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Short communication

Cuscuta chinensis Antidepressant-Like Effect, the Role of 5-HT and the Impact on Behavioral Response in Mice

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Abstract

Background and objectives: Depression is a chronic mental disorder that influences people's lives and functionality. The available medications do not give full guaranty of effectiveness and are not devoid of unwanted side effects. *Cuscuta chinensis* has been recommended for the treatment of depression in traditional medicine. In this study, the antidepressant-like activity of *C. chinensis* has been evaluated by using forced swimming test (FST) in mice. **Methods:** *Cuscuta chinensis* extract was provided by boiling in water. The antidepressant effect was evaluated by forced swimming test (FST) in mice with daily gavage of 270, 360 and 430 mg/kg of the treatments for four weeks. The immobility time and behavioral activity and also the blood levels of 5-HT and norepinephrine were measured. **Results:** The FST confirmed antidepressant effect of the extract with decreased time of immobility and increased swimming time alongside increase in serum 5-HT in all groups ($p<0.01$compared to the control) except for the extract at the dose of 270 mg/kg (MA270). This effect was not statistically significant with fluoxetine group. **Conclusion:** *Cuscuta chinensis* demonstrated antidepressant effects in mice model which is a confirmation for its traditional use in depression.

Keywords: *Cuscuta chinensis*; depression; Persian medicine; phenolics content

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Introduction

Depression, a chronic mental disorder, influences the quality of life of lots of people around the word. Depression is multifactorial and some anti-depressant medications are not successful in overcoming the disease or are accompanied by unwanted adverse reactions [1,2]. In persian medicine (Iranian traditional medicine), *Cuscuta epithymum* (called "Aftimun") and *C. chinensis* (called "Kashus") from Convolvulaceae family, are recommended for the treatment of depression. In the present study, we prepared an easy-to-use form of *Cuscuta chinensis* aqueous extract and evaluated the antidepressant effects in a mouse model.

Material and Methods

Ethical consideration

The study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1399.648).

Chemicals

Sodium carbonate (Sigma-Aldrich, USA), Folin-Ciocalteu, pyrogallola and fluoxetine (Merck,

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Germany) were used in the study.

Plant material

Cuscuta chinensis Lam. was provided from Tehran local herbal market and the identity was confirmed by botanists at the Herbarium of Traditional Medicine and Matreia Medica Research Center (TMRC), Shahid Beheshti University of Medical Sciences (HMS-530).

Preparation of the extract

To prepare *Cuscuta chinensis* for medicinal use, it is usually wrapped in cotton and deepened in warm boiled water or milk for a few minutes according to Iranian traditional medicine (ITM). To follow this preparation method and meanwhile maintain ease of access and use, we decided to provide a dry extract following the traditional preparation method. *Cuscuta chinensis* was boiled in water at 90 °C for 15 min. The extract was dried into a powder by spray drying method.

Total phenolics content

Total phenolics content was measured according to previously explained methods [3,4].

Dose determination

In ITM, the average daily dose of *C. chinensis* is 20 mg of the dried plant which is equal to 2.5 g of our dried extract for a normal adult person. To measure the doses for the animal study, this amount was multiplied by 10 and calculated per kg; which was 360 mg/kg. Considering a range of 80-120 %, the doses of 270, 360 and 430 mg/kg were applied in the animal study. Since the plant is used both in water and milk in traditional use, both solvents were used for preparing the extract.

Animals

Forty-eight male albino Balb C mice (6–8 weeks old) (Pasteur Institute of Iran), weighing 22-25 g, were used in the study. The mice were kept six in each cage and were kept at 22±2°C with 45–60% humidity, and 12-h light/ dark cycle), they had free access to food and water.

Treatment groups

Forty-eight mice were used in the study in two negative and positive groups and six treatment groups (six mice in each group). The control groups received distilled water and fluoxetine (18 mg/kg) as the negative and positive groups, respectively. Three groups received different doses of *C. chinensis* dried extract at concentrations of 270, 360 and 430 mg/kg dissolved in water (WA270, WA360, WA430, respectively) and three groups received different doses of *C. chinensis* dried extract at concentrations of 270, 360 and 430 mg/kg dissolved in milk (MA270, MA360, MA430. The mice received the treatments once daily for four weeks through gavage.

Forced swimming test (FST)

FST was performed according to Can et al., 2012 [5]. The mice behaviors were recorded by camera and the time recordings were done by using a chronometer.

Neurotransmitters analysis

The mice were anesthetized and the blood was collected from the heart. Norepinephrine and 5-HT and in the serum of mice were assessed with norepinephrine ELISA kit: catalog number MBS2600834 and serotonin ELISA kit: catalog number LS-F4120, respectively following the manufacturer's instructions. The samples were analyzed in triplicate.

Statistical analysis

The results were expressed as mean±SEM and were assessed by one way analysis of variance (ANOVA) with GraphPad Prism 5 software. Dunnett multiple comparisons post-test was used for comparing the result of *C. chinensis* to the control and fluoxetine. To compare the effect of different concentrations Tukey multiple comparisons test was used; p value level equal to 0.05 was considered as the significance level.

Results and Discussion

The results of FST in mice are presented in Figure 1. *Cuscuta chinensis* extract significantly reduced the immobility time compared to the control (MA360 and WA270, $p<0.05$; WA360 and WA430, $p<0.01$). This effect was not statistically different from fluoxetine group which implies that the effect t of the extract at the highest doses was similar to fluoxetine. The swimming time in treatment groups increased significantly in comparison to the control group in all treatment groups (except MA270). This increase was not different from the positive control, fluoxetine. The climbing time of the mice in different treatment groups did not increase significantly when compared to control.

The treatments were given to the mice for four weeks which resulted in increase of 5-HT in treatment groups. This increase was only significantly different from the control in the mice that received the highest concentration of the extract (430 mg/kg, $p<0.05$). Levels of norepinephrine were not different from the control after four weeks of the study.

Neurotransmitters level such as dopamine, norepinephrine, and serotonin are involved in major depressive disorder [6]. *Cuscuta* species have been evaluated for antidepressant properties in clinical studies and in vivo models and have shown positive results. Several categories of phytochemicals including flavonoids, glycosides, alkaloids, tannins and lignins have been reported form *Cuscuta* species while diverse flavonoids have been isolated from *C. chinensis* [7-10]. Flavonoids are suggested to be beneficent in depressive disorders; they target neuronal pathways such as noradrenergic, serotonergic, GABAnergic and dopaminergic systems [11,12] and can reverse the monoamine neurotransmitter attenuations by 5-HT, NA and DA, and 5-hydroxyindoleacetic acid [13]. Quercetin and other flavonoids have decreased the immobility time and increased 5-HT in FST in previous research [7,14]. Serotonin and norepinephrine have a relationship with depression and their action leads to antidepressant effects [6]. These two neurotransmitters have correlation with specific behavior of animal in FST, norepinephrine with climbing and serotonin with swimming behavior [15].

Considering the results of the FST, *C. chinensis* extract could significantly reduce the immobility time and increase the swimming time of the mice in comparison to control. These effects were similar to that of fluoxetine which suggest the antidepressant effects of the plant. The levels of 5-HT in the mice blood also confirm these findings, since previous investigations have found a correlation between the swimming time in FST and the levels of 5-HT, it can be suggested that the *C. chinensis* extract in the present study has shown antidepressant effects mediated by 5-HT increase.

The levels of norepinephrine did not change significantly in the mice receiving the treatment; on the other hand, the time of climbing behavior did not increase significantly in the treatment groups suggesting that the antidepressant activity of *C. chinensis* extract might not be mediated through enhancement of norepinephrine by this extract.

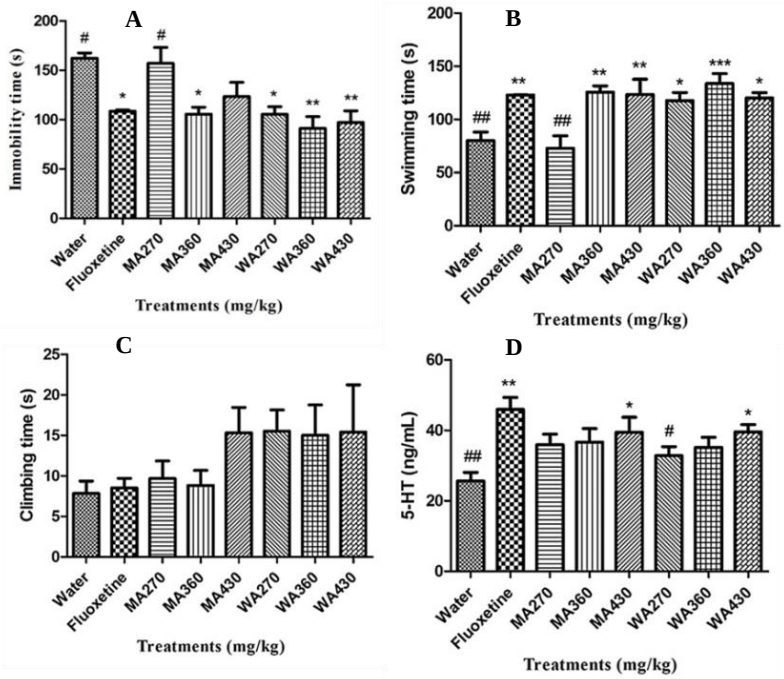

Figure 1. Effect of *Cuscuta chinensis* on time of immobility (A), swimming (B), climbing (C) and 5-HT serum levels (D); data are reported as mean±SEM (n = 6); *, ** and***: significant difference in comparison to negative control ($p<0.05$, $p<0.01$ and $p<0.001$ respectively); #and ## significant difference in comparison to fluoxetine; $p < 0.05$ and $p<0.01$, respectively; MA270, MA360, MA430: extract dissolved in milk at the doses of 270, 360 and 430 mg/kg, respectively; WA270, WA360, WA430: extract dissolved in water at the doses of 270, 360 and 430 mg/kg, respectively

Conclusion

Considering the antidepressant effects of *Cuscuta chinensis* in the present study and the traditional use of the plant for depression, the easy to use extract of this study can be evaluated in further in vivo and clinical studies.

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Author contributions

Maryam Hamzeloo-Moghadam was involved in conceptualization, funding acquisition, writing and editing of the manuscript; Leila Ara and Fatemeh Jafari were involved in data collection; Roshanak mokaberinejad contributed in conceptualization.

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

References

[1] Mao QQ, Ip SP, Xian YF, Hu Z, Che CT. Anti-depressant-like effect of peony: a mini-review. *Pharm Biol*. 2012; 50(1): 72–77.

[2] Park SW, Kim YK, Lee JG, Kim SH, Kim JM, Yoon JS, Park YK, Lee YK, Kim YH. Anti-depressant-like effects of the traditional Chinese medicine kami-shoyo-san in rats. *Psychiatry Clin Neurosci*. 2007; 61(4): 401–406.

[3] Peng FZ, Fan J, Ge TT, Liu QQ, Li BJ. Rapid anti-depressant-like effects of ketamine and other candidates: molecular and cellular mechanisms. *Cell Prolif*. 2020; 53(5): 1–13.

[4] Kahkeshani N, Hadjiakhoondi A, Navidpour L, Akbarzadeh T, Safavi M, Karimpour-Razkenari E, Khanavi M. Chemodiversity of *Nepeta menthoides* Boiss. & Bohse. essential oil from Iran and antimicrobial, acetylcholinesterase inhibitory and cytotoxic properties of 1,8-cineole chemotype. *Nat Prod Res*. 2018; 17(4): 544–552.

[5] Fahimi S, Mortazavi SA, Abdollahi M, Hajimehdipoor H. Formulation of a traditionally used polyherbal product for burn healing and HPTLC fingerprinting of its phenolic contents. *Iran J Pharm Res*. 2016; 15(1): 95–105.

[6] Can A, Dao DT, Arad M, Terrillion CE, Piantadosi SC, Gould TD. The mouse forced swim test. *J Vis Exp*. 2012; 59: 1–5.

[7] Gupta M, Mazumder UK, Pal D, Bhattacharya S, Chakrabarty S. Studies on brain biogenic amines in methanolic extract of *Cuscuta reflexa* Roxb. and *Corchorus olitorius* Linn. seed treated mice. *Acta Pol Pharm*. 2003; 60(3): 207–210.

[8] Ahmad A, Tandon S, Dang Xuan T, Nooreen Z. A review on phytoconstituents and biological activities of *Cuscuta* species. *Biomed Pharmacother*. 2017; 92: 772–795.

[9] Pan S, Wang X, Duan W, Yu Z, Zhang L, Liu W. Preparative isolation and purification of flavonoids from *Cuscuta chinensis* Lam. by high-speed counter current chromatography. *J Liq Chromatogr Relat Technol*. 2013; 37(15): 2162–2171.

[10] Li WL, Zhang Y, Bai J, Xiang Z, Ding JX, Ji YB. Identification of chemical constituents in *Cuscuta chinensis* using HPLC-ESI/ Q-TOF MS/MS. *Bio Technol Indian J*. 2013; 8(4): 563–567.

[11] Kwon YS, Chang BS, Kim CM. Antioxidative constituents from the seeds of *Cuscuta chinensis*. *Nat Prod Sci*. 2000; 6(3): 135–138.

[12] Hritcu L, Ionita R, Postu PA, Gupta GK, Turkez H, Lima TC, Carvalho C, de Sousa DP. Antidepressant flavonoids and their relationship with oxidative stress. *Oxid Med Cell Longev*. 2017; Article ID 5762172.

[13] Pannu A, Sharma PC, Thakur VK, Goyal RK. Emerging role of flavonoids as the treatment of depression. *Biomolecules*. 2021; 11(2): 1–49.

[14] Khan H, Perviz S, Sureda A, Nabavi SM, Tejada S. Current standing of plant derived flavonoids as an antidepressant. *Food Chem Toxicol*. 2018; 119: 176–188.

[15] Detke MJ, Rickels M, Lucki I. Active behaviors in the rat forced swimming test differentially produced by serotonergic and noradrenergic antidepressants. *Psychopharmacology (Berl)*. 1995; 121(1): 66–72.

Abbreviations

FST: forced swimming test; ITM: Iranian traditional medicine