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Antidepressant activities of *Feijoa sellowiana* fruit

M. MAHMOUDI, M.A. EBRAHIMZADEH[1], M. ABDI, Y. ARIMI[1], H. FATHI[1]

Department of Pharmacology, School of Medicine, [1]Pharmaceutical Sciences Research Center; Mazandaran University of Medical Sciences, Sari, Iran

Abstract. – OBJECTIVE: Many pharmacological activities have been reported for Feijoa sellowiana. The aim of present study was to investigate antidepressant activities of its leaf and fruit extracts.

MATERIALS AND METHODS: Antidepressant activities of methanolic extracts were evaluated by modified forced swimming test (FST) and tail suspension tests (TST) in male Swiss albino mice.

RESULTS: Extracts showed signicant antidepressant activity in both models. They shortened remarkably the immobility period in both FST and TST and exhibited a dose dependent activity ($p < 0.001$). Leaf extract showed better activity than fruit extract. At 800 mg kg-1, it showed far better activity than imipramine in FST ($p < 0.001$). Both extracts showed significantly better activity than imipramine in increasing climbing time ($p < 0.001$). They showed significant activity in increasing in swimming time as compared to the control group ($p < 0.001$).

CONCLUSIONS: Our studies indicate that Feijoa showed significant antidepressant activity. It produced dose dependent effect on both models. It seems this effect is mainly mediated by inhibition of reuptake of catecholamines. These results introduced these plants as easily accessible source of natural antidepressant.

Key Words:
Antidepressant, Forced swimming test, Tail suspension test.

Introduction

Depression is a common disorder with high lifetime rates with high morbidity and mortality. Because the mechanism of depression is quite complex, different synthetic chemical antidepressants have been introduced. Current antidepressant treatments are efficacious; however, just for 50% of the patients and it often takes more than 5-8 weeks until the patients respond to the treatment[1]. Accordingly, it is necessary to research and develop more effective antidepressants. There are a large number of herbal medicines whose therapeutic potential have been assessed in a variety of animal models. Most assessments of herbal antidepressant activity were conducted using forced swimming test (FST) and the tail suspension test (TST). These studies have provided useful information for the development of new pharmacotherapies from medicinal plants for use in clinical for treatment of depression. Plants, such as *Hypericum perforatum*[2], *Vicia sojakii*[3] and *Hibiscus esculentus*[4] may be an important source of new antidepressant drugs.

Feijoa sellowiana (Myrtaceae) is native to southern of South America. Owing to its easy adaptability in subtropical regions; nowadays, it is extensively cultivated in many countries and also in Iran where its fruit are very popular. Although the chemical composition of Feijoa has been clearly reported[5], pharmaceutical studies of its constituents have barely been carried out. Its fruits are rich in vitamin C, polyphenols, terpenes, tannins and flavonoids. In the literature various biological activities have been described. *Feijoa* showed potent antimicrobial and antifungal activity and a sensible activity against Helicobacter pylori[6]. Moreover, its antioxidant activities have been reported[5,6]. It has good nephroprotective activity[7]. To the best of the author's knowledge, antidepressant activity of *Feijoa* have not been reported to date and nothing was found about mechanism or antidepressant activity of this plant. Therefore, the aim of the present work is to determine the antidepressant activity by modified forced swimming test (FST) and tail suspension test (TST) in order to understand the usefulness of this plant in medicine.

Materials and Methods

Plants Materials and Preparation of Extracts

Feijoa fruit (at the ripening stage) and leaf were collected from Fajr citrus experimental in-

Corresponding Author: Mohammad Ali Ebrahimzadeh, Ph.D; e-mail: zadeh20@gmail.com

stitute in autumn 2013. After identification of the plant by Dr. Bahman Eslami a voucher (No. 194, 195) has been deposited in the Faculty of Pharmacy Herbarium. Parts were dried at room temperature and coarsely ground before extraction. 100 g of each part was extracted at room temperature by percolation method using methanol.

Animals

Male Swiss albino mice (20 ± 2 g) were randomly housed in groups of 10 in polypropylene cages at an ambient temperature, 25 ± 1°C and 45-55% relative humidity, with a 12 h light: 12 h dark cycle (lights on at 7 a.m.). The animals had free access to standard pellet and water and *libitum*. Experiments were conducted between 8:00 and 14:00 h. The experiments were conducted according to the norms of Committee for the Purpose of Control and Supervision of Experiments in Animal. Mice were divided into 22 different groups (n = 8) and tested in FST and TST.

Forced Swimming Test (FST)

The mouse was dropped into a glass cylinder (20 cm in height and 14 cm in diameter) containing 15-cm-deep water at 24-25°C and left there for 6 min. After the initial 2-3 min of vigorous activity, the animals show a period of immobility by floating with minimum movements. Each mouse was judged to be immobile when it stopped struggling and remained floating motionless in the water, making only those movements necessary to keep its head above water. The duration of immobility, climbing and swimming behaviors during the final 4-min interval of the swimming test were measured[3,8]. Control group was treated with Tween 80 plus 0.9% (w/v) saline solution. The other groups received an *i.p.* injection of extract (100-800 mg kg^{-1}) in Tween 80 plus 0.9% (w/v) saline solution and imipramine (10 mg kg^{-1}) (from Darupakhsh Co., Tehran, Iran), one hour before the experiment. The animals were used only once. A decrease in the duration of immobility is indicative of an antidepressant effect.

Tail Suspension Test (TST)

The tail suspension test was carried out as per the established method. Groups of 8 animals are treated with the extract (100-1200 mg kg^{-1}) by *i.p.* injection 30 min prior to testing. For the test the mice are suspended on the edge of a shelf 58 cm above a table top by adhesive tape placed approximately 1 cm from the tip of the tail. After 2-3 min of vigorous activity characterised by struggling movements, attempts to catch the adhesive tape, or body torsions or jerks, the mice hung passively and completely motionless. Immobility was defined as the absence of any limb or body movements, except for those caused by respiration or when they hung passively and completely motionless. The duration of immobility is recorded for a period of 5 min. Imipramine (10 mg kg^{-1}) was used as positive control[3,4]. A decrease in the duration of immobility is indicative of an antidepressant effect.

Non-fatal Dose

1500 and 2000 mg kg^{-1} doses of extracts were injected to separated groups of seven. After 72 hours, any mortality was considered as the maximum non-fatal dose[3].

Statistical Analysis

Experimental results are expressed as means ± SD. The data were analyzed by analysis of variance ($p < 0.05$) and the means separated by Duncan's multiple range test.

Results

Table I showed the effect of extracts on the duration of immobility during FST. Extracts in all tested doses showed significant activity as compared to control group ($p < 0.001$). Leaf extract showed better activity than fruit. Fruit extract at 800 mg kg^{-1} showed the same activity as imipramine ($p > 0.05$) but leaf extract at 800 mg kg^{-1} showed far better activity than imipramine ($p < 0.001$, 24.9 ± 5.5 *vs.* 44.3 ± 14.9 s, respectively).

Extract in all tested doses showed significant activity in increasing in climbing time as compared to control group ($p < 0.001$). Imipramine also increased climbing time respect to the control group significantly ($p < 0.001$) but extracts showed far better activity than imipramine in increasing climbing time. All groups were different from imipramine with $p < 0.001$. It seems *Feijoa* extract has antidepressant activity by inhibition of reuptake of catecholamines.

Extract in all tested doses showed significant activity in increasing in swimming time as compared to the control group ($p < 0.001$). Imipramine also increased swimming time respect to the control group significantly ($p <$

Table I. Antidepressant activities of Feijoa in modified FST.

Group	Dose (mg kg^{-1})	FST Immobility (s)[a,b,c]	Climbing (s)[a,b,d]	Swimming (s)[a,b,d]
Control	-	202.3 ± 14.9	6.5 ± 5.4	31.2 ± 7.8
Fruit	100	121.0 ± 18.2	79.3 ± 23.5	39.7 ± 3.4
	200	82.2 ± 12.99	104.4 ± 7.1	53.4 ± 9.5
	400	74.5 ± 17.3	109.4 ± 11.4	56.1 ± 8.7
	800	45.6 ± 6.19^{ns}	146.0 ± 11.5	48.4 ± 9.9
Leaf	100	118.9 ± 13.0	72.2 ± 5.3	48.9 ± 8.6
	200	114.8 ± 15.4	78.1 ± 12.4	46.1 ± 5.4
	400	59.2 ± 7.3*	136.3 ± 9.5	44.5 ± 6.9
	800	24.9 ± 5.5***	167.3 ± 20.9	47.8 ± 8.8
Imipramine	10	44.3 ± 14.9	43.1 ± 35.6	152.6 ± 28.6

[a]Data are expressed as mean ± SD (n = 8). bAll groups were different from control group with $p < 0.001$. [c]Groups are different from imipramine ($^{ns}p > 0.05$, $^{***}p < 0.001$). [d]All groups were different from imipramine with $p < 0.001$.

0.001) but the effect of extracts were not comparable with that of imipramine ($p > 0.05$).

All extracts in all tested doses showed significantly and dose dependently decreased in the immobility time as compared to control mice ($p < 0.001$). Both extracts in 1200 mg kg^{-1} showed the same activity as imipramine ($p > 0.05$) (Figure 1). The non-fatal doses of extracts were over 2 g kg^{-1}. No mortality was observed after 72 hours.

Discussion

There is an increasing interest in the study of the antidepressant effect of herbs, since treatment of depression with conventional antidepressants provides a complete remission just for the half of individuals[1]. There are many published papers that showed polyphenolic compounds such as flavonoids have antidepressant activity[9,10]. Because of high polyphenol and flavonoids contents of *Feijoa* fruit[6,7], it was selected for assay of antidepressant activity. FST and TST are the two well established animal models of depression which are used to screen the potential drugs for antidepressant activity. Behavioral despair was proposed as a model to test for antidepressant activity. It was suggested that mice forced to swim in a restricted space from which they cannot escape are induced to a characteristic behavior of immobility. This behavior can be reduced by agents that are therapeutically effective in human depression. There is a significant correlation between clinical potency and effectiveness of antidepressants in both models[11,12]. FST is the most widely used tool for assessing antidepressant activity preclinically. However, the major drawback of the traditional FST is that it is unreliable in the detection of the effects of selective 5-HT reuptake inhibitors[9,13], which are the most widely prescribed antidepressant drugs today. Several modifications have been made to enhance the sensitivity of the traditional FST[9,13]. These alterations enabled investigators to distinguish specific behavioural components of active behaviors: (1) climbing behavior, upward-directed movements of the forepaws along the side of the swim chamber; (2) swimming behavior, the movement throughout the swim chamber that

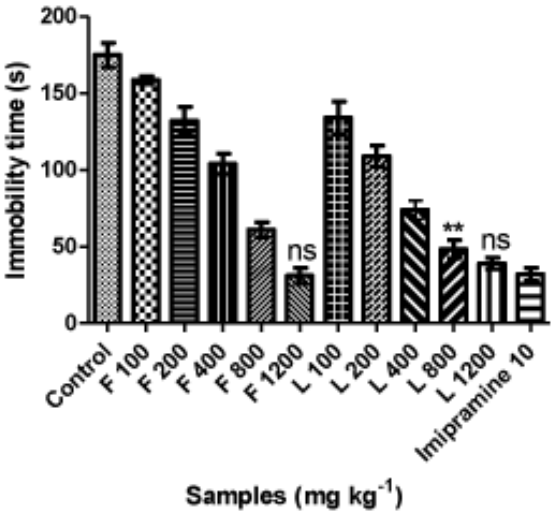

Figure 1. Antidepressant activities of Feijoa in TST. Groups are different from imipramine ($^{ns}p > 0.05$, $^{**}p < 0.01$).

also includes crossing into another quadrant; and (3) immobility as in the traditional test. The major advance of the this modified FST is that it reveals that catecholaminergic agents decrease immobility with a corresponding increase in climbing behavior, whereas 5-HT-related compounds decrease immobility but increase swimming behavior[9,13].

Extracts in all tested doses showed significant activity as compared to control group ($p < 0.001$). Leaf extract showed better activity than fruit. At 800 mg kg^{-1} it showed far better activity than imipramine ($p < 0.001$).

Extract in all tested doses showed significant activity in increasing in climbing time as compared to control group ($p < 0.001$). Extracts showed far better activity than imipramine in increasing climbing time ($p < 0.001$). It seems Feijoa extracts have antidepressant activity by inhibition of reuptake of catecholamines.

Extract in all tested doses showed significant activity in increasing in swimming time as compared to the control group ($p < 0.001$). This effect was not comparable with that of imipramine ($p > 0.05$). It seems, extracts have a weak activity on the reuptake of 5-HT.

TST has been described as a facile means of evaluating potential antidepressants[12]. The immobility displayed by rodents when subjected to an unavoidable and inescapable stress has been hypothesized to reflect behavioral despair which in turn may reflect depressive disorders in humans. Clinically effective antidepressants reduce the immobility that mice display after active and unsuccessful attempts to escape when suspended by the tail. All extracts in all tested doses showed significantly and dose dependently decreased in the immobility time as compared to control mice ($p < 0.001$). Both extracts in 1200 mg kg^{-1} showed the same activity as imipramine ($p > 0.05$).

Conclusions

Our studies indicate that *Feijoa* extract showed significant antidepressant activity. It produced dose dependent effect on both FST and TST. It seems, this effect is mainly mediated by inhibition of reuptake of catecholamines. However, further studies are necessary for complete understanding its antidepressant mechanism. This study introduced *Feijoa* as easily accessible source of natural antidepressant.

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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