Herbal Medicines Journal **2019; 4(3):119-26**
DOI: 10.22087/herb%20med%20j.v4i3.772 **ISSN:** 2538-2144

Original Article

Evaluation of the Phytochemistry and Antidepressant-Like Effect of *Cinnamomum verum* Essential Oil in Male Mice

Tannaz Moselm-Zadeh[1], Saeid Abbasi-Maleki[1*], Goudarz Sadeghi-Hashjin[2]

[1]Department of Pharmacology & Toxicology, Urmia Branch, Islamic Azad University, Urmia, Iran
[2] Dependent of Comparative Bioscience, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran

Received: 29.09.2019; Accepted: 01.02.2020

Abstract

Background and Aim: Previous studies have reported the antioxidant, analgesic, anti-inflammatory, and neuroprotective effects *of Cinnamomum verum* (CV). Hence, the phytochemistry and antidepressant-like effects of the CV essential oil were investigated in the present study by the forced swimming test (FST) and tail suspension test (TST) in male mice.

Materials and Methods: Seventy-two male NMRI mice (20-30 g) were randomly divided into the control or vehicle (10 ml/kg, i.p.), the fluoxetine (20mg/kg, i.p.), the imipramine (30mg/kg, i.p.), and the CV essential oil (5, 10 & 20 mg/kg, i.p.) groups. The immobility, swimming, and climbing times of the mice in FST, as well as the immobility time in TST were determined and recorded.

Results: Based on the GC-MS analysis, the main component was cinnamaldehyde (87.42%). Furthermore, all doses of the CV essential oil decreased immobility times in FST ($P< 0.001$ and $P<0.05$, respectively) and TST ($P<0.001$). Moreover, all doses of the essential oil increased swimming time ($P< 0.01$ and $P<0.001$), but the climbing time was only increased by 10 and 20 mg/kg of the essential oil ($P< 0.01$ and $P<0.001$, respectively).

Conclusion: According to the findings of the present study, the major components of the CV essential oil (e.g. cinnamaldehyde) are likely to have antidepressant effects due to its monoaminergic mechanism. Nevertheless, further studies are required to determine its exact mechanism of action.

Keywords: Antidepressant, *Cinnamomum verum*, *Forced swimming test*, *Tail suspension test*, Monoaminergic system, Mice

***Corresponding Author:** Saeid Abbasi-Maleki, Department of Pharmacology & Toxicology, Urmia Branch, Islamic Azad University, Urmia, Iran. Email: s.abbasi@iaurmia.ac.ir.

Please cite this article as: Moselm-Zadeh T, Abbasi-Maleki S, Sadeghi-Hashjin G. Evaluation of the Phytochemistry and Antidepressant-Like Effect of *Cinnamomum verum* Essential Oil in Male Mice. Herb. Med. J. 2019; 4(3):119-26.

Introduction

Depression is a common mental disorder that will be the most prevalent disease in the world by 2030 as the World Health Organization (WHO) has stated (1). The neurobiology of the disease is currently unknown. However, it has been shown that the monoaminergic system plays a vital role in the pathophysiology of depression (2). Studies have revealed that the common synthetic antidepressant agents (e.g. fluoxetine and imipramine) act via increasing the reuptake of amino acids such as

serotonin (5-hydroxy tryptamine; 5-HT), noradrenaline (NA), and dopamine (DA) in synaptic clefts (3). Although these drugs are currently available, their side effects, including sexual dysfunction, nausea, dry mouth, weight gain, and sleep disorder have restricted their use. Hence, drugs with low side effects, particularly medicinal plants and their derivatives, are probably better replacements with regard to the reduction of complications and treatment efficiency (4). In line with this, our previous studies have already investigated and demonstrated the antidepressant properties of several extracts or essential oils, including *Lavandula officinalis*, *Pimpinella anisum*, *Passiflora incarnata*, *Viola odorata*, *Origanum majorana* L., *Sesamus indicum* oil, *Mentha piperita*, and *Carthamus tinctorius* (5-12).

C*innamomum verum* (CV) is an evergreen tree of 7 meters height with ovate-oblong and sharp leaves grown reciprocally on the stem. The most important compound taken from this plant is its essential oil. On the other hand, beside some other compounds like mucilage, tannin, benzocyanidines, and coumarins, the major constituent present in the essential oil is cinnamaldehyde. This plant has been reported to have different pharmacological properties, including analgesic, anti-inflammatory, anesthetic, and antioxidant effects (13). Moreover, Fadaei *et al*. reported the anti-anxiety and anti-depressant effects of the CV extract on the rats which had received lead acetate (14). Nonetheless, no study has been carried out on the antidepressant effects of the CV essential oil (with far more cinnamaldehyde than the extract) in animal models of depression to date. Hence, this research was undertaken to investigate the phytochemistry, as well as antidepressant-like effects of the CV essential oil in FST and TST, as two animal models of depression, in male mice.

Materials and Methods

Preparation of C*innamomum verum* Essential Oil

The CV essential oil was purchased from Adonis Gol Daru Pharmaceutical Co. (Tehran, Iran), under Bath no: 010. The plant samples were dried by anhydrous sodium sulfate, and stored at 4°C in sealed brown vials before use.

The Gas Chromatography-Mass Spectrometry Analysis (GC-MS)

Like our recent study (12), we used Agilent 6890 GC apparatus equipped with an HP-5MS capillary column (30 m × 0.25 mm i.d., 0.25 μm) and an Agilent 5973 mass detector for the separation and detection of chemical compounds. Chemical components were identified as explained by Adams, 2007, and the data were presented in Table 1 (15). Identification was achieved using kovats index by a homologous series of n-alkanes (C8-C25). The mass spectra were finally compared with samples in Wiley library and the literature data.

Drugs

The drugs that were used include fluoxetine HCL (Abidi Pharmaceutical Co, Iran) and imipramine HCL (Pars Darou Co, Iran). The drugs and the CV essential oil were dissolved in normal saline and tween 80 (12%) respectively, and were administrated intraperitoneally (i.p.) at a constant volume of 10 ml/kg. The FST and TST were seen 60 min after the single injection of the drugs or essential oil.

Animals

Male NMRI mice, weighting 20-30g, were prepared from the Urmia University of Medical Science (Urmia, Iran). The mice were studied in cages (n=6) with standard condition including light/dark cycle (12 h light and 12h dark), temperature (23–25 ◦C), and humidity (50±10%). The mice had free access to standard commercial pellets food and water *ad libitum*. The **researchers** followed all the ethical principles confirmed by Urmia Branch, Islamic Azad University, for the care and use of Laboratory animals (IR.IAUrmia.REC.1397.07).

Forced Swimming Test (FST)

In the current study, the FST was applied as previously explained previously by Porsolt *et al.* (16). To this end, an open cylindrical container (10 cm diameter × 25 cm height) filled with 15 cm of water was prepared and the mice were forced to swim in the container at 25±1˚C. In the FST, the recorded behaviors were as follows:

1) immobility: a mouse was judged as immobile when the animal endeavored to remain floating on water without struggling and only attempted to keep its head above water; 2) swimming: in this stage, a mouse was judged on the basis of active swimming motions if the

mouse tried to maintain its head above water more than required, i.e. its movement around cylinder; 3) climbing phase: a mouse was judged on the basis of climbing if the mouse made active movements with its forepaws in and out of the water that the animal usually moves against the walls. In this test, we recorded the total duration of behaviors for the last 4 minutes by a 6-minute test using a video camera (Cannon, Japan) that was placed precisely above the cylinder. A decrease in immobility time and an increase in swimming or climbing behaviors were considered as the behavioral profiles consistent with an antidepressant-like activity (16).

Tail Suspension Test (TST)

In this test, the animals were kept away from any exposure to sound and vision. Moreover, they were kept suspended 50 cm above the floor by an adhesive tape that was positioned roughly 2 cm from the tip of the tail. In TST, immobility time was registered for the last 4 min within a 6-min test. A video camera (Canon, Japan) was used opposite from the apparatus to record the duration of immobility (17).

Experimental Design and Animal Grouping

A total of seventy-two NMRI mice were randomly divided into twelve groups of six mice as follows in both of the tests:

Group 1: vehicle (normal saline plus 2 % Tween 80; 10ml/kg).

Groups 2, 3 and 4: three doses (5, 10, and 20 mg/kg) of the CV essential oil.

Groups 5 and 6: fluoxetine (20 mg/kg) or imipramine (30 mg/kg) respectively.

In addition, the administration schedule and drugs as well as essential oil administration were determined based on our recent studies and different literature (9, 10 and 18).

Statistical Analysis

The data have been presented as mean ± standard error of the mean (S.E.M) (n=6), and they were analyzed by one-way ANOVA followed by Tukey's comparison test. $P<0.05$ as was considered statistically significant. All statistical analyses were performed using GraphPad Prism 7 (San Diego, CA, USA).

Results and Discussion

GC-MS analysis data

Based on the GC-MS analysis, the CV essential oil was comprised of 10 compounds (representing 99.14%). The main constituent was Cinnamaldehyde (87.42%) followed by Cinnamaldehyde dimethyl acetal (7.13%), and Para-Methoxy cinnamic aldehyde (1.88%), as it has been indicated in Table 1. These constituents (3) comprised 96.43% of the yield, whereas the other components that had been detected represented <1% (Table. 1).

Effects of the CV Essential Oil on Immobility, Swimming and Climbing Behaviors in FST

As illustrated in Figure 1, all doses of the CV essential oil decreased immobility time in FST (P< 0.001 and P<0.05, respectively,). Figure 2 illustrates that all doses of the essential oil significantly (P<0. 01 and P<0.001, respectively) increased the swimming time in comparison with the control group. Furthermore,

Table 1: The chemical compounds of *Cinnamomum verum* essential oil.

No	Name	RT (min)	Area%
1	Benzaldehyde	7.308	0.36
2	Linalool	13.116	0.23
3	Benzenepropanal	15.863	0.62
4	**Cinnamaldehyde**	**21.43**	**87.42**
5	1-(2-Ethoxyphenyl)acetone	23.643	0.23
6	**Cinnamaldehyde Dimethyl Acetal**	**26.812**	**7.13**
7	Trans-Cinnamyl Acetate	28.507	0.67
8	δ-Cadinene	31.182	0.28
9	**Para-Methoxy cinnamic aldehyde**	**31.393**	**1.88**
10	α-Cadinol	34.869	0.33
			99.14

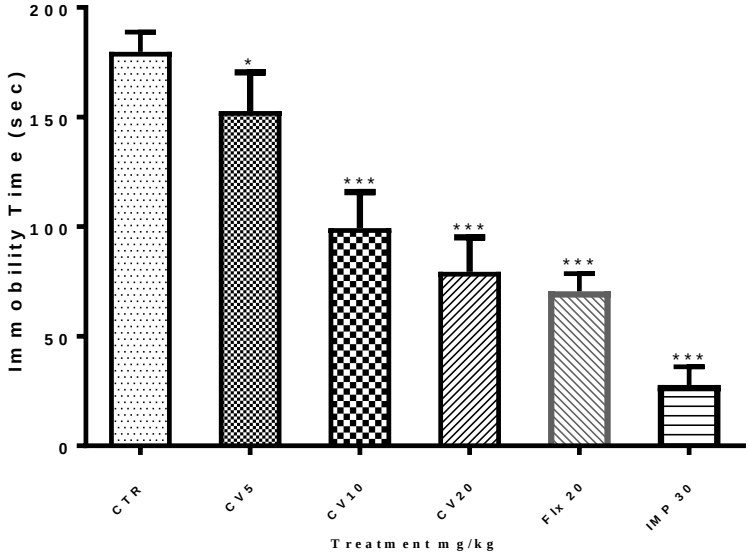

Figure 1. The effects of the i.p. administration of *Cinnamomum verum* essential oil, fluoxetine and imipramine on the mean immobility time in FST. Values are presented as mean ± S.D. (n= 6) mice/group. * and *** show significant differences between the vehicle (control) group at P < 0.05 and P < 0.001, respectively. Results were analyzed by one-way ANOVA followed by Tukey's post-hoc test.CTR=control; CV=*Cinnamomum verum;*Flx=Fluoxetine;IMP=Imipramine.

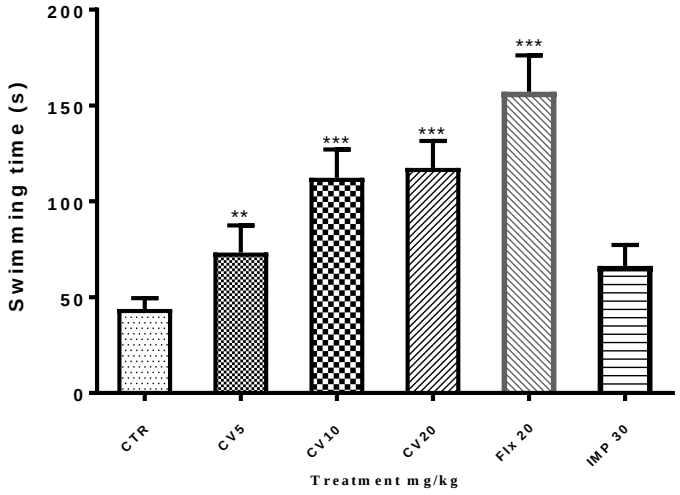

Figure 2. The effects of the i.p. administration of *Cinnamomum verum* essential oil, fluoxetine and imipramine on the mean swimming time in FST. Values are presented as mean ± S.D. (n= 6) mice/group. ** and *** show significant differences between the vehicle (control) group at P < 0.01 and P < 0.001, respectively. Results were analyzed by one-way ANOVA followed by Tukey's post-hoc test. CTR=control; CV=*Cinnamomum verum;*Flx=Fluoxetine;IMP=Imipramine.

figure 3 indicates that only 10 and 20 mg/kg of the essential oil remarkably P< 0. 05 and P<0.001, respectively,) increased the climbing time compared to the control group.

Effects of the CV Essential Oil on immobility Time in TST

As shown in figure 4, all doses of the CV essential oil decreased immobility time in TST (P< 0.001).

The aim of this research was to examine the

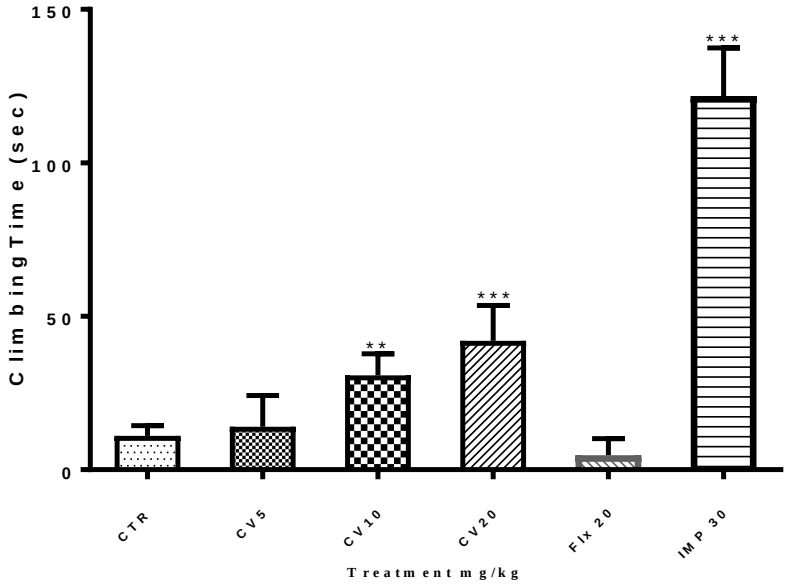

Figure 3. The effects of the i.p. administration of *Cinnamomum verum* essential oil, fluoxetine and imipramine on the mean climbing time in FST. Values are presented as mean ± S.D. (n= 6) mice/group. ** and *** show significant differences between the vehicle (control) group at $P < 0.01$ and $P < 0.001$, respectively. Results were analyzed by one-way ANOVA followed by Tukey's post-hoc test.CTR=control; CV=*Cinnamomum verum;*Flx=Fluoxetine;IMP=Imipramine.

phytochemistry and antidepressant-like effects of the CV essential oil in animal models of depression (FST and TST) in male mice. The findings indicated that all doses of the CV essential oil decreased immobility time in both tests compared to the vehicle (control) groups. In line with our results, Fadaei and Rousta also showed that a chronic 30-day consumption of the CV extract (200 mg/kg, orally) decreased immobility time in rats (receiving lead acetate) and, in other words, induced antidepressant-like effects (14). In another experiment, Sohrabi *et al*. (2017) reported that the i.p. administration of 0.5-2 mg/kg of the CV essential oil for 14 repeated days decreased immobility time in both FST and TST and exhibited the antidepressant-like activity (19). Unlike these findings, our results revealed that the acute i.p. of administration of the CV essential oil (5-20 mg/kg) decreased immobility time in both FST and TST. However, this difference in behavioral responses could accordingly vary due to different factors, including treatment schedule, different doses, and quality of the essential oil.

On the other hand and unlike the results of the two previous studies, the findings of the present research indicated that all doses of the CV essential oil also significantly increased swimming time. However, only 10 and 20 mg/kg of the essential oil could significantly increase the climbing time. In line with other findings, fluoxetine as a reference drug was also able to decrease immobility time, increase swimming time, and insignificantly increase climbing time. Moreover, similar to other findings, imipramine reduced immobility time, increased climbing time, and insignificantly increased swimming time (20). Our result is completely in line with a study revealing that the antidepressant agents selectively inhibiting noradrenaline reuptake (e.g. imipramine) would cause a reduction in immobility time and increase climbing time (21). On the other hand, selective serotonin reuptake inhibitors (e.g. fluoxetine) reduce immobility time and significantly increase swimming time without having any effect on climbing time (22). Considering our recent studies (12) and the other experiments, it is believed that those synthetic and/or medicinal herbs that decrease immobility and significantly increase the swimming and climbing behaviors in FST have monoaminergic mechanisms of action (23-25).

Given GC/MS and the study of CV's phytochemistry, different compounds were found in the CV essential oil. Our results supported the findings of previous

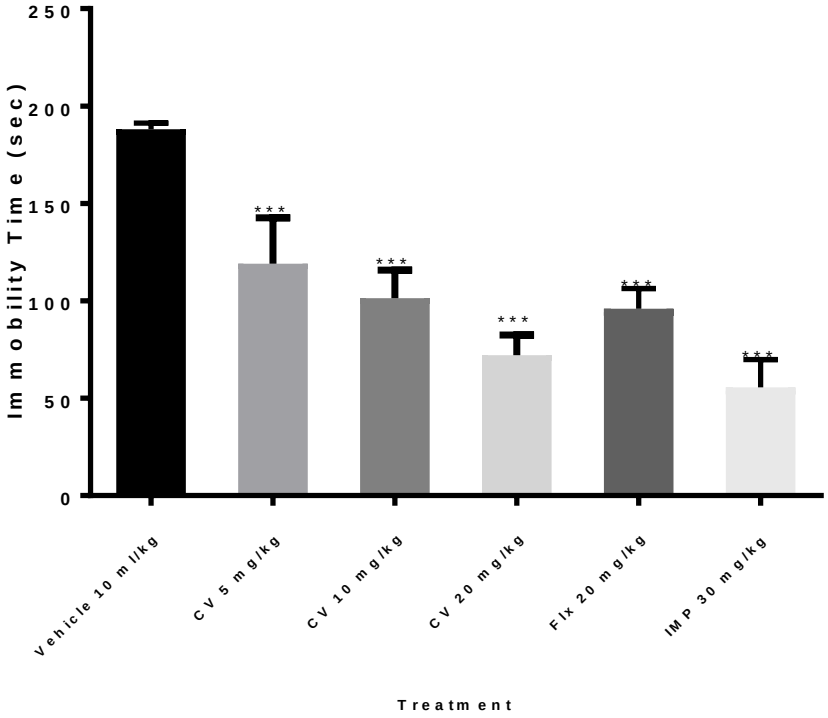

Figure 4. The effects of the i.p. administration of *Cinnamomum verum* essential oil, fluoxetine and imipramine on the mean immobility time in FST. Values are presented as mean ± S.D. (n= 6) mice/group. *** shows significant differences between the vehicle (control) group at P < 0.001. Results were analyzed by one-way ANOVA followed by Tukey's post-hoc test. CTR=control; CV=*Cinnamomum verum;*Flx=Fluoxetine;IMP=Imipramine.

studies and demonstrated that the main components of the CV essential oil were cinnamaldehyde followed by cinnamaldehyde dimethyl acetate, and para-methoxy cinnamic aldehyde (26, 27). On the other hand, the pharmacological properties of the C*innamomum verum* including anti-inflammatory, antioxidant, anti-diabetic, and anticancer effects have been attributed to the presence of cinnamaldehyde (28-30). In support of this finding, the antidepressant-like effect of the CV essential oil is possibly due to its major component, i.e., cinnamaldehyde. However, no study has been conducted on the direct effect of cinnamaldehyde, and even the CV essential oil itself, on the monoaminergic system (modulation of the serotonergic, dopaminergic, and noradrenergic systems) to date. Nevertheless, previous researches have reported the antioxidant effects of cinnamaldehyde (30). The antidepressant effects of antioxidants have also been shown in several studies, where it was believed that antioxidants could inhibit the reuptake of 5-HT (31). Hence, the antidepressant-like effects of the CV essential oil could be partially attributed to its antioxidant properties.

Beside the role of the serotonergic system in the antidepressant-like effects of the CV essential oil, free radicals increase following oxidative stress. According to certain reports, due to the high level of oxygen metabolism, dopaminergic system is also sensitive to oxidative stress and is injured following its occurrence (32). Mehraein *et al*. (2018) specified that cinnamaldehyde reduced the injury of dopaminergic system in substantia nigra (SN) pathway in the brain and could be helpful for patients with Parkinson's disease (PD) through its protective mechanism on the dopaminergic system (33). In another study, the neuroprotective effect of trans-cinnamaldehyde on the dopaminergic pathway was exhibited (34).

Previous studies have also indicated the role of noradrenergic system in cinnamaldehyde's effects. Accordingly, they have showed that trans-cinnamaldehyde could have a stimulating effect on the

release of NA at the myenteric ileum nerve endings of guinea pig (35). Another study also reported that cinnamaldehyde could cause the release of NA from the central nervous system by stimulating sensory neurons (36). **.** Hence, one of the highlighting points of the present study was to determine the effects of the acute antidepressant-like effects of the CV essential oil. The shortcoming of this study was the fact that the exact mechanism of this essential oil in animal models of depression was not specified.

Conclusion

According to the results of the present study, one of the components of the CV essential oil, e.g., cinnamaldehyde, is likely to cause antidepressant effects due to its monoaminergic mechanism. Nevertheless, further studies are required to confirm the exact mechanism of action of the CV essential oil.

Acknowledgment

This study is the result of a DVM thesis, (No.10310501972038), Urmia branch, Islamic Azad University. The authors would like to thank Adonis Gol Daru Pharmaceutical Co for preparing the essential oil.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Cohn DW, Kinoshita D, Palermo-Neto J. Antidepressants prevent hierarchy destabilization induced by lipopolysaccharide administration in mice: a neurobiological approach to depression. Ann NY Acad Sci.2012;1262: 67-73.
2. Nutt DJ. Relationship of neurotransmitters to the symptoms of major depressive disorder. J Clin Psychiatry.2008; 69: 4-7.
3. Lambert G, Johansson M, Agren H, Friberg P. Reduced brain norepinephrine and dopamine release in treatment-refractory depressive illness: evidence in support of the catecholamine hypothesis of mood disorders. Arch Gen Psychiatry.2000; 57: 787-93.
4. Wang R, Xu Y, Wu HL, Li YB, Li YH, Guo JB, et al. The antidepressant effects of curcumin in the forced swimming test involve 5-HT1 and 5-HT2 receptors. Eur J Pharmacology.2008; 578:43-50.
5. Jafarpoor N, Abbasi-Maleki S, Asadi-Samani M, MH. Khayatnouri. Evaluation of antidepressant- like effect of hydroalcoholic extract of Passiflora incarnata in animal models of depression in male mice. J Herb Med Pharmacol.2014; 3: 41-5.
6. Abbasi- Maleki S, Bekhradi R, Asgharpanah J, Abbasi Maleki F, Maleki AhangharіN. Antidepressant effect of aqueous and hydroalcoholic extracts of Lavandula officinalis in forced swim test and tail suspension test in male mice. J Arak Uni Med Sci. 2013; 16(78): 65-75. [In Persian]
7. Shahamat Z, Abbasi-Maleki S, Mohammadi Motamed S. Evaluation of antidepressant-like effects of aqueous and ethanolic extracts of Pimpinella anisum fruit in mice. Avicenna J Phytomed.2016; 6 (3): 322-8.
8. Abbasi-Maleki S, Mousavi Z. Hydroethanolic extract of Carthamus tinctorius induces antidepressant-like effects: modulation by dopaminergic and serotonergic systems in tail suspension test in mice. Iran J Basic Med Sci 2017; 20:1063-73.
9. Abbasi-Maleki S, Bakhtiarian A, Nikoui V. Involvement of the monoaminergic system in the antidepressant-like effect of the crude extract of Mentha piperita (Lamiaceae) in the forced swimming test in mice. Synergy 2017; 5: 21-8.
10. Eslami Yoshanloei J, Abbasi-Maleki S, Moradi-Kor N. 2016. Evaluation of the antidepressant effects of Sesamus indicum oil in forced swim test and tail suspension test in mice.1st International Conference on Medicine, Public Health and Biological Sciences (MPHBS), Sep. 2016.doi. 10.18869/MPHBS.2016.221.
11. Shafei Z, Abbasi Maleki S, Ghaderi-Pakdel F. Evaluation of the antidepressant-like effect of Viola odorata hydroalcoholic extract in male mice. J Birjand Univ Med Sci. 2018; 25 (4) :286-96.
12. Abbasi-Maleki S, Khadkhoda Z,Taghizad-Farid-R.The antidepressant-like effects of Origanum majorana essential oil on mice through monoaminergic modulation using the forced swimming test, J Tradit Complement Med.2020;10(4):327-35.
13. Salehi Surmaghi MH: Medicinal Plants and Phytotherapy. 3th ed.Tehran, Donyay Taghziah Press,2010.
14. Fadaei S, Asle-Rousta M. Anxiolytic and antidepressant effects of cinnamon (Cinnamomum verum) extract in rats receiving lead acetate. SJKU. 2018; 22 (6) :31-9.
15. Adams RP. Identification of Essential Oil Components by Gas chromatography/ Mass Spectrometry. Carol Stream IL: Allured Publishing Corporation; 2007.
16. Porsolt R, Bertin A, Jalfre M. Behavioral despair in mice: a primary screening test for antidepressants, Int Arch Pharmacol 1977; 229: 327-36.
17. Steru L, Chermat R, Thierry B, Simon P. The tail suspension test: a new method for screening antidepressants in mice. Psychopharmacol 1985; 85:367-70.
18. Rajbir B, Kaur S, Singh J, Ishar MPS. Ameliorative effect of volatile oil from Cinnamomum zeylanicum on hyperalgesia in alloxan diabetic rats. Can J Pure Appl Sci 2009; 3: 887-95.
19. Sohrabi R, Pazgoohan N, Seresht HR, Amin B. Repeated systemic administration of the cinnamon essential oil possesses anti-anxiety and anti-depressant activities in mice. Iran J Basic Med Sci. 2017;20(6):708-14.
20. Page ME, Detke MJ, Dalvi A, Kirby JG, Lucki I. Serotoninergic mediation of the effects of fluoxetine, but not desipramine, in the rat forced swimming test. Psychopharmacol 1999;147(2):162-7.
21. Detke MJ, Rickels M, Lucki I. Active behaviors in the rat forced swimming test differentially produced by serotonergic and noradrenergic antidepressants. Psychopharmacol 1995;121(1): 66-72.
22. Consoni FT, Vital MA, Andreatini R. Dual monoamine modulation for the antidepressant-like effect of lamotrigine in the modified forced swimming test. Eur Neuropsychopharmacol. 2006;16(6):451-8.
23. Indulkar P and Prabhavalkar K: Evaluation of the efficacy of combination therapy of agomelatine, duloxetine and sertraline in the management of stress induced depression. Int J Pharm Sci Res 2018; 9(8): 3210-22.

24. Reneric JP, Lucki I. Antidepressant behavioral effects by dual inhibition of monoamine reuptake in the rat forced swimming test. Psychopharmacology (Berl). 1998;136(2):190-7.
25. Sanmukhani J, Anovadiya A, Tripathi CB. Evaluation of antidepressant like activity of curcumin and its combination with fluoxetine and imipramine: an acute and chronic study. Acta Pol Pharm. 2011;68(5):769-75.
26. Mousavian M, Bazgir, E, Moradpour A. Cinnamon bark essential oil compounds and its antifungal effects against fungal rotting of fruits. *J Crops Improv*. 2018; 19(4): 907-20.
27. Ainane T, Khammour F, Merghoub N, et al. Cosmetic bio-product based on cinnamon essential oil "Cinnamomum verum" for the treatment of mycoses: preparation, chemical analysis and antimicrobial activity. MOJ Toxicol. 2019;5(1):5-8.
28. Lee SC, Wang SY, Li CC ,Liu CT. Anti-inflammatory effect of cinnamaldehyde and linalool from the leaf essential oil of Cinnamomum osmophloeum Kanehira in endotoxin-induced mice. J Food Drug Anal..2018;26(1):211-20.
29. Guo X, Sun W, Huang L, et al. Effect of Cinnamaldehyde on Glucose Metabolism and Vessel Function. Med Sci Monit. 2017; 23:3844-53.
30. Sharma UK, Sharma AK, Gupta A, Kumar R, Pandey A, Pandey AK. Pharmacological activities of cinnamaldehyde and eugenol: antioxidant, cytotoxic and anti-leishmanial studies. Cell Mol Biol (Noisy-le-grand). 2017. 31;63(6):73-8.
31. Khanzode SD, Dakhale GN, Khanzode SS, Saoji A, Palasodkar R. Oxidative damage and major depression: the potential antioxidant action of selective serotonin re-uptake inhibitors. Redox Rep 2013; 8: 365-70.
32. Guo JD, Zhao X, Li Y, Li GR, Liu XL. Damage to dopaminergic neurons by oxidative stress in Parkinson's disease (Review). Int J Mol Med. 2018;41(4):1817-25.
33. Mehraein, F., Zamani, M., Negahdar, F., Shojaee, A. Cinnamaldehyde attenuates dopaminergic neuronal loss in substantia nigra and induces midbrain catalase activity in a mouse model of Parkinson's disease. *J Basic Clinic Pathophysiol*. 2018; 6(1): 9-16.
34. Pyo JH, Jeong YK, Yeo S, Lee JH, Jeong MY, Kim SH, et al. Neuroprotective effect of trans-cinnamaldehyde on the 6-hydroxydopamine-induced dopaminergic injury. Biol Pharm Bull. 2013;36(12):1928-35.
35. Cheng JT, Liu IM, Huang WC, Kou DH. Stimulatory effect of trans-cinnamaldehyde on noradrenaline secretion in guinea-pig ileum myenteric nerve terminals. Life Sci. 2000;66(11):981-90.
36. Iwasaki Y, Tanabe M, Kobata K, Watanabe T. TRPA1 agonists-allyl isothiocyanate and cinnamaldehyde – induce adrenaline secretion. Biosci Biotechnol Biochem. 2008;72(10):2608-14.