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Original Article

An Investigation of the Protective Effects of the Hydroalcoholic Extract of Persian Yellow Rose (*Rosa foetida Herrm.*) on Rats with Parkinson's Disease Induced by 6-Hydroxydopamine

Nahid Jivad[1*], Zahra Forouzandeh Shahraki[2], Amir Mahdi Naseri[3]

[1]Department of Neurology, School of Medicine, Kashani Hospital, Shahrekord University of Medical Sciences
[2]Deputy of Technology and Research, Shahrekord University of Medical Sciences, Shahrekord, Iran
[3]Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran

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Abstract

Background and Aim: This study was carried out to investigate the protective impacts of *Rosa foetida* extract on Parkinson's disease.

Materials and Methods: Seventy rats were divided into 7 groups of 10, including a sham group, the Parkinsonian group (received 6OHDA), pretreatment and post-treatment groups with Persian yellow rose extract (150 mg/kg and 300 mg/kg), and the positive control (L-DOPA). Animal behavior was evaluated using behavioral tests, including muscle stiffness test, rotarod, and elevated body swing test (EBST). The data were analyzed using SPSS statistical software.

Results: The frequency of turning to the right in the EBST test, the muscle stiffness score, and the right as well as left-hand scores in the muscle stiffness test were significantly higher in the Parkinsonian group than in the sham group ($P<0.05$). The frequency of turning to the right in the post-treatment group with Persian yellow rose extract in doses 150 and 300 mg/kg and in pre-treatment with Persian yellow rose extract in dose 300 was significantly lower than that of the Parkinsonian group ($P<0.05$). The score of the left and right hand in the pre-treatment group of Persian yellow rose extract at a dose of 300 significantly decreased compared with the Parkinsonian group ($P<0.05$). The time to maintain balance in the rotarod test was significantly reduced in the Parkinsonian group compared with the sham, and post-treatment as well as pre-treatment groups with different doses of Persian yellow rose extract ($P<0.05$).

Conclusion: According to the results of this study, it can be said that the Persian yellow rose extract protects nerve cells against oxidative damage caused by 6-hydroxydopamine and improves motor symptoms and balance disorders caused by Parkinson's disease.

Keywords: Persian yellow rose, Parkinson, Dopamine, L-DOPA, Rat

***Corresponding Author:** Nahid Jivad, Assistant Professor, Department of Neurology, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran. Email: jivad_395@yahoo.com.

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Introduction

Parkinson's disease is a neurodegenerative and progressive disease which is related to several movement disorders, including bradykinesia, muscle stiffness, tremors at rest, and postural imbalance. The hallmark of the disease in terms of pathology is the slow and gradual degeneration of dopaminergic neurons in the dense part of the substantia nigra, which reduces dopamine levels in the striatum, caudate nuclei and putamen (1). This disease is associated with movement disorders, including muscle stiffness, tremors and tremors of arms and legs at rest, akinesia or difficulty in starting movements, reduction of spontaneous movements and slowness of movements, or bradykinesia, weakness in maintaining balance, reduction of dependent movements, i.e. unconscious movements, and natural body movements such as facial expressions when talking. Moreover, some behavioral and anxiety disorders are observed in Parkinson's patients, particularly panic disorder, simple and social phobia, and generalized anxiety (2).

Although the cause of Parkinson's disease is not completely clear, it is known that both genetic and environmental factors are effective in its occurrence. Among these factors, age, family history of Parkinson's disease, genetic mutations, gender, exposure to pesticides, some drugs, and history of brain injury can be mentioned as risk factors of this disease (3). In most people with Parkinson's disease in the first 5 years of the disease, levodopa is used as the first line of treatment and is prescribed in the amounts of 300 to 600 mg/kg per day. Movement symptoms in these people improve by 20-70%. Two to three weeks after treatment with this drug, the feeling of fatigue decreases, and the slowness of movements, stiffness, and continuous walking improve within 3 months, but the tremor response varies from person to person and it may take several years to improve. Speech disorders and instability improve at the beginning of treatment, but central symptoms generally do not respond to this drug. Early side effects of this drug include nausea, loss of appetite, and fainting. Thus, doctors gradually increase the dose of the drug to develop tolerance to this drug. Among the other side effects of this drug, we can mention prominent tremors, and some patients are not even able to tolerate a low dose (4).

Figure 1. Persian yellow rose *(Rosa foetida)*.

One of the complementary and alternative medicinal methods used in the treatment of Parkinson's disease is the use of herbal medicine. The widespread use of herbal medicines and natural products in general in the world can be attributed to the side effects of chemical drugs. In the last three decades, a growing trend has been observed in the tendency to use medicinal plants and the revival of traditional medicine (5). Currently, there is a noticeable lack of neuroprotective drugs that stop the processes of neuronal degeneration. Since treatment with herbal medicines has fewer side effects, scientists have recently turned to herbal medicines (7, 6). This plant is rich in vitamin C and can exhibit antioxidant effects against free radicals (8). The antioxidant effects of Persian yellow rose have been shown in vitro (9) (Figure 1). However, its antioxidant effects in animal models have not been investigated. Hence, the effect of *Rosa feotida* on the improvement of the motor activity of Parkinsonian rats was investigated in this study.

Materials and Methods

This research is an experimental study. After receiving the code of ethics (IR.SKUMS.REC.1397.157) from the Ethics Committee of Shahrekord University of Medical Sciences and the thesis project code by the number of 3769, flowers of the Persian yellow rose were collected and after herbarium approval, they were used for extraction. The flower parts of the plant were placed at room temperature to dry. Then, the dry sample

of the plant was powdered by an electric mill, and 10 ml of 70% ethanol was added to each 1 gram of the resulting powder and kept at room temperature for 48 hours. Subsequently, the extract was filtered by filter paper and the resulting liquid was centrifuged at 3000 rpm for 15 minutes, and this process was repeated 3 times to filter the extract. The supernatant was collected and then concentrated using a rotary and the extract obtained after drying at 37°C was stored in an incubator at -20°C until the experiments.

Grouping of the Mice

Seventy male Wistar mice were purchased from Razi Vaccine and Serum Institute and kept for one week in order to adapt to the environment and relieve stress in the animal cage of the Faculty of Medicine under conditions of 12 hours of light - 12 hours of darkness, and the temperature of 22-24 degrees Celsius. They were kept ad libitum with the same food and water. Then, the mice were randomly divided into 7 groups of 10 as follows:

The first group (Parkinsonian group): 6-OHDA induced Parkinsonian rats that received normal saline intraperitoneally for 14 days after the 14th day of 6-OHDA injection.

The second group (sham): the rats that were subjected to the same process as the Parkinsonian group, but 6-OHDA solvent (saline) was injected instead of 6-OHDA (10).

The third and fourth groups (extract post-treatment): 6-OHDA induced Parkinsonian rats that received doses of 150 and 300 mg/kg of Persian yellow rose extract intraperitoneally for 14 days after the 14th day of 6-OHDA injection (11).

The fifth and sixth groups (extract pretreatment): 6-OHDA-induced Parkinsonian rats that received doses of 150 mg/kg and 300 mg/kg of Persian yellow rose extract intraperitoneally for 14 days before 6-OHDA injection (11).

The seventh group (L-DOPA treatment): 6-OHDA-induced Parkinsonian rats received a dose of 50 mg/kg of L-DOPA intraperitoneally for 14 days after the 14th day of 6-OHDA injection.

Induction of Parkinson's Disease

In creating the Parkinson's model, the method of Rodrigues et al. (2001) was used through the injection of a single dose of hydroxydopamine in the third ventricle. First, the mice were anesthetized by the intraperitoneal injection of ketamine/xylazine (100.5 mg/kg). Then, a fixed mouse head stereotaxic device and intraventricular injections were used for MFB coordinates (DV: -8.3, AP: -3.8, ML: ± 1.8) by 6-hydroxydopamine (200 micrograms in a volume of 5 microliters of saline containing ascorbic acid). After 5 minutes, the needle remaining in the injection site was slowly removed. Fourteen days after the induction of Parkinson's disease, EBST and barfix tests were performed to confirm the Parkinsonization of the mice (10).

Elevated Body Torsion Test (EBST)

The elevated body twist test (EBST) was carried out according to the method described by Borlongan *et al.* in 1995. Briefly, tails of the mice were taken from the 2 cm range of the connection with the body and brought up so that the animals' nose would be placed 2 cm above the support surface. In this case, the animal twists its body to the right or left, and the number of twists to each side indicates the severity of the disease (12).

Muscle Stiffness Test

In this test, the animal is placed on the table. If the way the animal stands and walks is normal, it will not receive a score (score 0). If the animal is placed on the table and remains motionless due to muscle stiffness or begins to move with difficulty by moving its arms and legs, the animal is given a score of 0.5. Then, the animal's right hand is placed on a wooden platform with a height of 3 cm. If the animal does not remove its hand from the platform for at least 10 seconds, it will receive a score of 0.5. This test is also done for the left hand, and this step has 1 point in total. Subsequently, the animal's right hand is placed on the 9 cm platform. If the animal does not remove its hand from the platform for at least 10 seconds, it gets a score of 1, and the left hand is also tested in the same way. This stage has a total of 2 scores. A completely Parkinsonian animal gets a score of 3.5 and a healthy animal gets a score of zero. (11)

Measurement of Motor Activity and Balance

The movement and balance activities of the animals were determined by the rotarod device. To evaluate the balance performance by the rotarod device, the animal was placed on a rotating horizontal rod with a diameter of 3 cm rotating at an initial speed of 10 rpm, and the ultimate speed was raised from 10 to 20 rpm within 20 seconds. The time to keep balance and stay on the bar

was recorded for each animal. After the induction of Parkinson's disease, each animal was first given two opportunities to get used to and adapt to the device (the learning criterion is staying on the rod for 5 minutes). To carry out the test, the animal was placed on the device three times and the average time obtained was calculated. After placing the animal on the machine every time, the animal was given 30 minutes to rest, and then the balance activity was measured again (13).

Measurement of Antioxidant Capacity

Antioxidant capacities of whole serum and brain tissue homogenate were determined by FRAP method. The FRAP working solution was prepared by adding 2.5 mL of 0.25 mM acetate buffer with pH=3, 2.5 mL of 10 mM TPTZ prepared in 40 mM hydrochloric acid, and 2.5 mL of 20 mM FeCl6 in water. Twenty-five microliters of serum sample or tissue homogenate was mixed with 1.5 ml of FRAP working solution, and after 10 minutes at 37°C, the optical absorption at 593 nm was read by a spectrophotometer. (14)

Measuring the Amount of Malondialdehyde

Two hundred µl of serum/brain tissue homogenate was mixed with 1.5 ml of 20% acetic acid, 1.5 ml of 0.8 thiobarbituric acid (TBA) and 200 µl of 8.1% SDS solution. Then, the samples were placed in a boiling water bath for 60 minutes. Subsequently, the samples were cooled and 1 ml of distilled water and 5 ml of n-butanol-pyridine mixture were added to them and shaken. Then, the present mixture was centrifuged at 4000 rpm for 10 minutes and the optical absorption of the supernatant solution was recorded at a wavelength of 523 nm (14).

Data Analysis Method

The data were analyzed using SPSS version 20 software, one-way analysis of variance, and Tukey's post hoc test. A significance level of less than $P<0.05$ was considered.

Results and Discussion

Based on a one-way analysis of variance and Tukey's post hoc test, the antioxidant capacity of serum in the Parkinsonian group was significantly decreased compared with the sham group ($P<0.01$). In the post-treatment group with a dose of 300 mg/kg of Persian yellow rose extract, the antioxidant capacity of the serum was significantly higher than the Parkinson's group ($P<0.001$). In the pretreatment groups of Persian yellow rose in doses of 150 and 300 mg/kg, the antioxidant capacity of serum was significantly higher than in the Parkinsonian group ($P<0.001$). In the group receiving L-DOPA, the antioxidant capacity of serum was significantly higher than in the group with Parkinson's disease ($P<0.01$). Based on one-way analysis of variance and Tukey's post hoc test, serum malondialdehyde increased significantly in the Parkinsonian group compared with the sham group ($P<0.001$). In the post-treatment groups with doses of 150 and 300 mg/kg of Persian yellow rose extract, malondialdehyde serum was significantly lower than the Parkinsonian group ($P<0.01$ and $P<0.001$). In the pretreatment groups with doses of 150 and 300 mg/kg of Nestern Z malondialdehyde extract, the serum was significantly lower than in the Parkinsonian group ($P<0.001$). In the group receiving L-DOPA, serum malondialdehyde was not significantly different from the Parkinson's group. In the present study, muscle stiffness, EBST and rotarod tests were used to evaluate the behavior of Parkinsonian animals. The results showed that the frequency of turning to the right in the EBST test and the muscle stiffness score and right and left-hand score in the muscle stiffness test increased significantly in the Parkinsonian group compared with the sham group, while the time to maintain balance in the rotarod test decreased significantly.

Based on one-way analysis of variance and Tukey's post hoc test, the antioxidant capacity of serum in the Parkinsonian group was remarkably decreased compared with the sham group ($P<0.01$). In the post-treatment group with a dose of 300 mg/kg of Persian yellow rose extract, the antioxidant capacity of the serum was significantly higher than the Parkinson's group ($P<0.001$). In the pretreatment groups of Persian yellow rose extract in doses of 150 and 300 mg/kg, the antioxidant capacity of serum was significantly higher than the Parkinsonian group ($P<0.001$). In the group receiving L-DOPA, the antioxidant capacity of serum was noticeably higher than the group with Parkinson's disease ($P<0.01$). Moreover, the antioxidant capacity of the brain tissue in the Parkinsonian group was significantly reduced compared with the sham group ($P<0.001$). In the post-treatment group with doses of 150 and 300 mg/kg of Persian yellow rose extract, the antioxidant capacity of the brain tissue was not

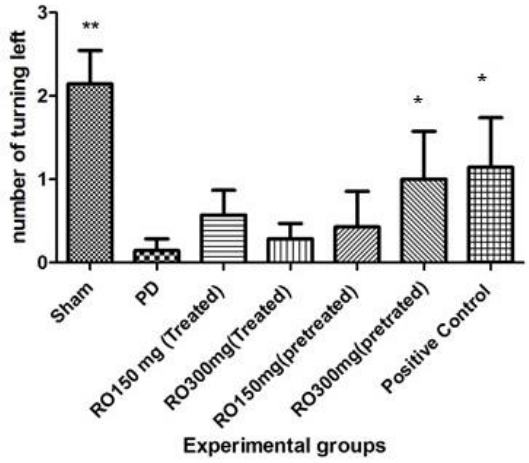

Chart 1: A comparison of the frequency of turning left in the EBST test in the studied groups (analysis of variance test and Tukey's post hoc test). PD: Parkinsonian rats. RO: hydroalcoholic extract of Persian yellow rose. Positive control: A group receiving L-DOPA. *Indicates a significant difference with the Parkinsonian group (**P<0.01 and *P<0.05).

significantly different from the Parkinson's group. In the pretreatment groups of Persian yellow rose extract in doses of 150 and 300 mg/kg, the antioxidant capacity of the brain tissue was significantly higher than that of the Parkinsonian group (P<0.05, P<0.001). In the group receiving L-DOPA, the antioxidant capacity of the brain was significantly higher than in the Parkinson's group. Based on one-way analysis of variance and Tukey's post hoc test, serum malondialdehyde increased significantly in the Parkinsonian group compared with the sham group (P<0.001). In the post-treatment groups with doses of 150 and 300 mg/kg of Persian yellow rose extract, malondialdehyde serum was significantly lower than the Parkinsonian group (P<0.01 and P<0.001). In the pretreatment groups with doses of 150 and 300 mg/kg of Nestern Z malondialdehyde extract, the serum was significantly lower than the Parkinsonian group (P<0.001). In the group receiving L-DOPA, serum malondialdehyde was not noticeably distinct from the Parkinson's group (P<0.001). Brain tissue malondialdehyde increased significantly in the Parkinsonian group compared to the sham group (P<0.001). In the post-treatment group with a dose of 300 mg/kg of the Persian yellow rose malondialdehyde extract, the brain tissue was significantly lower than the Parkinsonian group (P<0.001). In the pretreatment groups with doses of 150 and 300 mg/kg of Nestern Z malondialdehyde extract, the brain tissue was significantly lower than the Parkinsonian group (P<0.001). In the group receiving L-DOPA, malondialdehyde in the brain tissue was not significantly different from the Parkinson's group.

A Comparison of the Frequency of Turning Left in the EBST Test in the Studied Groups

According to the results of a one-way analysis of variance and Tukey's post hoc test, the frequency of turning to the left in the EBST test was significantly lower in the Parkinsonian group than in the sham group (P<0.01). The frequency of turning to the left in the EBST test was significantly higher in the pretreatment groups with 300 doses of Persian yellow rose extract and L-DOPA than in the Parkinsonian group (P<0.05). (Chart 1).

A Comparison of the Frequency of Turning to the Right in the EBST Test in the Studied Groups

According to the results of a one-way analysis of variance and Tukey's post hoc test, the frequency of turning to the right in the EBST test was remarkably greater in the Parkinsonian group than in the sham group (P<0.01). The frequency of turning to the right in the EBST test was significantly lower in the post-treatment groups with doses of 150 and 300 mg/kg of *Rosa foetida* extract than in the Parkinsonian group (P<0.01 and P<0.05). The frequency of turning to the right in the EBST test in the pretreatment group with the Persian yellow rose extract at a dose of 300 mg/kg

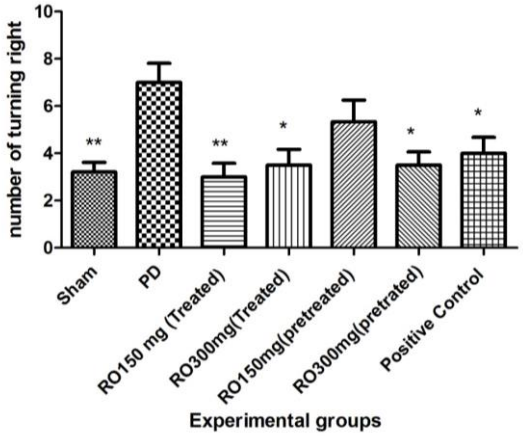

Chart 2: A comparison of the frequency of turning to the right in the EBST test in the studied groups (analysis of variance test and Tukey's post hoc test). PD: Parkinsonian rats. RO: hydroalcoholic extract of Persian yellow rose. Positive control: A group receiving L-DOPA. *Indicates a significant difference with the Parkinsonian group (**P<0.01 and P<0.05).

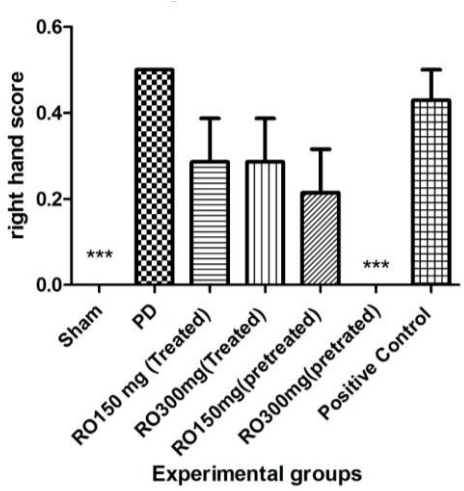

Chart 3: A comparison of the right-hand score in the muscle stiffness test in the studied groups (analysis of variance test and Tukey's post hoc test). PD: Parkinsonian rats. RO: hydroalcoholicextract of a Persian yellow rose. Positive control: group receiving L-DOPA. *Indicates a significant difference with the Parkinsonian group (*** P<0.001).

and L-DOPA was significantly lower than in the Parkinsonian group (P<0.05). (Chart 2).

A Comparison of the Right Hand Score in the Muscle Stiffness Test in the Studied Groups

According to the results of a one-way analysis of variance and Tukey's post hoc test, the right hand score in the Parkinsonian group was significantly higher than the sham group (P<0.001). The score of the right-hand in the pretreatment group with the Persian yellow rose extract at a dose of 300 mg/kg was significantly decreased compared with the Parkinsonian group (P<0.001). The score of the right hand in the extract post-treatment and extract pre-treatment groups at a dose of 150 was not noticeably distinct from the Parkinsonian group (Chart 3).

A Comparison of the Left-Hand Score in the Muscle Stiffness Test in the Studied Groups

According to the results of a one-way analysis of variance and Tukey's post hoc test, the left-hand score in the Parkinsonian group was significantly higher than the sham group (P<0.001). The score of the left hand in the pretreatment group with the Persian yellow rose extract at a dose of 300 mg/kg was significantly decreased compared with the Parkinsonian group (P<0.001). The score of the left hand in the extract post-treatment and extract pre-treatment groups at a dose of 150 was not significantly

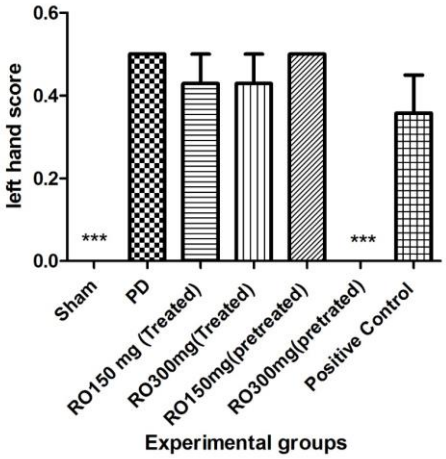

Chart 4: A comparison of the left-hand score in the muscle stiffness test in the studied groups (analysis of variance test and Tukey's post hoc test). PD: Parkinsonian rats. RO: hydroalcoholic extract of Persian yellow rose. Positive control: group receiving L-DOPA. *Indicates a significant difference with the Parkinsonian group (*** P<0.001).

different from the Parkinsonian group (Chart 4).

A Comparison of the Muscle Stiffness Score in the Muscle Stiffness Test in the Studied Groups

According to a one-way analysis of variance and Tukey's post hoc test, the duration of maintaining balance in the rotarod test was noticeably reduced in the Parkinsonian group compared with the sham group (P<0.001). In the post-treatment group with doses of 150 and 300 mg/kg of Persian yellow rose, the duration of maintaining balance in the rotarod test was

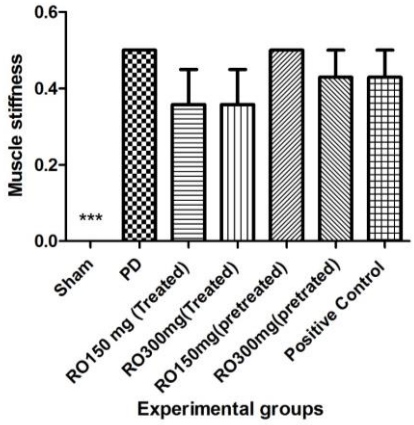

Chart 5: A comparison of the muscle stiffness score in the muscle stiffness test in the studied groups (analysis of variance test and Tukey's post hoc test). PD: Parkinsonian rats. RO: hydroalcoholic extract of Persian yellow rose. Positive control: group receiving L-DOPA. *Indicates a significant difference with the Parkinsonian group (*** P<0.001).

significantly longer than that of the Parkinsonian group (P<0.05 and P<0.001). In the pretreatment groups of Persian yellow rose extract in doses of 150 and 300 mg/kg, the duration of maintaining balance in the rotarod test was significantly longer than in the Parkinsonian group (P<0.001). In the group receiving L-DOPA, the duration of maintaining balance in the rotarod test was significantly longer than that in the Parkinsonian group (P<0.001) (Chart 5).

A Comparing the Duration of Maintaining Balance in the Rotarod Test in the Studied Groups

According to one-way analysis of variance and Tukey's post hoc test, the duration of maintaining balance in the rotarod test was significantly reduced in the parkinsonian group compared to the sham group (P<0.001). In the post-treatment group with doses of 150 and 300 mg/kg of yellow nester extract, the duration of maintaining balance in the rotarod test was significantly longer than in the parkinsonian group (P<0.05 and P<0.001). In the pretreatment groups of Persian yellow extract in doses of 150 and 300 mg/kg, the duration of maintaining balance in the rotarod test was significantly longer than the parkinsonian group (P<0.001). In the group receiving L-DOPA, the duration of maintaining balance in the rotarod test was significantly longer than the group with Parkinson's disease (P<0.001) (Chart 6).

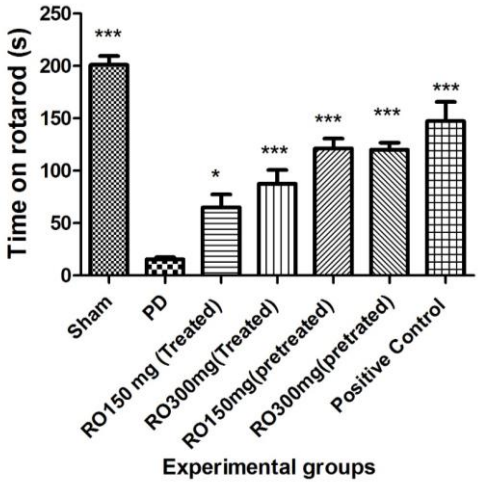

Chart 6: Comparison of the duration of maintaining balance in the rotarod test in the studied groups (analysis of variance test and Tukey's post hoc test). PD: Parkinsonian rats. RO: hydroalcoholic extract of Persian yellow rose. Positive control: group receiving L-DOPA. * Indicates a significant difference with the Parkinsonian group (*P<0.05 and ***P<0.001).

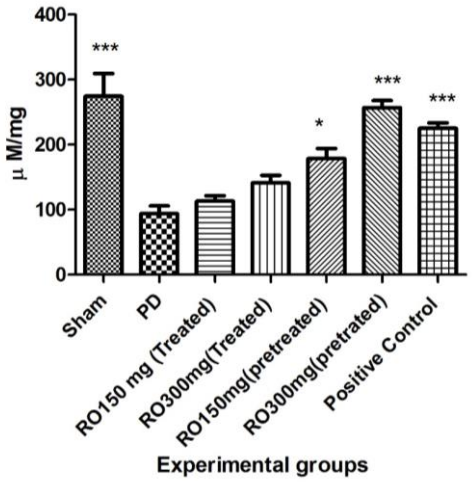

Chart 7: Comparison of the antioxidant capacity of the brain tissue in the studied groups (analysis of variance and Tukey's post hoc test). PD: Parkinsonian rats. RO: hydroalcoholic extract of Persian yellow rose. Positive control: group receiving L-DOPA. * Indicates a significant difference with the Parkinsonian group (*P<0.05, and ***P<0.001).

A Comparison of Oxidant Tissues in the Studied Groups

Based on one-way ANOVA and Tukey's post hoc test, the antioxidant capacity of the brain tissue in the parkinsonian group was significantly reduced compared to the sham group (P<0.001). In the post-treatment group with doses of 150 and 300 mg/kg of yellow nester extract, the antioxidant capacity of the brain tissue was not significantly different from the Parkinson's group. In the pretreatment groups of Persian yellow rose extract in doses of 150 and 300 mg/kg, the antioxidant capacity of the brain tissue was significantly higher than that of the parkinsonian group (P<0.05, P<0.001). In the group receiving L-DOPA, the antioxidant capacity of the brain was significantly higher than in the Parkinson's group (P<0.001) (Chart 7).

It was shown in the present study that Persian yellow rose could have protective effects in Parkinsonian rats. This plant decreased immobility in the muscle stiffness test as well as the frequency of twisting in the EBST test, and improved the ability to maintain balance in the rotarod test. Persian yellow rose extract also increased the antioxidant capacity and decreased malondialdehyde in the brain and serum of the Parkinsonian rats. Thus, it can be said that Persian

yellow rose extract improves motor symptoms and balance disorders by protecting nerve cells against oxidative damage caused by 6-hydroxydopamine. It comes from Parkinson's disease. It has been indicated that there is a positive relationship between the death of nigral dopaminergic cells and the severity of behavioral symptoms in the 6-hydroxydopamine animal model (15). The most reliable test in the acute assessment of Parkinson's patients in the laboratory is the elevated body torsion test or EBST, which can detect partial or almost complete damage in the substantia nigra. In this test, the induction of Parkinson's disease is related to a rise in the number, intensity and degree of twisting deviations (15, 16). Moreover, the time spent on the rotation of the rotard apparatus has an inverse relationship with cell damage in this nucleus (17).

Furthermore, an increase in the duration of immobility in the muscle stiffness test in Parkinsonian rats has been reported in the studies conducted by Reyhani *et al*. in 2015 (18), Setreki *et al*. in 2018 (19) and Nasri in 2012 (15). The immobility or akinesia that occurs in Parkinson's disease is often due to the reduction of dopamine secretion in the basal ganglia. Its secretion also decreases in the limbic system, which may severely reduce the nerve stimulation to perform motor activity (19). In the present study, post-treatment of the Parkinsonian rats with Persian yellow rose extract in doses of 150 and 300 mg/kg and pre-treatment with Persian yellow rose extract in dose of 300 caused significant decreases in the frequency of turning to the right. Moreover, pretreatment of the Parkinsonian rats with Persian yellow rose extract in a dose of 300 resulted in a significant decrease in left- and right-hand scores. Furthermore, the duration of maintaining balance in the rotarod test was significantly increased in the groups receiving the extract as post-treatment and pre-treatment, which indicates the protective effects of the Persian yellow rose extract against muscle stiffness and movement as well as balance disorders caused by reviewing the sources. Protective effects of the yellow nasturtium against nerve damage have not been investigated to date. However, protective effects of other rose species on the nervous system have been shown. These protective effects include the protective effect of Rosa canina L in increasing hippocampal neuronal density (20), improving depression, and cognitive impairment in diabetic rats (21), the protective effect of *Rosa laevigata* on PC12 nerve cells against damage caused by hydrogen peroxide (22), and the protective effects of *Rosa damascena* against neurological damage caused by Alzheimer's (23). Neuroprotective effects of rose species have been attributed to the antioxidant and anti-inflammatory activities of the phenolic compounds present in them (22).

In the present study, in order to determine the mechanism of the protective effects of Persian yellow rose extract against Parkinson's disease, some oxidative stress parameters were determined in the studied groups and it was observed that the induction of Parkinson's disease through intracerebral injection of 6-hydroxydopamine caused a significant decrease in the antioxidant capacity of the brain and serum. A significant increase in MDA was observed. In physiological conditions, 6-hydroxydopamine poison is oxidized very quickly and turns into hydrogen peroxide and then turns into hydroxyl radical, which is one of the most destructive free radicals for living cells. Some degrees of oxidative damage in Parkinsonian rats treated with 6-hydroxydopamine have been reported in some studies (20), which is consistent with the findings of this study. The progressive loss of dopaminergic neurons in the basal ganglia is the most important pathological finding in the brain of patients with Parkinson's disease. The destruction of these neurons results in the reduction of the dopamine neurotransmitter in this area. As long as 50-60% of dopaminergic neurons have not been destroyed and 80-85% of the amount of dopamine in the striatum has not decreased, symptoms of the disease will not appear (24). Regarding the death of dopaminergic cells, there are several hypotheses such as mitochondrial complex I defects related to the electron transport chain, iron accumulation, protein accumulation, inflammatory immune responses, dysfunction of liver cytochrome p450 and oxidative stress, and increased formation of free radicals (25). The increase in lipid peroxidation in the body area of patients with Parkinson's disease can be a result of increased iron ion, disruption of mitochondrial complex 1 activity, and increased nitric oxide production. The role of each of these factors has been shown in increasing the production of free radicals as well as the brain of Parkinson's patients. Moroever,

a reduction in the activity of brain antioxidant enzymes has been reported in patients with Parkinson's disease (26, 27). In the present study, pretreatment and posttreatment of the Parkinsonian rats with Persian yellow rose extract caused a noticeable increase in the antioxidant capacity and a significant decrease in MDA in the brain and serum. So far, the antioxidant effects of Persian yellow rose have been shown in 2 studies conducted by Norouzi *et al*. in 2020 and Noor Alizadeh *et al*. in 2018 in an in vitro environment (28, 29). Also, in a study conducted in Turkey, it was reported that the extract of Persian yellow rose exhibited a greater degree of antioxidant activity in chelating metals than other plant extracts tested (30). In general, antiParkinsonian drugs are a series of drugs that are prescribed to treat and decrease the symptoms of Parkinson's disease. These drugs, including safinamide which is effective on non-motor symptoms in Parkinson's disease, are used to either modulate the level of dopamine in the brain or to simulate the function of dopamine (31). Since there is no definitive cure for Parkinson's disease, it can be said that Persian yellow rose extract also improves motor symptoms and balances disorders by protecting nerve cells against the oxidative damage caused by 6-hydroxydopamine.

Conclusion

It was found in the present study that Persian yellow rose extract could have protective effects on Parkinsonian rats. This extract caused a decrease in immobility in the muscle stiffness test, reduced the frequency of twisting in the EBST test, and improved the ability to maintain balance in the rotarod test. Persian yellow rose extract also increased the antioxidant capacity and decreased malondialdehyde in the brain and serum of the Parkinsonian rats. Thus, it can be said that Persian yellow rose extract could improve motor symptoms and balance disorders by protecting nerve cells against the oxidative damage caused by 6-hydroxydopamine that comes from Parkinson's disease.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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