The Quarterly Scientific Journal of Applied Biology
Vol.35, No.1, Ser.70, Spring 2022, P: 28 - 31
Journal homepage: https://jab.alzahra.ac.ir
10.22051/JAB.2021.34043.1392

Research Paper

The effect of four weeks of exercise and oleuropein supplementation on anxiety and depression behaviors in an animal model of Parkinson's disease

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Received: 2021.07.06 **Accepted: 2021.10.26**

Introduction

Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's and the most common cause of dementia (Nagatsu, 2002). Movement disorders due to Parkinson's disease are related to damage to the dense structure of the substantia nigra, which is usually visible macroscopically (Mahmoudi et al., 2018). Studies show that the initial manifestations of Parkinson's disease occur outside the central nervous system, including sleep disorders, anxiety disorders, and depression (Savica et al., 2010).

Degradation of dopaminergic neurons in the negro-striatal region and decreased dopamine levels are associated with the development of mood behaviors (Happe et al., 2001).

Studies have shown the role of various neurotransmitters in the phenomenon of anxiety; But the GABAergic system and the GABA A receptor are among the most important systems responsible for anxiety (Bueno et al., 2005). Oxidative stress is also a major cause of dopaminergic neuronal degeneration in Parkinson's disease, which is associated with anxiety-like behaviors (Dissanayaka et al., 2010; Dexter-David & Jenner, 2013).

Numerous studies have reported that consumption of plant-based foods or polyphenol-rich supplements may delay the onset and progression of diseases such as Alzheimer's, Parkinson's, and related neurological disorders (Vauzour et al., 2010). Among natural antioxidants, oleuropein is one of the most abundant polyphenols in olive leaves (Lockyer et al., 2015).

Oleuropein is the main bioactive compound in the leaves and unprocessed fruit of olives that has beneficial pharmacological effects including antioxidant, anti-inflammatory, and neuroprotective properties (Omar, 2010). Evidence suggests that exercise activates the brain's dopaminergic system and increases dopamine in the striatum. These findings increase the likelihood that exercise reduces the vulnerability of dopaminergic neurons to 6-hydroxy dopamine (Yoon et al., 2007). Due to the relatively high prevalence of anxiety and depression in Iran and the side effects of the drugs used in these patients, it is necessary to achieve many less complicated and more effective treatments. Therefore, the aim of this study was to evaluate the effect of four weeks of exercise and oleuropein supplementation on anxiety and depression behaviors induced by 6-hydroxy dopamine in adult male rats.

Materials and Methods

The aim of this study was to investigate the effect of oleuropein and exercise on anxiety and depression in animal models of Parkinson's disease. In this experimental study, 40 rats were divided into five groups: control, Parkinson's (6-hydroxy dopamine to the striatum area unilaterally), swimming practice (five sessions per week and 30 minutes each session) (Jafari et al., 2020), oleuropein recipient for 4 weeks (20 mg per kilogram of body weight per day) (Pourkhodadad et al.,2016) and combined with swimming practice and oleuropein. To create the Parkinson's model, the animals were first weighed, then anesthetized by intraperitoneal injection of ketamine hydrochloride (90 mg / kg body weight) and xylazine (10 mg / kg body weight) (Jafari et al., 2020). The rats were then placed in a stereotaxic device. Then, according to the coordinates extracted from the brain surgery atlas, the MFB coordinates (anterior-posterior = 4.6, lateral medial = 1.6 and

dorsal = 8.2 mm) were determined (Jafari et al., 2020). To assess anxiety, the elevated plus-maze test was performed and to assess depression, the open field test was performed (Rafieirad & Abbaszadeh, 2017). One-way ANOVA and Tukey's post hoc test were used to determine the differences between the groups.

Results and Discussion

The results showed that the use of oleuropein with exercise significantly increased the duration of Parkinson's model animal presence in the open arms of elevated plus-maze (P <0.05) and the number of border crossings in the open field test in the Parkinson's group. Consumption of oleuropein (P <0.01), Parkinson-swimming exercise (P <0.01), Parkinson-swimming exercise combined with consumption of oleuropein (P <0.05) significantly increased compared to the Parkinson group. In addition, the use of oleuropein with exercise in open field box testing significantly increases the number of animals crossing the central square and significantly reduces the number of crossings of marginal squares and the number of hands raised (P<0.05). On the other hand, the number of crosses of the central square in the open field test in the Parkinson-Oleuropein consumption group (P <0.05), Parkinson-swimming exercise (P <0.05), Parkinson-swimming exercise with oleuropein consumption (P <0.05) were significantly increased compared to Parkinson's group. The results showed that the number of excretions in the groups of oleuropein-Parkinson extract, swimming-Parkinson exercise and exercise with oleuropein-Parkinson's consumption had a significant decrease compared to the Parkinson group (P <0.001). Moreover, the number of hand raisings in the groups of oleuropein-Parkinson extract (P <0.001) and exercise with oleuropein-Parkinson's consumption (P <0.001) and swimming-Parkinson exercise group (P <0.05) were statistically significant compared to the Parkinson group and indicates a decrease in anxiety. The results showed that in the plus maze test for adult rats, in the oleuropein-Parkinson extract groups, exercise with oleuropein-Parkinson's consumption (P <0.05) and the swimming-Parkinson exercise group (P <0.001) compared to the Parkinson's group. There is a statistically significant difference and there is an increase in the percentage of visits to the open arm. The results of this study showed that Parkinson's group was significantly different from the control group in terms of mean anxiety. There is also a significant difference and reduction in anxiety in the group that took oleuropein compared to the Parkinson's group. The group that received exercise training showed a significant difference and decreased anxiety compared to the Parkinson's group, and the

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group that received both oleuropein and exercise showed a significant difference and decreased anxiety compared to the Parkinson's group. In this regard, Tadaiesky et al. Reported that the lesion caused by 6-hydroxy dopamine in the rat striatum increases anxiety responses in the maze behavioral test in addition to the elevated form (Tadaiesky et al., 2008). Polyphenols in plant extracts have many antioxidant and anti-oxidative properties (Vauzour et al., 2010). Shrivastava et al. Suggested that piperine has a protective effect on 6-OHDA-induced Parkinson's disease due to its antioxidant properties through its anti-apoptotic mechanism (Shrivastava et al., 2013). Prolonged exercise, on the other hand, increases the levels of endogenous antioxidants that can protect the brain from oxidative damage. On the other hand, it has been found that exercise in humans can improve anxiety and depression behaviors (Anderson & Shivakumar, 2013). Exercise in rats and mice also reduces anxiety in open-environment testing, maze plus elevation, and dark-light boxing (Pietrelli et al., 2012). Short-term exercise, including resistance exercise, can also improve the signs and symptoms of anxiety (Herring et al., 2011). Previous studies have shown that exercise can reduce anxiety in athletes (Heidarya et al., 2011). In terms of mechanism of action, exercise has been shown to release endorphins from the brain and endorphins play an effective role in reducing anxiety (Torabi et al., 2014). Exercise can also alter several hormonal and neurotransmitter systems in the body, including changes in GABA, serotonin, and atrial natriuretic levels, each of which can alter anxiety levels following exercise (Strohle, 2009).

Conclusion

The results of this study showed that exercise combined with oleuropein consumption can improve anxiety and depression behaviors in Parkinson's rats with its antioxidant effect.

Keywords: *anxiety, depression, exercise, oleuropein, Parkinson's.*

Acknowledgements

The authors would like to thank the Research Deputy of Ahvaz branch, Islamic Azad University for its support to carry out this study.

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Declaration of conflict of interest

The authors declare that they have no conflicts of interest.