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Potential of the *Allium jesdianum* Extract in Suppression of Anxiety and Depression in Mice

Raziyeh Mousavi, Zahra Haghighi Fashi, Mahsa Hadipour Jahromy* and Rokhsna Rasooli

Department of Pharmacology, Faculty of Medicine, Islamic Azad University, Tehran, Iran

***Corresponding author:** Mahsa Hadipour Jahromy, Associate Professor of Pharmacology, Herbal Pharmacology Research Center, Faculty of Medicine, Islamic Azad University, Tehran Medical Sciences Branch, Tehran, Iran, Tel: +98 21 2200 66 60 7; E-mail: Jahromymh@yahoo.com

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Abstract

Background: Herbal medicine has been widely applied as effective remedy by extensive spectrum of cultures. Psychiatric patients usually don't accept their disease and also refuse drug therapy. It seems that by herbal remedies we can perform more successful in treatment. *Allium jesdianum* is an endemic plant of Zagros Mountains of Iran which possessing various applications in traditional food.

Objectives: The aim of this study was to evaluate anxiolytic and antidepressant effect of *Allium jesdianum* hydro alcoholic extract in mice.

Methods: Antidepressant and anxiolytic effect of *Allium jesdianum* hydro alcoholic extract were evaluated by elevated plus maze (EPM), open field test (OFT) and force swimming test (FST).

Results: In open field test *Allium jesdianum* extract significantly decreased number of lines crossed at the doses of 500 mg/kg compared to the control and diazepam group ($p<0.05$), besides it could significantly increase the number of lines crossed at the doses of 1000 and 2000 mg/kg compared to the control ($p<0.01$) and fluoxetine groups($p<0.05$). In elevated plus maze, *Allium jesdianum* extract significantly increased time spent ($p<0.01$) and number of enters in open areas ($p<0.05$) at the doses 500 and 1000 mg/kg compared to the control group. Moreover it significantly ($p<0.01$) decreased time spent and number of enters in open areas compared to diazepam group. In forced swimming test, the immobility time for all groups significantly decreased in contrast to the control group ($p<0.01$).

Conclusion: Results indicated that *Allium jesdianum* extract has antidepressant effect with stimulator effect in adult male mice, moreover it showed anxiolytic effect.

Keywords: *Allium jesdianum*; Antidepressant; Anxiolytic; Open field test; Forced swimming test; Elevated plus maze

Introduction

Among many psychiatric and behavioral problems, anxiety and depressive disorders are the most frequent which have been identified to be associated whit common stress-related mood disorders leading to disability and premature death [1].

Depression occurs in of all ages with an average of 17% lifetime prevalence in general population [2]. It usually disposes the patient to ischemic heart disease and also increases the risk of suicide attempt [3]. Refusing of disease acceptance and subsequent drug consumption as well as suffering from many side effects make about one third of patient do not respond to the existing medication [4].

Anxiety, the other most common and important psychiatric disorder, causes considerable decrease in the life quality of the people who suffer from that. According to World Health Organization (WHO) estimation, 400 million people all over the world have anxiety disorders, but only one-third of them receive treatment [5,6] therefore their treatment is of crucial importance.

Although, there are many classical and reference anxiolytic and antidepressant drugs, treatment by them usually accompany whit undesirable side effects including cardiovascular toxicity, sexual dysfunction, weight gain, and drug interactions [7,8]. Furthermore, psychiatric patients usually don't accept their disease and also refuse drug therapy.

Today, herbal medicine has been widely applied as effective remedy by extensive spectrum of cultures for health care, not only because they are inexpensive but also for stronger cultural acceptability, better compatibility with the human body as well as minimal side effects [9]. Even though, much evidence suggests that all herbal medicines may not be safe, most of them are faced to highly demand and acceptance rather than chemical drugs [10].

It seems that by herbal remedies we can perform more successful in treatment. Previous evidence confirms successful anxiety and depression therapy by traditional medicinal plants such as *Acanthopanax sen*ticosus [11], *Acorus calamus* [12], *Albizia julibrissin* [13], *Ginkgo biloba* [14], *Paeonia lactiflora* [15],

and *Hypericum perforatum* [16]. The plant *Allium jesdianum* belongs to Liliace family and grows on the 1800-2600 meters altitudes of Zagros Mountains of Iran. Native people of this region use the aerial parts of the plant for the treatment of abdominal pain, rheumatic pain and urinary stones [17].

In the recent studies some beneficial effects of *Allium jesdianum* has reported. Gholami et al. demonstrated the antibacterial activity of aqueous and methanol extracts of AJ plant on a number of pathogenic bacteria resistant to antibiotics [18]. In another study the effect of *Allium jesdianum* extract on renal stone was investigated [19]. Furthermore it is reported that AJ extract has anti nociceptive effects that is opposite to Naloxone [17].

To the best of our knowledge, no study has been carried out to investigate the possible therapeutic effects of *Allium jesdianum* in depression and anxiety. Hence, the primary aim of the present study was to investigate the possible antidepressant and anxiolytic-like effects of ethanol root extract of *Allium jesdianum* using batteries of behavioral models.

Experimental

Plant materials and preparation of extract

The plant *Allium jesdianum* was collected from Zagros Mountains north-eastern of Khouzestan, Iran, in spring 2015. After identification of the plant, a voucher (NO: 2252) has been deposited in the agriculture research center herbarium.

The aerial part of plant was washed in cold water, dried in shade and room temperature and coarsely ground before extraction. 500 grams of plant was extracted by percolation method using ethanol. The resulting extract was concentrated over a rotary vacuum until a crude solid extract was obtained.

Chemicals

Fluoxetine and diazepam were purchased from Darupakhsh Co. (Tehran, Iran) and used as the reference drug (positive control). They were dissolved in normal saline as solvent.

Animals

Forty eight male mice weighting 20-25 grams were kept at ambient temperature (25 ± 1°C) and 40-45% relative humidity, with a 12 hr. light: 12 hr. dark cycle. The animals had free access to standard pellet and water. The 48 rats were randomly divided into six groups of 8 in cages (n=8 per group); Control group (received I.P normal saline), Diazepam group (received I.P diazepam 5 mg/kg), Fluoxetine group (received I.P Fluoxetine 10 mg/kg), *Allium jesdianum* extract groups (Hib ext which received I.P extract with the doses of 500, 1000 and 2000 mg/kg).

Treatment

The extract of *Allium jesdianum* was freshly dissolved in normal saline and administered intraperitoneally. Diazepam and Fluoxetine were dissolved in normal saline and administered in I.P route. The control group received normal saline (10 ml/kg) intraperitoneally. All groups received their treatments once a day for 10 constitutive days and the animals were subjected to various behavioral tests 30 minutes after the last injection.

The experiments were conducted according to the norms of committee for the purpose of control and supervision of experiments in animal. All animals were treated humanely according to the guidelines on ethics standard for investigation of experimental pain in animals and approved by the Animal Experimentation Ethics Committee of Kerman Neuroscience Research Center (EC/KNRC/90).

Open field test

The open field is a 40 X 40 X 30 cm arena with walls to prevent escape. Commonly, the field is marked with a grid and square crossings. The center of the field is marked with a different color to differentiate from the other squares. Mouse was placed in the center of area and the observer quantified the spontaneous ambulatory locomotion of each mouse for 5 min.

A blind observer registered the number of times the animal entered each square (counts per 5 min), a count is considered when the animal totally crosses from one square to the next. A change in the number of counts with respect to the control group is considered as an alteration of locomotor activity [20].

Force swimming test

The Force swimming test is the most widely used model for assessing antidepressant activity and was employed in this study as described by Porsolt et al. [21]. For this purpose, the mouse was dropped into a glass cylinder (20 cm in height and 12 cm in diameter) containing 8 cm-deep water at 24-25°C and left there for 6 minute. Two minutes to adapt to the environment and 4 minute to record immobility time [22].

The mice were considered immobile when they remained floating in the water, without struggling, making only very slight movements necessary to keep its head above water. Drugs with antidepressant activity reduce that parameter (immobility time), while depressant drugs exert the opposite effect.

The control group was treated with distilled water and the other groups of mice received intra peritoneal injection of AJ extract (500, 1000 and 2000 mg/kg) for 10 days. Fluoxetine (10 mg/kg) was used intraperitoneally as positive control of the test.

Elevated plus maze

The elevated plus maze test was carried out as described previously by Lister [23] to measure anxiolytic and/ or anxiogenic activity of different agents. The maze consisted of two open (30 X 5 X 0.2 cm) and two closed (30 X 5 X 15 cm) arms, extending from a center platform (10 X 10 cm) and elevated to a height of 50 cm above the floor.

Mice were individually placed on the center of the maze facing an open arm, and the number of entries and the time spent in closed and open arms were recorded during a 5 min observation period.

The maze was wiped clean with 10% ethanol and dried after each trial. The number of open and closed-arm entries and the time spent in open arms were recorded. The time spent in the open arms and the number of open-arm entries was used as measures of anxiety [24].

Total closed-arm entries were analyzed as measures of non-specific changes in locomotor activity. The experimental animals were intra peritoneal treat with diazepam (20 mg/kg) and the extract (500, 1000 and 2000 mg/kg), 30 min respectively, before evaluation in the maze.

Statistical analysis

The data were analyzed by origin 6 software. One-way ANOVA was performed. A probability level of 0.05 or less was accepted as significant.

Result

Open field test

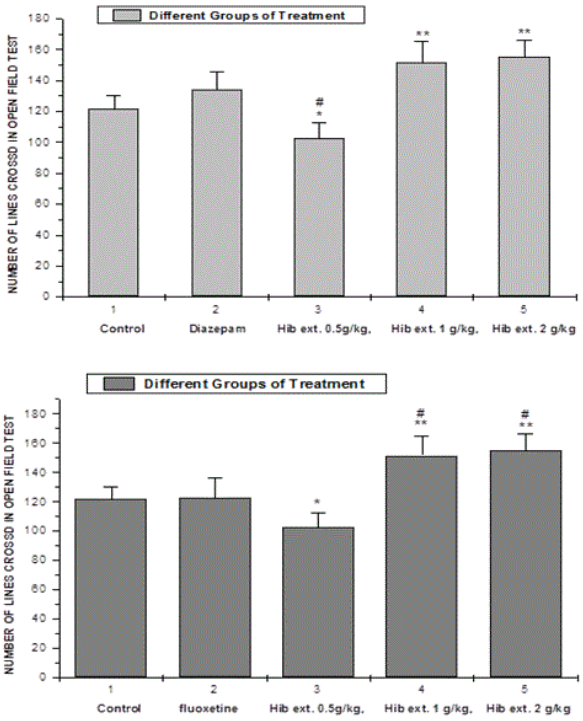

Figure 1: Locomotor activity in the open field test of mice that received saline vehicle (control), *Allium jesdianum* (500 mg/kg, 1000 and 2000 mg/kg), Diazepam (5 mg/kg) and Fluoxetine (10 mg/kg) [n=6, *p<0.05 compared to control group; **p<0.01 compared to control group, #p<0.05 compared to fluoxetine or diazepam group].

Diazepam produced a slight non-significant increase in the number of rearing compared to control. At the doses of 500 mg/kg, ethanol extract of AJ produced a significant (p<0.05) decrease in the number traveled by the mice in contrast to diazepam (p<0.05) and fluoxetine (p<0.05).

At the doses of 1000 and 2000 mg/kg, AJ administration significantly increased number of lines crossed compared to the control (p<0.01) and fluoxetine (p<0.05).

Fluoxetine (10 mg/kg) didn't affect locomotion activity in contrast to the saline control group (**Figure 1**).

Forced swimming test

As shown in **Figure 2**, in forced swimming test, the immobility time for all treated groups which had received fluoxetine and AJ extract (500, 1000 and 2000 mg/kg), significantly decreased compared to the control group (p<0.01) (**Figure 2**).

No significant difference was observed between AJ extract groups (500, 1000 and 2000 mg/kg) and fluoxetine group.

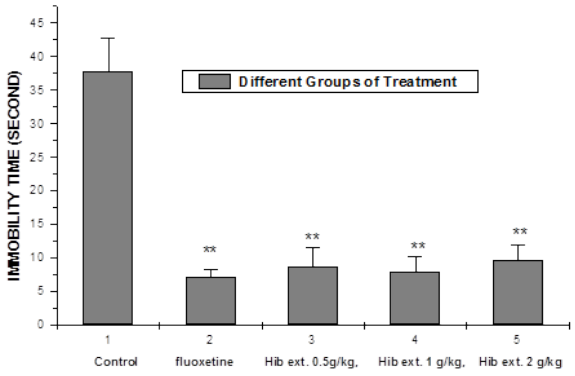

Figure 2: Immobility time in the forced swimming test of mice that received saline vehicle (control), *Allium jesdianum* (500 mg/kg, 1000 and 2000 mg/kg) and fluoxetine (10 mg/kg) [n=6, **p<0.01 compared to control group].

Elevated plus maze test

The number of enters to open arms (p<0.01) and time spent in open arms (p<0.01) significantly increased after treatment with AJ extract at the doses of 500 and 1000 mg/kg compared to control. Diazepam (5 mg/kg) also significantly increased both the open arm entry and the time spent in the open arms (p<0.01).

The effect produced by the extract at the dose of 2000 mg/kg seemed to be stronger than diazepam (**Figure 3**).

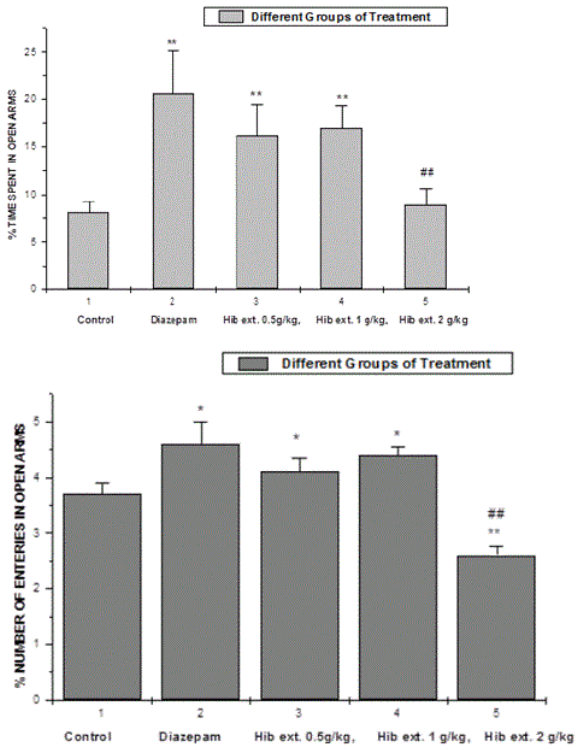

Figure 3: Number of entries and time spent in open arm in elevated plus maze test of mice that received saline vehicle (control), *Allium jesdianum* (500 mg/kg, 1000 and 2000 mg/kg) and diazepam (5 mg/kg) [n=6, *p<0.05, **p<0.01 compared to control group. ##p<0.01 compared to diazepam group].

Discussion

Most findings of the preliminary neuropharmacological screening of different doses (500, 1000 and 2000 mg/kg body weight) of ethanol extract from AJ root provide evidence of anxiolytic- and antidepressant-like effects induced by this herb.

The AJ extract was first studied using the open field which provides a better indication of the animal's emotional state. Evaluating locomotor activity, as measured by open field test, showed that ethanol extract from the AJ at the dose of 500 mg/kg decreased the frequency of movements. Since locomotor activity is a measure of the level of excitability of the CNS [25], this decrease in spontaneous motor activity could be attributed to the sedative effect of the plant extracts in this dose.

To evaluate anxiolytic property of AJ extract, Elevated plus maze test was applied. It is a well-known model which has been validated to determine the fear of rodents to avoid open and elevated places and assess the anti-anxiety effects of pharmacological agents [26].

Inherent reaction of naive mice to this test is manifested as preferring to spend much time in the closed arms. An increase in open arm activity either duration or entries, reflects anti-anxiety behavior. Agents which increase open and close arm exploration are respectively considered as anxiolytics and anxiogenics.

As expected, here the typical benzodiazepine drug diazepam produced significant increase in the latency of time spent in open arm and also increased number of entries to open arm. Administration of 500 and 1000 mg/kg AJ also significantly increased the number of entries to open arm and the latency of spent time in open arm. It shows that AJ has anxiolytic effect and its anxiolytic effect is comparable whit diazepam.

On the other hand, we found a more consistent antidepressant-like activity. AJ, in all administered doses, reduced immobility time and simultaneously enhanced swimming behavior in mice by using the forced swimming test. The forced swimming model is used to evaluate the depressive phenotype of mice. It provides a rapid and reliable behavior screening test for anti-depressants [27].

In the forced swimming test, a longer duration of immobility is thought to reflect greater behavioral despair or depression after persistent stress. We hypothesized that administration of AJ would decrease mean immobility time, and accordingly our findings showed AJ at all doses significantly decreased the immobility time of mice in FST and it was comparable with standard anti-depressant drug Fluoxetine. As Fluoxetine exerts its antidepressant effect by blockage of 5-HT reuptake, the observed effect may be attributed to blockage of 5-HT reuptake or MAO inhibition.

Taking together it is interesting that although AJ at the dose of 500 mg/kg showed sedative effect, it could decline immobility of animals in forced swimming test and increase the number of entry and time spent in open arms in plus maze test. It means that antidepressant and anxiolytic effects of AJ has not related to stimulation of motor activity and movement.

From the above observations, it can be concluded that AJ possesses both anxiolytic and anti-depressant activity which is comparable with the standard treatments including diazepam and fluoxetine. However, further studies are required to know the exact mechanism.

Conclusions

In conclusion, our study provides evidence for antidepressant activity of *Allium jesdianum* extract. At antidepressant doses, it also had anxiolytic effects. However, further studies must be carried out to detect and isolate the active constituent which is responsible for its pharmacological activity.

Conflict of Interest

The authors declare that there is no conflict of interest.

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References

1. He D, Zhang P, Luo X, Li X, Wang L, et al. (2015) Evaluation of the anxiolytic and antidepressant activities of the aqueous extract from Camellia euphlebia Merr. ex Sealy in Mice. J Evid Based Complementary Altern Med p: 618409.
2. Lépine JP, Briley M (2011) The increasing burden of depression. Neuropsychiatr Dis Treat 7: 3-7.
3. Ferrari AJ, Charlson FJ, Norman RE, Patten SB, Freedman G, et al. (2013) Burden of depressive disorders by country, sex, age, and year: findings from the global burden of disease study 2010. PLoS Med 10: e1001547.
4. Emami M (2002) Treatment of diseases by plants, Tehran, Iran.
5. Sadock BJ, Sadock VA (2011) Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry: Lippincott Williams & Wilkins, USA.
6. Ceremuga TE, Valdivieso D, Kenner C, Lucia A, Lathrop K, et al. (2015) Evaluation of the anxiolytic and antidepressant effects of asiatic acid, a compound from Gotu kola or Centella asiatica, in the male Sprague Dawley rat. AANA J 83: 91-98.
7. Rothschild AJ (2000) Sexual side effects of antidepressants. J Clin Psychiatry 47: 24.
8. Masand PS, Gupta S (2002) Long-term side effects of newer-generation antidepressants: SSRIS, venlafaxine, nefazodone, bupropion, and mirtazapine. Ann Clin Psychiatry 14: 175-182.
9. Rivera J, Loya A, Ceballos R (2013) Use of herbal medicines and implications for conventional drug therapy medical sciences. Altern Integr Med 2: 130.
10. Pal SK, Shukla Y (2003) Herbal medicine: Current status and the future. Asian Pac J Cancer Prev 4: 281-288.
11. Jin L, Wu F, Li X, Li H, Du C, et al. (2013) Antidepressant effects of aqueous extract from Acanthopanax senticosus in Mice. Phytother Res 27: 1829-1833.
12. Pawar VS, Anup A, Shrikrishna B, Shivakumar H (2011) Antidepressant like effects of Acorus calamus in forced swimming and tail suspension test in mice. Asian Pac J Trop Biomed 1: S17-S9.
13. Kim JH, Kim SY, Lee SY, Jang CG (2007) Antidepressant-like effects of Albizzia julibrissin in mice: Involvement of the 5-HT 1A receptor system. Pharmacol Biochem Behav 87: 41-47.
14. Kalkunte SS, Singh AP, Chaves FC, Gianfagna TJ, Pundir VS, et al. (2007) Antidepressant and antistress activity of GCMS characterized lipophilic extracts of Ginkgo biloba leaves. Phytother Res 21: 1061-1065.
15. Mao Q, Huang Z, Ip S, Che C (2008) Antidepressantlike effect of ethanol extract from Paeonia lactiflora in mice. Phytother Res 22: 1496-1499.
16. Butterweck V, Jürgenliemk G, Nahrstedt A, Winterhoff H (2000) Flavonoids from Hypericum perforatum show antidepressant activity in the forced swimming test. Planta medica 66: 3-6.
17. Khaksarian M, Meshkat AM, Farazifard R, Safarpour F (2008) A study of chemistry and antinociceptive properties of medicinal plant Allium jesdianum leaves and the probable role of opioidergic system. Yafteh 18: 107-112.
18. Gholami A, Arabestani MR, Ahmadi M (2016) Evaluation of antibacterial activity of aqueous and methanol extracts of Allium jesdianum plant on a number of pathogenic bacteria resistant to antibiotics. Pajouhan Scientific Journal 14: 18-26.
19. Vahdani R, Mehrabi S, Malekzadeh J, Jannesar R, Sadeghi H (2012) Effect of hydrophilic extract of Allium jesdianum on ethylene glycol-induced renal stone in male wistar rats. Armaghane danesh 16: 566-577.
20. Gould TD, Dao DT, Kovacsics CE (2009) The open field test. Mood and anxiety related phenotypes in mice: Characterization using behavioral tests. Springer protocols pp: 1-20.
21. Porsolt R, Bertin A, Jalfre M (1977) Behavioral despair in mice: A primary screening test for antidepressants. Arch Int Pharmacodyn Ther 229: 327-336.
22. Amaral JF, Silva MIG, De Aquino Neto MR, Moura BA, De Carvalho AMR, et al. (2013) Antidepressantlike effect of biseugenol in the mice forced swimming test: Evidence for the involvement of the monoaminergic system. Fundam Clin Pharmacol 27: 471-482.
23. Lister RG (1987) The use of a plus-maze to measure anxiety in the mouse. J Psychopharmacology 92: 180-185.
24. Abdolmaleki A, Moghimi A, Ghayour MB, Rassouli MB (2016) Evaluation of neuroprotective, anticonvulsant, sedative and anxiolytic activity of citicoline in rats. Eur J Pharmacol 789: 275-279.
25. Nagaraju K, Carlson G, De Luca A (2010) Behavioral and locomotor measurements using open field animal activity monitoring system. J Vis Exp 91: 51785.
26. Walf AA, Frye CA (2007) The use of the elevated plus maze as an assay of anxiety-related behavior in rodents. Nature protocols 2: 322-328.
27. Castagné V, Moser P, Roux S, Porsolt RD (2011) Rodent models of depression: Forced swim and tail suspension behavioral despair tests in rats and mice. Curr Protoc Neurosci 55: 8.