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## Comparison of *Salix aegyptiaca* Extract and Fluoxetine in Reducing Depression in Animal Models

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### ABSTRACT

The aim of this study was to compare the effect of *Salix aegyptiaca* extract and Fluoxetine in reducing depression. In this experimental study used 60 laboratory mice weighting approximately 25 to 30 grams. Mice were divided in to the six groups: control, depression, Fluoxetine and three groups received different doses of 50, 100 and 200 mg/kg intraperitoneal injection of hydro alcoholic *Salix aegyptiaca* extract. After intraperitoneal injection, Forced swimming test and the tail suspension test was used to determine the level of depression. Mobility and immobility time of mice in each test indicates animal level of depression. The results were analyzed using humanities statistical software. The results showed that *Salix aegyptiaca* extract at a dose of 200 mg/kg was significantly effective in increasing mobility time in both tests compared with control and fluoxetine groups, indicating depression improvement. According to the results, *Salix aegyptiaca* hydro alcoholic extract with a dose of 200 mg/kg can be a good alternative to fluoxetine and can be utilized in reducing depression symptoms.

**Keywords:** *Salix aegyptiaca*, Depression, Fluoxetine, Forced swimming test, Tail suspension test, Laboratory small mice

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### INTRODUCTION

Depression is one of the most common mental disorders throughout the world. Reports of World Health Organization (WHO) show that depression is the second most debilitating factor after cardiovascular disease which causes severe social and economic losses [1]. About 340 million people in the world are depressed and according to the WHO, by 2020, the disease will be the second most commonly reported disease in the world after heart failure [2].

The statistics show that of every five women and every ten men, one person experiences the disease throughout their lives. In Iran, 305 million people were depressed until 1999. Depression is accompanied by reduced energy and interest, feeling guilty, difficult concentrating, thinking about death and suicide [3]. Depression is the result of brain biochemical changes and is one of the most common diseases in adults. About 70% of depressed patients respond to anti-depressants. Shock therapy is an alternative treatment for people who do not respond to medications. The most important medication is drug which can be done with psychotherapy. For the treatment of mild depression, psychotherapy can be beneficial on its own, but in the treatment of moderate and severe depression, medication is the first choice [4].

Fluoxetine is the first proposed selective serotonin reuptake inhibitor (SSRI). This drug was produced in early 1970's and introduced in 1998 for US market and since then has been one of the most widely used medicines. Therapeutic effects of SSRI family are due to their ability to prevent serotonin reuptake in the pre-synaptic section of the nerves endings. It is necessary to know that drugs of this family affect also other transmitters. Over the past two decades, evidence has been obtained that neural transmission of serotonin has been reduced during periods of depression. SSRI drugs have similar performance in curing depression. Fluoxetine has the longest half-life (26-220 hours) in this family. This length is due to an active metabolite known as norfluoxetine. All drugs of this family are well absorbed after oral ingestion and heavily metabolized in the liver [5].

Forced Swimming Test is one of the common animal pharmacological models for estimating anti-depressant effects of chemical and herbal compounds in rodents such as mice. This method is sensitive to all antidepressant drugs. One of the additional supplementary tests to estimate the anti-depressant effects of drugs is Tail Suspension Test. This method doesn't have temperature drop and stress of forced swimming test [6].

Pussy willow is a plant from willow genus which has fragrant catkins. It has a cold, tonic, and laxative nature and also relieves warm headaches [7]. Considering no extant study about the antidepressant effects of aquatic and hydro alcoholic extracts of this plant, current study was carried out.

## MATERIALS AND METHODS

Sixty mature mice in the weight range of 25 to 30 gram were selected and kept under controlled temperature and humidity with sufficient water and food for one week to adapt to environment. At first day of test, depression, fluoxetine and three extract groups received tetrabenazine injections to enforce depression. After that, fluoxetine group received fluoxetine injections whereas extract groups received 50, 100, and 200 mg/kg of pussy willows' extract intraperitoneal. At the end, forced swimming and tail suspension tests were taken [8].

Forced swimming test is one of the most valid and commonly used animal tests for studying depression. According Martin Sligman notion of helplessness, if animal is exposed to constant stress and doesn't have escape choice, it will lose its hope gradually and stop its activities and becomes helpless [9].

In this method, a cylindrical glass container with 25 cm height and 12cm diameter containing 25°C water is used to measure movement activities of sample. Mice are placed slowly in water from a height of 20 centimeters. In this situation, animal swims to maintain its stability. After a while, animal stops activity which is known as immobility. To measure the immobility time, a

chronometer was used. Increase in immobility time is ascribed to depression whereas decrease of this time is known as efficiency of antidepressant treatment. Environment conditions were similar and the test time was six minutes [10].

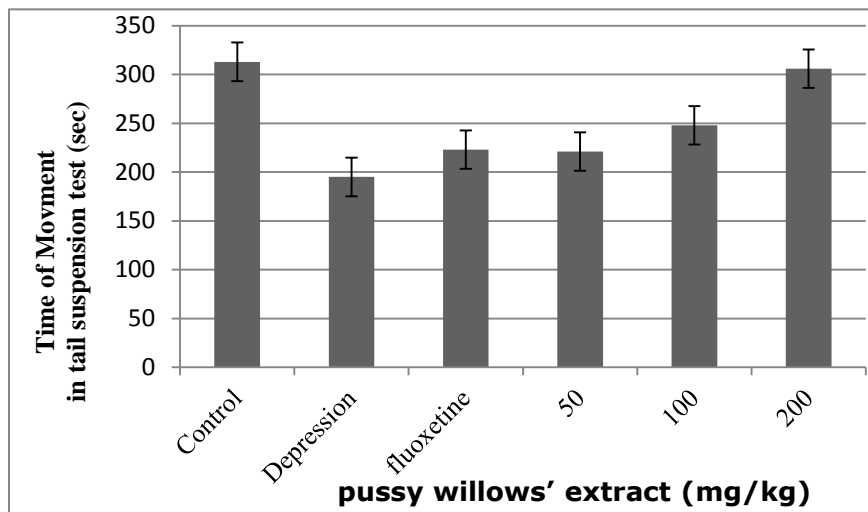
Tail suspension test was also used in this study as supplementary test. In this test, metal bases with 70cm height plus 50 cm ropes between two bases were used. Mice tails were tied up to this rope and the animal was hanged from tail, then, test was begun with a severe movement of the mouse [11]. The time which animal was motionless, inactive and unresponsive was considered as immobility time. Total suspension time was six minutes which first two minutes was considered for adaption and immobility in next four minutes was measured by chronometer in seconds. In both tests, all variables were recorded by one person which was not aware of samples groups [12].

In the present study, ethical principles were observed in accordance with the rules of support and maintenance of laboratory animals and statements of Islamic Azad University (Isfahan Branch).

Obtained data were analyzed at two descriptive and inferential levels. Average and standard deviation were calculated in descriptive level whereas one-way variance analysis plus Duncan test were used for inferential. Data were analyzed using SPSS 22 program.

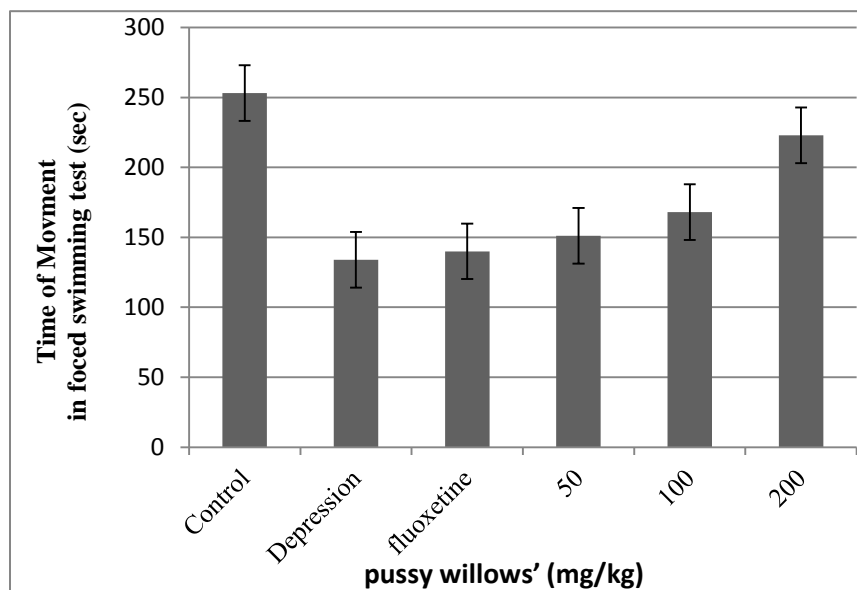
## RESULTS AND DISCUSSION

Average mobility time of 200 mg/kg group (in seconds) was more than all other groups in suspension test. Also, 200 mg/kg group had the lowest amount immobility time ( $p < 0.05$ ). Figure 1 shows the difference between the groups in relation to this activity.



**Figure 1:** Time of movement in second at the tail suspension test in all groups

In forced swimming test, the results showed that *Salix aegyptiaca* extract at a dose of 200 mg/kg was significantly effective in increasing mobility time in compared with control and fluoxetine groups. Also, depression group had the lowest mobility time ( $p < 0.05$ ). Figure 2 shows the differences between groups in terms of motor activity.



**Figure 2:** Time of movement in second at the forced swimming test in all groups

Results of paired comparison of mean differences showed that 200 mg/kg group was significantly different from depression and control groups in mobility and immobility indices but not from fluoxetine group. This was observed in both swimming and suspension tests.

In this study, the effects of pussy willows' extract and fluoxetine were compared on depression reduction of mice. According to results, there were significant difference between six groups ( $p < 0.01$ ) in swimming and suspension tests. Results also showed that about 42.8% of individual differences were related to differences between six groups which confirms hypothesis of study.

Pussy willow is an effective treat for reducing depression of mice. There is not any similar study about comparing fluoxetine and pussy willows. Result of this study showed that 200mg/kg dose of pussy willows extract reduced immobility time of mice in both tests which is evaluated as reduction index of depression. Also, it increased movement in both tests which again indicates decrease in depression.

In pathology, decrease in function of some neurotransmitters such as serotonin, epinephrine and dopamine leads to depression and almost all chemical drugs with anti-depression properties increase function of at least one of these chemical messengers. Previous studies have shown that there is some amount of flavonoid in this extract and it may react with dopamine receptors and inhibit them and thus can decrease depression symptoms in patients [11].

It should be said that dopamine receptors placed pre-synaptic on the dopamine terminals and inhibition of them leads to releasing dopamine as an effective neurotransmitter that can decrease depression severity [13].

In conclusion, depression as a commonest disorder has economic, emotional and social costs for patients and their families. It was estimated that 12 months procedure rate of this disorder is about 2.9 to 12.6% [14]. It seems that 50 and 200 mg per kg hydro alcoholic extract of passion fruit, compared with fluoxetine, can significantly decrease depression symptoms in tiny laboratory rat and it means that this study can be as a guide for finding similar anti-depression drugs with plant origin.

On the whole, pussy willows' extract can be a good alternative to fluoxetine in 200 mg/kg dose. In order to better understand of the effect of this extract, the investigation of interaction between extract and dopamine system can be suggested. At the other hand, studies on pussy willows' extract and component in its stem, leaf, flower and overhead organs showed that there is a large amount of flavonoid and alkaloid in this plant [15]. Based on these results, the investigation of pussy willows' extract in light of existence of other substances that may have anti-depression properties seems to be necessary.

### CONCLUSION

Hydro alcoholic extract of *Salix aegyptiaca* in 200 mg/kg compared to control group significantly increased the duration of mobility, which indicates a decrease in depression. From these findings, it can be concluded that the hydro alcoholic extract of the *Salix aegyptiaca* in the dose-dependent manner is effective in reducing depression.

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### REFERENCES

1. Jafari, F., Khosravi, M., and Bagherpour, M., Assessment of the antidepressant effect of *Rosa canina* L. petal extracts in mice by forced swimming stress model. *Physiol Pharmacol*, **2013**. 17: 231– 239.
2. Mahmoodi, M., Maymandi, SM., and Fremdi, A., The quality of prescribing in general practice in Kerman, Iran. *Journal of Kerman University of Medical Sciences*, **2005**. 12(4): 244-251.
3. Dolatabadi, Sh., et al. Stochastic risk-constrained scheduling of smart energy hub in the presence of wind power and demand response. *Applied Thermal Engineering*, **2009**. 14(3): 83-90.
4. Kaplan, E., and Sadok, B., Comparing the effects of hop's hydro alcoholic extract and diazepam on
5. reducing the anxiety in mice. *Der Pharmacia Lettre*. **2016**. 184-188
6. Qaeli, P., Kamkar, M., and Mesbahi, M., Comparing the effects of 8- week treatment with fluoxetine and imipramine on fasting blood glucose in patients with major depression disorder. *Journal of Diabetes and Metabolism of Iran*, **2004**. 3(2): 155-159.
7. Maleki, AS., Panahj, AM., and Abbasi, C., Conceptual definition and operationalization of spiritual health: A methodological study. *Journal of Arak University of Medical Sciences*, **2013**. 16 (9): 12-18.

8. Zargari, A., Introduction of medicinal plants species with the most traditional usage in Alamut region. Medical plants, Tehran University press, **2002**. 1-154
9. Alasvand, MS., and Modaresi, M. The effects of hydro alcoholic extract of *Boswellia carteri* on reproductive hormones in male mice. *J. Chem. Pharm. Res*, **2015**,7(11): 556-560
10. Adem, C., The mouse forced swim test. *J Vis Exp*. **2012**. (59): 3638.
11. Szegedi, A., et al. Acute treatment of moderate to severe depression with hypericum extract WS 5570 (St John's wort): randomised controlled double blind non-inferiority trial versus paroxetine. *Bmj*, **2005**. 330(7490): 503-5011.
12. Dalvand, Z., Modaresi, M., and Sajjadian, Comparing the effects of cannabis and paroxetine on depressive symptoms by using forced swimming test in mice. *Der Pharma Chemica*, **2016**. 8(16): 112-115.
13. Sun, LQ., Pharmacokinetics of multi-dose D-polymannuronic acid tablets in Chinese healthy volunteers. *Asian Journal of Drug Metabolism and Pharmacokinetics*, **2013**. 4(4): 261-284.
14. Mann JJ. The medical management of depression. *NEngl J Med*, **2005**. 353: 1819-34.
15. Modaresi, M., Basravi, M., and Sajadia I., Comparative effects of balm hydro alcoholic extract and diazepam on reducing anxiety of in mice. *Armaghane danesh*. **2016**. 20(10):848-857.