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

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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 with common stress-related mood disorders leading to disability and premature death [1]. Depression occurs in all ages with an average of 17% lifetime prevalence in general population [2]. It usually exposes 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 patients 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 with 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 senticosus* [11], *Acorus calamus* [12], *Albizia julibrissin* [13], *Ginkgo biloba* [14], *Paonia 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 Khuzestan, 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 animal 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.

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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

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.

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).
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 wht 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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