosa damascena* Mill. essential oil on the lung injury in the CLP model. J Med Plants. 2020;19:277–94. [DOI]
30. Alizadeh Z, Fattahi M. Essential oil, total phenolic, flavonoids, anthocyanins, carotenoids and antioxidant activity of cultivated Damask Rose (*Rosa damascena*) from Iran: With chemotyping approach concerning morphology and composition. Sci Hortic. 2021;288:110341. [DOI]
31. Akbar S. *Melissa officinalis* L.(Lamiaceae). In: Handbook of 200 Medicinal Plants: A Comprehensive Review of Their Traditional Medical Uses and Scientific Justifications. Cham: Springer; 2020. pp. 1177–88.
32. Chindo BA, Howes MR, Abuhamdah S, Yakubu MI, Ayuba GI, Battison A, et al. New Insights Into the Anticonvulsant Effects of Essential Oil From *Melissa officinalis* L. (Lemon Balm). Front Pharmacol. 2021;12:760674. [DOI] [PubMed] [PMC]
33. Ghazizadeh J, Hamedeyazdan S, Torbati M, Farajdokht F, Fakhari A, Mahmoudi J, et al. Melissa officinalis L. hydro-alcoholic extract inhibits anxiety and depression through prevention of central oxidative stress and apoptosis. Exp Physiol. 2020;105:707–20. [DOI] [PubMed]
34. Miraj S, Azizi N, Kiani S. A review of chemical components and pharmacological effects of *Melissa officinalis* L. Der Pharmacia Lettre. 2016;8:229–37.
35. Chindo BA, Howes MR, Abuhamdah S, Mallam D, Micah T, Awotula RI, et al. Evaluation of the anti-nociceptive profile of essential oil from *Melissa officinalis* L. (lemon balm) in acute and chronic pain models. J Ethnopharmacol. 2024;321:117500. [DOI] [PubMed]

36. Ortiz-Mendoza N, Martínez-Gordillo MJ, Martínez-Ambriz E, Basurto-Peña FA, González-Trujano ME, Aguirre-Hernández E. Ethnobotanical, Phytochemical, and Pharmacological Properties of the Subfamily Nepetoideae (Lamiaceae) in Inflammatory Diseases. Plants (Basel). 2023;12:3752. [DOI] [PubMed] [PMC]
37. Das G, Das S, Talukdar AD, Venil CK, Bose S, Banerjee S, et al. Pharmacology and Ethnomedicinal Potential of Selected Plants Species from *Apiaceae* (Umbelliferae). Comb Chem High Throughput Screen. 2023;26:256–88. [DOI] [PubMed]
38. Hosseini M, Boskabady MH, Khazdair MR. Neuroprotective effects of *Coriandrum sativum* and its constituent, linalool: A review. Avicenna J Phytomed. 2021;11:436–50. [DOI] [PubMed] [PMC]
39. Santibáñez A, Jiménez-Ferrer E, Angulo-Bejarano PI, Sharma A, Herrera-Ruiz M. *Coriandrum sativum* and Its Utility in Psychiatric Disorders. Molecules. 2023;28:5314. [DOI] [PubMed] [PMC]
40. Sahoo S, Brijesh S. Anxiolytic activity of *Coriandrum sativum* seeds aqueous extract on chronic restraint stressed mice and effect on brain neurotransmitters. J Funct Foods. 2020;68:103884. [DOI]
41. Mahdavi AM, Javadivala Z. Systematic review of preclinical studies about effects of *Coriandrum sativum* L. on inflammatory mediators. Inflammopharmacology. 2022;30:1131–41. [DOI] [PubMed]
42. Jiao Y, Wang X, Chen J. Biofabrication of AuNPs using Coriandrum sativum leaf extract and their antioxidant, analgesic activity. Sci Total Environ. 2021;767:144914. [DOI] [PubMed]
43. Adams RP, editor. Identification of essential oil components by gas chromatography/mass spectrometry. 5 online ed. Gruver: Texensis Publishing; 2017.
44. Hano C, Tungmunnithum D. Plant Polyphenols, More than Just Simple Natural Antioxidants: Oxidative Stress, Aging and Age-Related Diseases. Medicines (Basel). 2020;7:26. [DOI] [PubMed] [PMC]
45. Pratt D. Natural antioxidants from plant material. In: Phenolic Compounds in Food and Their Effects on Health II. Washington: ACS Publications; 1992.
46. Dudonné S, Vitrac X, Coutière P, Woillez M, Mérillon J. Comparative study of antioxidant properties and total phenolic content of 30 plant extracts of industrial interest using DPPH, ABTS, FRAP, SOD, and ORAC assays. J Agric Food Chem. 2009;57:1768–74. [DOI] [PubMed]
47. Ainsworth EA, Gillespie KM. Estimation of total phenolic content and other oxidation substrates in plant tissues using Folin-Ciocalteu reagent. Nat Protoc. 2007;2:875–7. [DOI] [PubMed]
48. Ahmad M, Ghazali N, Samsuri S, Ruslan M, editors. Comparative study of total phenolic content and total flavonoid content extraction from guava juices by progressive freeze concentration and evaporation. In: IOP conference series: materials science and engineering; 2019 Oct 30–31; Kuala Lumpur, Malaysia. IOP Publishing; 2020.
49. Sparkman OD. Identification of essential oil components by gas chromatography/quadrupole mass spectroscopy Robert P. Adams. J Am Soc Mass Spectrom. 2005;16:1902–3. [DOI]
50. Thipprakmas R. Prevalence and factors associated with depression in the elderly: A systematic review. J Health Promot Environ Health Reg Health Cent 9. 2021;15:325–38.
51. Nemenzo EP, Palompon DR, Bejoc JA. Social factors as antecedents of depression among community-dwelling older persons. Ageing Int. 2022;47:38–54. [DOI]
52. Emamghoreishi M, Khasaki M, Aazam MF. Coriandrum sativum: evaluation of its anxiolytic effect in the elevated plus-maze. J Ethnopharmacol. 2005;96:365–70. [DOI] [PubMed]
53. Mahendra P, Bisht S. Anti-anxiety activity of Coriandrum sativum assessed using different experimental anxiety models. Indian J Pharmacol. 2011;43:574–7. [DOI] [PubMed] [PMC]
54. Pathan A, Alshahrani A, Al-Marshad F. Neurological assessment of seeds of Coriandrum sativum by using antidepressant and anxiolytic like activity on albino mice. Inventi Impact: Ethnopharmacology. 2015;3:102–5.
55. Shakeri A, Sahebkar A, Javadi B. *Melissa officinalis* L. - A review of its traditional uses, phytochemistry and pharmacology. J Ethnopharmacol. 2016;188:204–28. [DOI] [PubMed]

56. Pereira RP, Boligon AA, Appel AS, Fachinetto R, Ceron CS, Tanus-Santos JE, et al. Chemical composition, antioxidant and anticholinesterase activity of Melissa officinalis. Ind Crops Prod. 2014; 53:34–45. [DOI]
57. Emamghoreishi M, Talebianpour MS. Antidepressant effect of Melissa officinalis in the forced swimming test. DARU J Pharm Sci. 2009;17:42–7.
58. Zarghami M, Farzin D, Bagheri K. Anti depressant effects of Rosa Damascena on laboratory rats (A controlled experimental blind study). J Mazandaran Univ Med Sci. 2001;11:27–33.
59. Dolati K, Rakhshandeh H, Shafei MN. Antidepressant-like effect of aqueous extract from Rosa damascena in mice. Avicenna J Phytomed. 2011;1:91–7.
60. Boskabady MH, Shafei MN, Saberi Z, Amini S. Pharmacological effects of rosa damascena. Iran J Basic Med Sci. 2011;14:295–307. [PubMed] [PMC]
61. Weston-Green K, Clunas H, Naranjo CJ. A Review of the Potential Use of Pinene and Linalool as Terpene-Based Medicines for Brain Health: Discovering Novel Therapeutics in the Flavours and Fragrances of Cannabis. Front Psychiatry. 2021;12:583211. [DOI] [PubMed] [PMC]
62. Dos Santos ÉRQ, Maia JGS, Fontes-Júnior EA, do Socorro Ferraz Maia C. Linalool as a therapeutic and medicinal tool in depression treatment: A review. Curr Neuropharmacol. 2022;20:1073–92. [DOI] [PubMed] [PMC]
63. 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;26:5128–33. [DOI] [PubMed]
64. Guzmán-Gutiérrez SL, Bonilla-Jaime H, Gómez-Cansino R, Reyes-Chilpa R. Linalool and β-pinene exert their antidepressant-like activity through the monoaminergic pathway. Life Sci. 2015;128:24–9. [DOI] [PubMed]
65. Coelho V, Mazzardo-Martins L, Martins DF, Santos ARS, da Silva Brum LF, Picada JN, et al. Neurobehavioral and genotoxic evaluation of (-)-linalool in mice. J Nat Med. 2013;67:876–80. [DOI] [PubMed]
66. Aprotosoaie AC, Hăncianu M, Costache II, Miron A. Linalool: a review on a key odorant molecule with valuable biological properties. Flavour Fragr J. 2014;29:193–219. [DOI]
67. Khushboo, Kumar A, Sharma B. Biomedical Implications of Plant-based Principles as Antidepressants: Prospects for Novel Drug Development. Mini Rev Med Chem. 2022;22:904–26. [DOI] [PubMed]