

ORIGINAL RESEARCH

Medicine Science 2019;8(2):436-9

Investigation of antidepressant-like effect of pari-flo product on forced swimming test in balb-c mice

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Received 12 February 2019; Accepted 04 March 2019

Available online 27.03.2019 with doi:10.5455/medscience.2019.08.9022

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Abstract

Pari-flo is a commercial preparation in the form of a solution containing standardized *Passiflora incarnata* plant extract. We hypothesized that Pari-flo may have antidepressant potential with its content. Therefore, the aim of this study was investigation of the antidepressant-like effect of Pari-flo product comparing with imipramine based on Forced Swimming Test (FST) in Balb-c Mice. Forty-two male Balb-c mice were divided into 6 equal groups as follows: group 1 (control) were fed with normal rat chow and tap water, groups (2, 3, 4 and 5) were given 125, 250, 500 and 1000 mg/kg/day dose Pari-flo respectively, group (6) were given 15 mg/kg/day dose imipramine. After 7 days of treatment, the FST was carried out. Pari-flo significantly reduced the immobility time while increased the climbing time in FST at the dose of 500 and 1000 mg/kg/day. At the 1000 mg/kg/day dose of Pari-flo was increased the swimming time in FST. Imipramine was also increased the swimming and climbing time, while reduced the immobility time. Based on FST test results, it is concluded that Pari-flo product has antidepressant-like activity comparable to those of imipramine in experimental animal models.

Keywords: Antidepressant, Forced Swimming Test, Pari-flo, Mice

Introduction

Affecting millions of people per year, depression is a serious psychiatric problem with lifetime prevalence of 2% to 15% globally, and a major contributor to the global burden of disease and disability [1]. Many drugs and herbal extracts are being tested to use in the treatment of depression since the current treatment approaches remain insufficient [2,3]. For this purpose, we have tested Pari-flo product in animal model of depression in this study.

Pari-flo is a commercial preparation in the form of a solution containing 200 mg/ml standardized *Passiflora incarnata* plant extract, 20 mg/ml L-Glycine, 30 mg/ml magnesium L-threonate and 0,1 mg/ml L-methylfolate. The main component of the Pari-flo, *P. incarnata*, a perennial herb, is used as an ornamental plant in Turkey. The plant, which has major active ingredients as flavonoids and alkaloids, is also used for complaints such as restlessness, anxiety, insomnia, epilepsy, various disorders in menstruation and menopausal periods, and known to have antitussive, antiasthmatic, aphrodisiac and anti-inflammatory effects [4,5]. Although *P. incarnata* extract has been tested in many preclinical studies, its

mechanism of action is still being discussed. The sedative effects of *P. incarnata* have been showed in rodents [6]. Furthermore, *P. incarnata* was found to have anxiolytic effects [7-10].

The effect of L-methylfolate, which is one of the other substances in the content of the product, can support the sufficient synthesis of biochemical compounds, such as serotonin, norepinephrine and dopamine, which are necessary for the alleviation of depression [11]. Other substance of the product, L-Glycine, reduces emotional stress, increases mental efficiency, improves nervous system metabolism, as well as having anti-stress and sedative effects [12]. Among the other substances of preparation, magnesium plays a critical role in some brain-related and neurological disorders such as depression, anxiety, bipolar disorder, schizophrenia, and L-methylfolate, is known to be effective in the treatment of depression, dementia and schizophrenia, in addition, it increases the effect of serotonin and norepinephrine reuptake inhibitors (SNRI) and selective serotonin reuptake inhibitors (SSRI) [13,14].

In our literature research, we did not find any study about investigating of antidepressant effect of Pari-flo in Mice. According to above information, we hypothesized that Pari-flo may have antidepressant potential with its content and therefore, we aimed to investigate (as a preliminary study) the antidepressant-like effect of Pari-flo product at four different doses comparing with imipramine based on FST in mice.

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Material and Methods

Animals: Forty-two male Balb-c mice, weighing 34–38 g, were provided from the Experimental Animal Research and Production Center of Inonu University and the study protocol was approved by the Ethic Committee of Inonu University Faculty of Medicine (2018/A-26). They were randomly divided into six groups (n=7 mice in each group). Animals were treated humanely in accordance with the NIH Guide for the Care and Use of Laboratory Animals and were housed at room temperature ($21^{\circ}\text{C} \pm 2^{\circ}\text{C}$) with relative humidity of $52\% \pm 3\%$ with a 12 h light/dark cycle.

Experimental Design

Forty-two male Balb-c mice were divided 6 equal groups as follows: group 1 (control) were fed with normal rat chow and tap water, group 2 were given 125 mg/kg/day, group 3 were given 250 mg/kg/day, group 4 were given 500 mg/kg/day, and group 5 were given 1000 mg/kg/day dose Pari-flo (Grand Medical Group/İstanbul/Türkiye) via drinking water, group 6 were given 15 mg/kg/day dose imipramine (Novartis Pharmaceuticals) via drinking water. Before we started this study, daily water consumption of mice was measured and found to be an average of 7 ml per animal/day. Dose adjustments of animals were made based on this measurement. After 7 days of treatment, the forced swimming test (FST) was carried out with pretest. The number of animals in each group, the doses and administration times of pari-flo and imipramine were determined by considering similar studies [15, 16].

Forced swimming test (FST)

FST was performed according to the method of Porsolt et al. [17]. Mice were forced to swim in a cylindrical tank filled with 15 cm deep water, 18 cm in diameter and 40 cm in height. In the 5-min test, the animals' swimming, climbing, and immobility times were measured with the help of a stopwatch. When each animal test was completed, the water in the tank was changed so that the mice were not affected from each other. Animals were accepted as immobile when they remained motionless and only doing those movements necessary to keep the noise above the water.

Statistical Analysis

GraphPad Instat Version 3.10 package software was used for statistical analyses. The data were expressed as mean $\pm$ standard error of mean ($\pm$ SEM). Significance between the groups was analyzed using the one-way variance analysis (ANOVA). Comparisons of groups with significant differences were made using the Tukey-Kramer test. A value of $p < 0.05$ was considered statistically significant.

Results

Figure 1 shows the immobility time of mice in FST. Significant reduction in immobility time was noted in the animals treated with 15 mg/kg/day imipramine ($p < 0.001$), 1000 mg/kg/day Pari-flo ($p < 0.01$) and 500 mg/kg/day Pari-flo ($p < 0.05$) compared with control group. Figure 2 shows the swimming time of mice in FST. Significant increase in swimming time was noted in the mice treated with 15 mg/kg/day imipramine ($p < 0.001$) and Pari-flo 1000 mg/kg/day ($p < 0.05$) compared with control group. Figure 3 shows the climbing time of mice in FST. Significant increase in climbing time was noted in the animals treated with imipramine ($p < 0.001$), 1000 mg/kg/day Pari-flo ($p < 0.01$) and 500 mg/kg/day Pari-flo

($p < 0.05$) compared with control group.

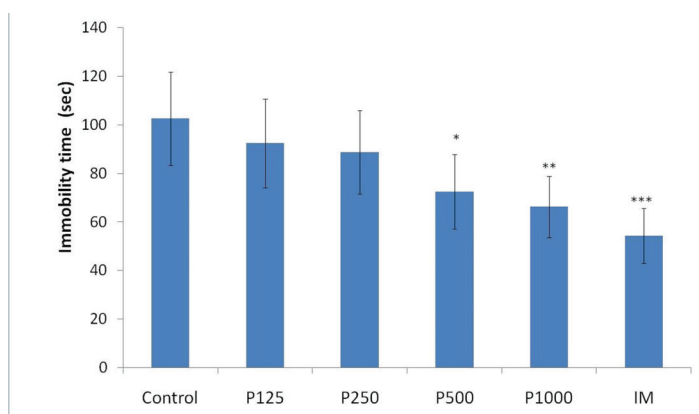


Figure 1. Effects of imipramine (15 mg/kg/day) and Pari-flo (125, 250, 500 and 1000 mg/kg/day) on immobility time in the forced swimming test. (IM: imipramine treated group, P125: 125 mg/kg/day Pari-flo treated group, P250: 250 mg/kg/day Pari-flo treated group, P500: 500 mg/kg/day Pari-flo treated group, P1000: 1000 mg/kg/day Pari-flo treated group, * $p < 0.05$, significant change vs. control group; ** $p < 0.01$, significant change vs. control group, *** $p < 0.001$, significant change vs. control group).

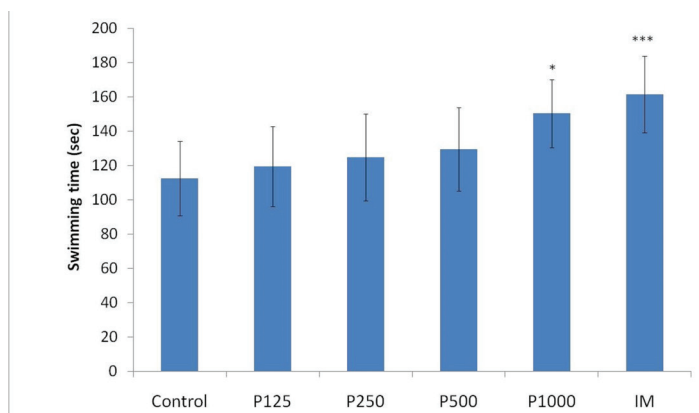


Figure 2. Effects of imipramine (15 mg/kg/day) and Pari-flo (125, 250, 500 and 1000 mg/kg/day) on swimming time in the forced swimming test. (IM: imipramine treated group, P125: 125 mg/kg/day Pari-flo treated group, P250: 250 mg/kg/day Pari-flo treated group, P500: 500 mg/kg/day Pari-flo treated group, P1000: 1000 mg/kg/day Pari-flo treated group, * $p < 0.05$, significant change vs. control group; *** $p < 0.001$, significant change vs. control group).

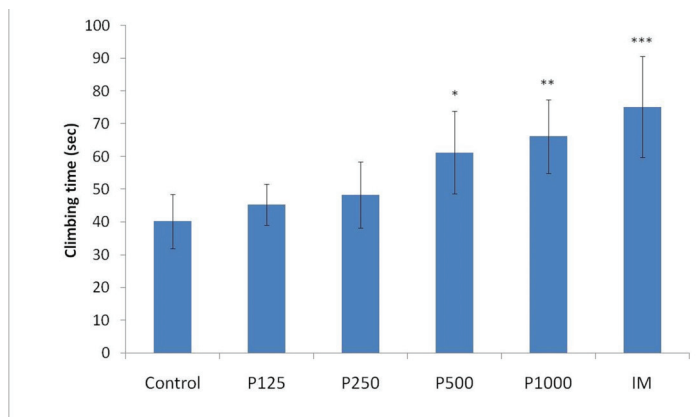


Figure 3. Effects of imipramine (15 mg/kg/day) and Pari-flo (125, 250, 500 and 1000 mg/kg/day) on climbing time in the forced swimming test. (IM: imipramine treated group, P125: 125 mg/kg/day Pari-flo treated group, P250: 250 mg/kg/day Pari-flo treated group, P500: 500 mg/kg/day Pari-flo treated group, P1000: 1000

mg/kg/day Pari-flo treated group, * $p < 0.05$, significant change vs. control group; ** $p < 0.01$, significant change vs. control group, *** $p < 0.001$, significant change vs. control group).

Discussion

Forced swimming test is one of the most commonly used animal models for investigating the antidepressant-like effects of conventional drugs and herbal substances in mice and rats. This model is sensitive to the effects of drugs and herbal extracts [18]. While decreasing the duration of immobility in FST is considered as an indicator of antidepressant-like effect, it has been suggested that the increase in noradrenergic activity induces the climbing behavior of animals, and increase in serotonergic activity may be related to swimming behavior [19]. In our study, imipramine reduced the immobility times of animals as in other studies [20]. As a tricyclic antidepressant, imipramine increased both swimming and climbing behavior, which may be due to its effect on noradrenergic and serotonergic pathways. Pari-flo was also found to decrease the immobility time of mice as dose-dependent manner, which indicating antidepressant-like effect. It was observed that Pari-flo increased both swimming and climbing behavior, and the effect on climbing behavior was more pronounced, which may be attributed to a prominent noradrenergic effect. The major component of Pari-flo, *P. incarnata* plant extract, known to contain alkaloids such as harmaline, harmine and harmalol, which are the irreversible monoamine oxidase-A (MAO-A) inhibitors, and known to have antidepressant properties [21,22]. These alkaloids may have played a major role in antidepressant-like activity. Besides MAO-A inhibition, *P. incarnata* plant extract is known to have an effect on GABAergic system, which may have contributed to antidepressant activity [23,24]. Some studies have shown that *P. incarnata* plant extract has no significant effect on swimming behavior in FST when used alone [15]. This difference may indicate that the other components in the content of Pari-flo have contributed to the antidepressant-like effect, via augmenting the serotonergic mechanisms, further studies are needed to determine the exact mechanism of Pari-flo. In addition, we believe that determining of the components responsible for pharmacological activity in Pari-flo, and removal of other substances will improve the formulation.

Conclusion

It is concluded that Pari-flo may have antidepressant-like effects comparable to those of imipramine in experimental animal models of Mice. However, this issue should be investigated with further experimental and clinical studies to determine the action mechanism and/or efficacy of Pari-flo as an antidepressant in the treatment of depression.

Acknowledgments

This work was supported by Grand Medical Group, Istanbul, Turkey.

Competing interests

The author confirms that this article content has no conflict of interest.

Financial Disclosure

All authors declare no financial support.

Ethical approval

Inonu University and the study protocol was approved by the Ethic Committee of Inonu University Faculty of Medicine (2018/A-26).

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