



Research Paper: Effects of Mallow, (*Malva Sylvestris*) Extract on Reducing Anxiety in Animal Model



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ABSTRACT

Background: Anxiety is an unpleasant and obscure sense of fear with unknown origin. It is characterized by distrust, prostration, and physiological arousal which is associated with one or more signs or symptoms such as nausea, chest tightness, palpitation, sweating, and headache. The purpose of this study was to evaluate the effects of mallow's extract on reducing dark anxiety in mice.

Materials and Methods: Forty laboratory mice were divided into 5 treatment groups: control, dark anxiety, and 50, 100, and 200 mg/kg doses of the mallow's extract.

Results: Based on the results, anxiety decreases significantly spending time in open arm while all doses of mallow extract increases it. Also, anxiety reduces mean open arm entrance and the extract increases it in all doses.

Conclusion: According to results, hydroalcoholic extract of mallow could reduce the anxiety in 100 and 200 mg/kg groups by effecting nervous system.

1. Introduction

Anxiety is a complex mental state that is sometimes useful. It can even be used as a natural and adaptive response to acute stress in situations where individual's integrity is being threatened or there is a pathologic disorder that disrupts the patient's life [1].

Anxiety is a warning signal of a probable danger. It prepares person to deal with threats and warn him of possible

physical injury, pain, distress, punishment, or loss of his social or physical desires [2]. Anxiety disorders are common mental disorders. One out of every 4 people show diagnostic criteria for at least one type of anxiety disorder and the 12-month prevalence rate of these disorders is 17.7% [3].

Currently, most drugs prescribed for anxiety treatment are sedatives and hypnotics. These drugs are mainly benzodiazepines used to treat social phobia and anxiety due to the facilitation of Gamma-Aminobutyric Acid (GABA) and selective serotonin reuptake control [4].

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Among anxiety medications, benzodiazepines are effective on sleeping. However, about 4 out of every 10 people who use these medications daily for more than 8 weeks, develop addiction. Long-term use of benzodiazepines can produce cognitive, behavioral and emotional problems, a sense of chaos and confusion, difficulty in correct and logical thinking, decreased sexual performance, social phobia, anxiety and depression, decreased interest in favorite activities, and inability to express feelings. Side effects are not common but at least one or two may appear. Benzodiazepines can interrupt learning ability and remembering new information and interfere with physical or mental works. By quitting the drug, memory and performance will return to normal condition. Side effects such as confusion, disorientation, insomnia, depression and dizziness may be seen among some consumers. Other rare effects are agitation and hallucinations.

Medicinal herbs are important in traditional medicine of many countries and have special values in new therapeutic approaches. Medicinal herbs are important not only for treating diseases, but also preventing them. In recent years, there is also a growing use of herbs in traditional medicine in Iran [5]. The chemical compounds present in the extract of these plants are natural, do not accumulate in the body, and do not have side effects, so they are superior to chemical drugs [6]. Mallow (*Malva sylvestris*) is a biennial plant from Malva family. It has a stem with a height of 50 to 120 cm and fleshy white roots. Its leaves have 5 to 7 lobes and are serrated. Flowers are rose-violet colored with purple lines [7].

The leaves and flowers of this plant are often used in traditional medicine. Vitamins A, B, and C are found in large amounts in the extract of this plant, and can therefore be used to treat and reduce symptoms of cold such as cough, as well as the treatment of inflammation of the respiratory system, urinary tract, digestive system, and skin rashes. Clinical research suggests that the plant has antibacterial, antifungal and antiviral effects and can fight against human pathogens. Due to the presence of large amounts of phenol and flavonoids, mallow extract with its sedative effects reduces anxiety [6]. Considering the side effects of chemical drugs and re-emerging of medicinal plants in treating diseases, a comparative study was conducted to investigate mallow's flower extract in reducing anxiety.

2. Materials and Methods

The study animals' weight ranged between 25 and 30 g. They were kept at controlled temperature and humidity for two weeks to be adapted to the environment with free access to food and water. In this research, experimental groups were placed in a dark box with dimensions of 10×10×15 cm for 10 minutes. This action will increase activity and anxiety.

Samples were divided into 5 groups with 8 mice in each group: 1. Control group received only physiological serum injections; 2. Dark anxiety group experienced anxiety by being in dark boxes; 3, 4, and 5. Three experimental groups which received 50, 100, and 150 mg/kg of mallow extracts. To prepare the extract, the plant was chopped and then powdered by mill. A total of 200 g of this powder was weighed and placed in a sterilized erlen plus 40 mL of ethyl alcohol. Erlen was shaken for few minutes and after sealing kept for 48 hours in a cool environment.

Watman paper was used to filter the extract. The paper was weighed at first, then the extract was passed through the paper. Watman paper and residual powder were kept at room temperature to dry completely. Weight of the dried powder and paper were measured. Alcohol was added to the powder and after 48 hours, the erlen contents were mixed completely for 5 minutes. To reach the desired doses, the base extract was used.

The extracts at 50, 100 and 200 mg/kg were injected with insulin syringes, i.p. 50 minutes before the test. Plus elevated maze was used an anxiety evaluation tool. This maze has two open arms (10×50 cm) and two closed arms (50×40×10 cm) and about 50 cm above the floor. This experimental model does not need training that is its advantage. In the morning of experiment, the extract was injected and then the animal was placed on maze for 5 minutes and standard anxiety indices were recorded. Increase in Open Arm Entries (OAE%) and open arm spending time were treated as anxiety reduction. Increases in both indices and at least significant difference of one of them from those in the control group is considered as significant change in anxiety level.

Measured parameters were the number of times the animal enters or stays in open or closed arms. Presence of all four legs in arms (open or closed) is evaluated as "staying". Percentage of entrance to Open Arm Entries (OAE%) and percentage of staying in Open Arms Time (OAT%) and movement activity were calculated as follows:

$OAE\% = \frac{\text{The number of entrance to open arms}}{\text{total number of entrances to open and close arms}} \times 100$

$OAT\% = \frac{\text{Open arm time}}{\text{total time in both arms}} \times 100$

$\text{Movement activity} = \frac{\text{The number of entrance to closed arm} + \text{the number of entrance to open arm}}{\text{total number of entrances}}$

Significant increase in the percentage of entrance to open arms and percentage of staying in open arms plus no movement activity shows anxiety reduction in this test. However, OAE% in proportion to OAT % has less sensitivity in recording

anxiety and anti-anxiety actions of animal [8]. After collecting data, they were analyzed by both descriptive and inferential statistics in SPSS 22. At descriptive level, average and standard deviation were calculated whereas 1-way analysis of variance was used in inferential level.

3. Results

According to the results of variance analysis, average Open Arm Time (OAT%) of three experimental groups were significantly more than control group ($P < 0.05$) while anxiety group had less significant open arm time than control group (Figure 1). Open Arm Entries (OAE%) of the experimental groups were almost similar to that in the control group, but OAE% of the anxiety group had significant difference ($P < 0.05$) with that in the control group (Figure 2). Movement activity of mice in the experimental groups were significantly ($P < 0.05$) more than the anxiety groups (Figure 3).

4. Discussion

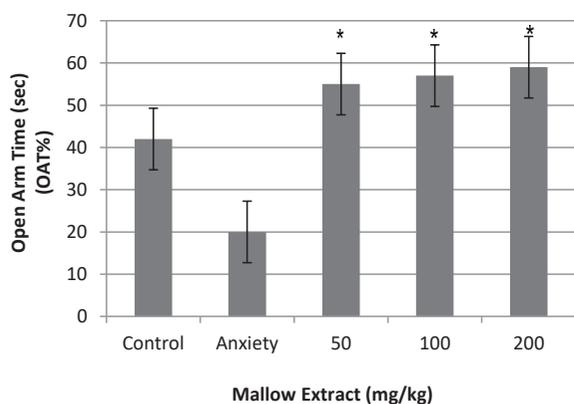
Nowadays, many people experience anxiety because they have to deal with various problems. Anxiety can disturb a person's life if it continues [8]. Anxiety disorders increase suicide attempts 2-5 times more. Anxiety is associated with an increase in the use of drugs, cigarettes, and alcohol. Based on Macney and MCCape report, about 19.1 million people (13.3%) aged 18-54 years in the United States suffer from anxiety disorders [9]. According to Sadock and Sadock (2007) report, anxiety has increased in the US (about 30 million people) and women suffer two times more than men. Costs of anxiety disorders in the United States is about \$42 billion which accounts for one third of \$ 148 billion spent on mental diseases [3].

In this study, adjusting effects of mallow's hydroalcoholic extract on dark anxiety of laboratory mice were evaluated using plus elevated maze method. Results showed that anxiety reduced open arm entrance and open arm time and the extract increased it to as much as that in the control group or even more.

The results of this study indicate that anxiety causes a significant reduction in the movement activity of the mice. Administration of the extract significantly increased the activity of the movement in the control group. While the anxiety significantly reduced the amount of entrance to the open arm, the use of extract in doses of 50, 100 and 200 mg/kg increased it to as much as that in the control group [3].

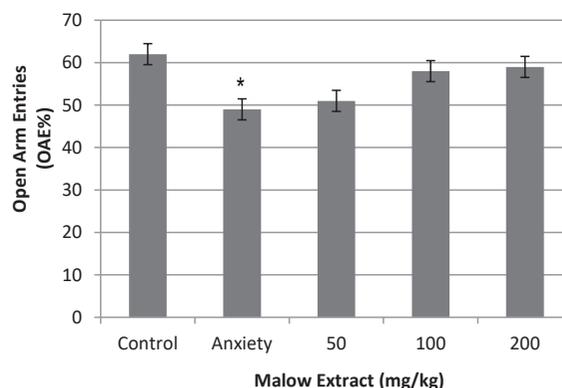
In Hosseini et al. (2015) study, 50 male rats were divided into 6 groups including no treatment (control 1), distilled water (control 2), plus maze, and 3 experimental groups which received 100, 200 and 400 mg/kg of wild poppies alcoholic extract. Their results show that the extract reduces anxiety which is in agreement with results of this study [10]. In a similar study, Komaki et al. (2015) studied the effects of garden thyme on male Wistar rats and reported that thyme might have anti-anxiety effects on mice behavior in plus elevated maze [11].

There is a lot of mucus, tannin, flavonoids, essential oil, vitamin C in the leaf and flower of the mallow. Anthocyanin is a natural chemical that is found only in flowers. Due to the large amounts of mucilage in the flower of this plant, its extract is widely used in herbal medicine. The presence of this mucilage can increase the production of neurotransmitters and the level of GABA [12]. This plant is not poisonous with no reports of contraindications, side effects or interactions with other drugs.



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Figure 1. Time spent in open arm (OAT%) by the anxiety, control and three experimental groups



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Figure 2. Open Arm Entry (OAE%) by the anxiety, control, and three experimental groups

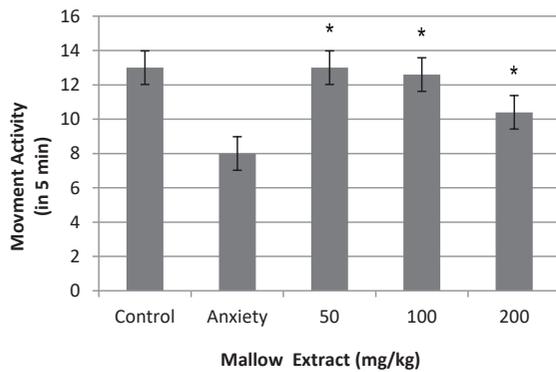
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Figure 3. Movement activity level in the anxiety, control and three experimental groups

5. Conclusion

Stress can significantly reduce the movement of the mice but the use of the mallow extract could offset this decline. Accordingly, the use of this extract, can be effective in reducing the amount of anxiety with dose-dependent effects.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were observed in accordance with the principles of working with laboratory animals approved by the university and approved by the Code of Ethics Committee for Biomedical Research, IR.IAU.NAJAFABAD.REC.1396.60.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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