A Study of the Effects of Pistaciavera (Pistachio) Seed Oil on Working Memory as Well as Spatial Learning and Memory

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Abstract

Introduction: Pistaciavera (pistachio) seeds are well-known medicinal herbs with several important pharmacological properties, including antioxidant and anti-inflammatory effects. The effects of pistachio oil (PO) have not yet been studied on the cognition performance. The current study was designed to investigate the nootropic effects of PO on male Wistar rats.

Materials and Methods: A total of 21 male Wistar rats were randomly divided into three experimental groups. Group1 was kept under normal conditions. Groups 2 and 3 were orally treated with PO, 1 and 4 mL/kg, respectively, for 21 days. Next, cognition was evaluated using the Morris water maze (MWM) and the Y-maze continuous alternation task (Y-CAT).

Results: The results showed that PO improved the working memory in Y-CAT, but it failed to exert positive effects on the spatial learning and memory in MWM.

Conclusion: The findings of the current study suggest that PO enhances the working memory and remedies memory impairments and cognitive deficits.

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1. Introduction

Learning and memory are the most important functions of the human brain. Due to the increase in human lifespan and neurodegenerative diseases, memory and cognitive impairments, e.g. dementia, turn into major public health problems [1]. A large body of evidence has demonstrated that working memory abilities decline across the lifespan, especially after the age of 70 [2]. Such a decline in the mentioned abilities reduces the quality of life and increases the disability rate in the elderly. Every natural and synthetic material that enhances brain functions suggests some clinical indications [3].

Besides, several reports have demonstrated that some medicinal plants, such as *Erythrinafalcata*, *Ginkgo biloba*, and ginger have memory-enhancing properties [4, 5]. *Pistaciavera* (*P. vera*), a member of the Anacardiaceae family, is a plant distributed widely in Iran. *P. vera* has a long history of local usage [6]. It sseeds (pistachios) are nuts rich in alkaloids and flavonoids, such as α-tocopherol, β-carotene, and lutein [7]. Past reports have demonstrated that P. vera possesses numerous pharmacological properties, including antioxidant [8], anti-nociceptive, and anti-inflammatory effects [9, 10].

Considering the literature review, the nootropic and memory-enhancing effects of *P. vera* have not yet been studied. The current study has been conducted aimed at investigating the effects of pistachio oil (PO) on the cognitive function. The Morris water maze (MWM) and the Y-maze continuous alternation task (Y-CAT) were performed to determine the effects of PO on learning and memory in normal rats.

2. Materials and Methods

2.1. Plant's material collection and oil extraction

In this study, pistachios from Akbari species obtained from the Rafsanjan region of Iran (with the genetic code of M30) were used. A pressure system (the cold extraction method) was used to extract oil [11].

2.2. Animals

Twenty one adult male Wistar rats (200-250 g) were obtained from the animal house of Rafsanjan University of Medical Sciences. The rats were housed under controlled temperature and light conditions (at 20–23◦C under a 12 h light/dark cycle) with standard rat chow diet and drinking water. The experiment was conducted in compliance with the recommendations of the Animal Care Committee of Rafsanjan University of Medical Sciences.

2.3. Experimental design

The rats were acclimatized for one week and then randomly assigned to three groups (normal, PO1, and PO4), with 7 animals existing in each group. The normal group served as healthy animals with no intervention applied to it. Group PO1 received PO (1 ml/kg) for 21 days, and group PO4 received PO (4 ml/kg) for 21 days [12].

After 24 hours from the last administration of PO, the rats were subjected to behavioral tests, with all experiments done at the same time of the day. The tests were done in the order of Y-maze (on the 22nd day of the experiment) and MWM (23rd-27th days of the experiment), respectively.

2.4. Y-CAT

Y-CAT was used to evaluate the working memory performance. Y-maze had three arms (40×4.5×12 cm, 120°). The floor and walls of the maze were made of opaque polyethylene plastic. The animals were initially put in an arm, and the time for each mouse entering the arms within 8 minutes was manually recorded. Consecutive entries into a new arm before returning into the two already visited arms were defined as the successful alternation. At the end of each test, the chamber was completely cleaned with ethanol (50%) to eliminate odor and stains. A higher percentage of alternations was used in the test [(number of alternations/total number of arm entries−2)× 100] as the index of the enhanced performance [13].

2.5. MWM

MWM has been utilized as the indicator of spatial learning and memory in rodents. It consists of a black circulation pool (120cm diameter and 40cm height) and a black platform (10cm diameter). To monitor the activities of the animals in the maze, a digital camera was used. Next, the data obtained were analyzed using the Ethovision software (version 7.1, Noldus Information Technology, Ethovision, Wageningen, the Netherlands). The MWM pool was divided into four equal quadrants, with different shapes of papers pasted on the room walls serving as the marker for the animals to find the hidden platform. The hidden platform was placed at the center of the target quadrant, 2 cm below the water.

The animals underwent 4 trials per day for 4 consecutive days (23^{rd}-27^{th} days of the experiment). In brief, the rats were put into the water at 4 points of different quadrants, and the escape latency was measured. The cut-off time for each test was 120 seconds. If the rats did not find the escape platform within 120 seconds, they would be directed to it by the examiner and stayed there for 15 seconds. Besides, 24 hours after the last trial, the probe test was done. In the probe test, the escape platform was removed, and the animals were put into the water at the selected points of the pool quadrants. The frequency of crossing through the escape platform, the time spent in the target quadrant, and the swimming speed of the animals in different experimental groups were recorded [14].

2.6. Statistical analysis

The statistical analysis was performed using the GraphPad Prism program (version 6.01, GraphPad Software, USA). The results were expressed as mean± SEM, and the differences among the groups were tested by Kruskal-Wallis followed by the Mann–Whitney U test. The differences among the groups would be considered statistically significant if p was less than 0.05.

3. Results

3.1. The effects of PO on working memory

The working memory was evaluated using the Y-CAT test (Fig. 1). The results demonstrated that the PO administration at the dose of 4 ml/kg increased the mean percentage of the alternations in the animals ($p<0.05$).

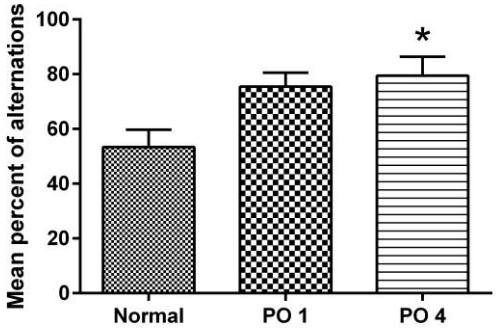

Fig. 1: The effect of PO treatment on working memory in different experimental groups. Each block represents the mean percent of alternations of different experimental groups in Y-maze continuous alternation task. Data are presented as mean± SEM; n= 7. *p<0.05 vs. normal group

3.2. The effects of PO on spatial learning and memory

Spatial learning and memory were evaluated using the MWM test (Fig. 2-4). The results demonstrated that the swimming times were similar among all experimental groups (Fig. 2).

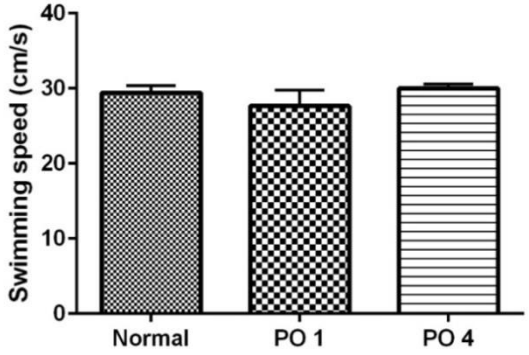

Fig. 2: The effect of PO treatment on locomotor function in different experimental groups. Each block represents the average of swimming speed of different experimental groups in day 5 of morris water maze test. Data are presented as mean± SEM; n= 7

As shown in fig. 3, during the learning phase, the rats in different experimental groups learned how to find the escape platform (escape latency decreased after the subsequent days of training). In addition, the results showed that PO administrations (1 ml/kg and 4 ml/kg) did not influence escape latency, as against the normal group, on the same day. As demonstrated in fig. 4, during the memory retrieval phase, the animals in all experimental groups showed no significant difference in the number of times crossing the platform and the percentage of the time spent in the target quadrant.

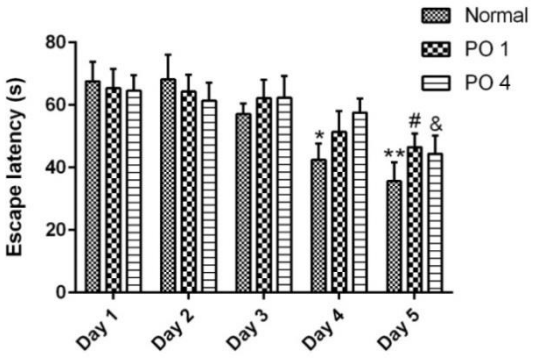

Fig. 3: The effect of PO treatment on spatial learning function in different experimental groups. Each block represents the average of escape latency in the morris water maze test for 5 consecutive trial days. Each value is the mean± SEM. n= 7. *p<0.05 and **p<0.01 vs. day 1 of normal group; #p<0.05 vs. day 1 of PO 1 group; & p<0.05 vs. day 1 of PO 4 group.

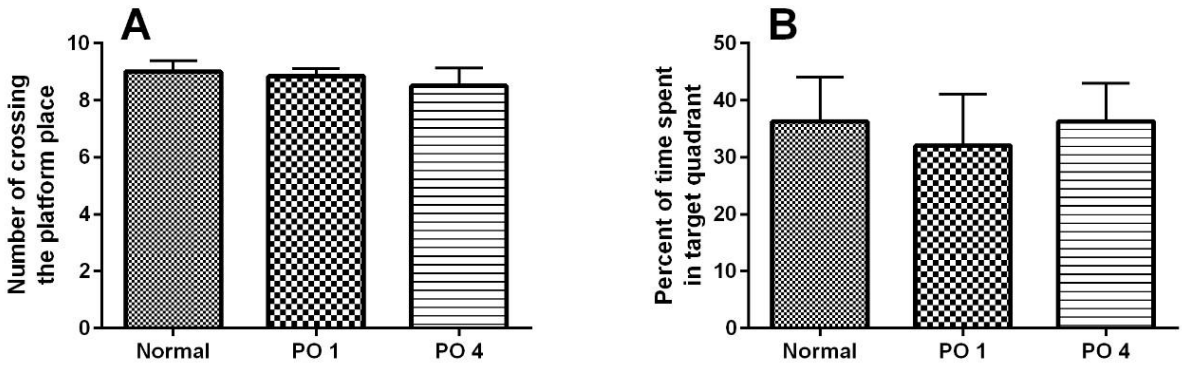

Fig. 4: The effect of PO treatment on spatial memory function. The number of crossing the platform place (A) and the percentage of time spent in the target quadrant (B) in the probe task in the morris water maze test. Data are presented as mean± SEM; n= 7

4. Discussion

The major finding of the current study is that PO administration improved the working memory in Y-CAT but failed to lead to any significant effect on the spatial cognition (learning and memory retrieval) in the MWM test.

Pistachios have various active constituents, including α-pinene, β-pinene, phytosterol, flavonoids, and α-Tocopherol [15-18].

These active constituents are responsible for various pharmacological properties of pistachios, such as neuroprotective, hepatoprotective, nephroprotective, and cardioprotective effects [19-22]. In a study, it was demonstrated that *Pistacialentiscus* oil (one of the species of *Pistacia*) improved memory dysfunction. Ammari et al., showed that *Pistacialentiscus* oil reduced LPS-induced memory impairments in rats. They found out that *Pistacialentiscus* oil improved the activities of superoxide dismutase (SOD) and catalase (CAT) in the brain tissue [23]. It is well established that pistachios have significant antioxidant properties due to the presence of anthocyanins, flavonoids, phytosterols, and luteolin in them [8]. In addition, pistachios are rich in campesterol, stigmasterol, and β-sitosterol, implying that pistachios have potent antioxidant effects [24]. In addition, clinical studies have demonstrated that the consumption of pistachios increases the blood levels of lutein, β-Carotene, and vitamin E [25]. Hence, the nootropic property of PO, at least partially, may be related to its antioxidant nature.

Studies have shown that herbs and their active ingredients demonstrate promising nootropicroperties.

Many researchers have recently focused on developing memory-improving agents of medicinal plants under normal conditions. It has been demonstrated that *Erythrinafalcata* enhances memory acquisition and the spontaneous recovery of fear [5]. Sahak et al., in another study, demonstrated that *Nigella sativa* improved learning and memory in healthy animals and humans [26]. In the same vein, Sirichoat et al. demonstrated that asiatic

acid, an active ingredient of *Centellaasiatica*, improved the spatial working memory in rats, by proliferating hippocampus cells [27]. Furthermore, *Zingiberofficinale* had been shown to enhance the cognitive function of mice in the novel object recognition test, by activating the signaling pathways of the nerve growth factor [4].

5. Conclusions

In conclusion, the current study results showed that PO administration exerted nootropic effects on the working memory but not on spatial learning and memory in rats. Therefore, pistachios could be a potential drug candidate for the improvement of cognitions in normal people. However, more studies are required to reveal the possible underlying mechanisms.

Conflict of interest

The authors declare no conflict of interest.

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