Studying the Effect of *Cyperus rotundus* Hydroalcoholic Extract on Memory Retrieval Disorder Caused by Acute Stress in Mice

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ABSTRACT

There are several reports that stress causes memory impairment. On the other hand, research has shown that *Cyperus Rotundus* (*C. rotundus*) extract improves memory and enhances information retrieval. In the current study, the possible ameliorating impacts of *C. rotundus* hydroalcoholic extract on stress-induced memory retrieval impairment were investigated. In this study, adult male laboratory mice were divided into two groups: stressed and non-stressed, and each of these groups was further divided into two subgroups: control groups receiving saline and those treated with *C. rotundus* extract. First, the mice received the substances by gavage for 21 or 7 days. One day after the last gavage, the animals were trained using a passive avoidance memory test device, and 24 hours after teaching, they were subjected to acute stress and immediately underwent a memory test. The latency to enter the dark room and the time spent in the darkroom of the device were recorded as a measure of passive avoidance memory retrieval. According to the findings obtained, pre-test stress significantly decreased the latency to enter the dark room and increased the time spent in the dark room. Pre-training gavage of the extract reversed the latency to enter and also significantly decreased the time spent in the dark room. It seems that the hydroalcoholic extract of *C. rotundus* improves the ability to retrieve information from long-term memory and reduces the destructive impact of acute stress on memory retrieval, depending on the time of consumption.

Key Words: *Hydroalcoholic extract, Cyperus rotundus, Memory, Acute stress*

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INTRODUCTION

Learning is a neuronal mechanism by which an individual changes his or her knowledge or behavior as a result of acquiring information or skills, while memory refers to the storage mechanism for what has been learned [1-3].

Neurobiological studies on memory in invertebrates and mammals have shown that synaptic changes in different areas of the brain play a major role in memory formation and synapses are the most important storage sites for information [4, 5]. Neuroimaging findings have shown that the amygdala, prefrontal cortex, and temporal lobe cooperate in memory formation. The amygdala is a memory modulator, the prefrontal cortex mediates memory encoding and formation, and the cerebellum is effective in successful learning and long-term memory retention [6, 7]. Information processing in memory and learning processes is the result of the interaction of neurotransmitter systems in different areas of the brain, especially the hippocampus and amygdala [8, 9].

Stress is one of the mental disorders that is known as the disease of the century due to its prevalence and spread in various forms among all ages [10]. Emotional memories are encoded, consolidated, and retrieved better than neutral memories, and stress, as a negative emotional state [3, 11], typically impairs memory retrieval by increasing cortisol, and these negative impacts of stress on information

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retrieval occur at the peak of cortisol (approximately 20 minutes after the stressor) [12, 13].

Cyperus rotundus (*C. rotundus*) is a medicinal plant with a wide variety of therapeutic uses that has been used since ancient times. The rhizomes of this plant are considered one of the best medicines in Ayurveda (ancient and ancient science) and its Ayurvedic name is Nagamotha [14]. This plant is used to treat stomach and intestinal disorders, inflammatory diseases, menstrual irregularities, cancer, aging, atherosclerosis, pain, cystitis (bladder inflammation), prostatitis (prostate inflammation), arthritis, malaria, seizures, obesity, diarrhea, diabetes mellitus, and allergies [15, 16].

Since stress is one of the undesirable characteristics of current societies and the use of medicinal plants has increased due to their safety and effectiveness in preventing and treating chronic diseases, and due to the effect of *C. rotundus* on memory in traditional medicine and the lack of reports of side effects, the current study was conducted to investigate the impacts of hydroalcoholic extract of *C. rotundus* rhizome on memory impairment caused by elevated platform.

MATERIALS AND METHODS

Laboratory animals

To carry out this research work, adult male mice weighing 25-30 grams were used. The mice were provided from the Laboratory Animal Breeding and Breeding Center of the Faculty of Veterinary Medicine and, after grouping, were kept in the animal house of the Biology Department under appropriate conditions with a temperature range of 23 ± 2 °C and a 12-hour light-dark cycle from 7 am to 7 pm. Except for the time of the experiment, they had sufficient water and food at all times.

Ingredients used

In this study, the rhizome of the *C. rotundus* plant identified by the Botany Department of the Faculty of this university, 96% ethanol, saline, and plate was used as food. *C. rotundus* extraction was performed by maceration method [17] and to increase the contact surface of the plant rhizomes with 70% ethanol (solvent), the rhizomes dried in the shade had to be powdered with an electric grinder. Finally, by dissolving the resulting extract in saline, different concentrations were prepared.

Passive avoidance memory measurement

Passive avoidance learning is a suitable method for examining the learning and memory process in laboratory animals. In this study, a step-through or shuttle box device was used to evaluate this type of memory in small laboratory mice (squirrels). This device is a Plexiglas box consisting of two light and dark sections that are connected by a guillotine door located at the bottom of the wall between the two sections. The stimulator device passes an electric current (shock agent) of 1 mA intensity for 3 seconds at a frequency of 50 Hz through a communication cable through steel rods embedded in the floor of the dark section.

When the mouse is placed in the light section, it immediately goes to the dark section based on its innate desire for darkness; however, if the animal has previously been shocked in this place, it avoids going into the dark section during the test phase, contrary to its innate desire; therefore, passive avoidance learning has been formed. This learning can be short-term or long-term and can be strengthened or weakened by drugs. In connection with this behavioral test, 3 specific stages were considered: the adaptation stage, the learning acquisition stage (training), and the retrieval stage (test). To measure long-term memory, the test stage was done 24 hours after the training stage.

Adaptation and training stages

In the adaptation stage, to familiarize the mouse with the device, we gently placed it into the light section of the device without causing stress to the mouse. After 10 seconds, the guillotine door was opened so that the animal could enter the dark section of the device based on its inherent desire. As soon as the animal entered the dark section of the device, the door was closed. Then the animal was removed from the dark section and returned to its cage. In this way, the animal was familiarized with the device. Mice whose entry delay time was more than 100 seconds were removed from the experimental group. After 30 minutes, the animal's training stage took place. This phase was similar to the adaptation phase, except that immediately after the animal entered the dark compartment, the valve was closed and an electric shock was given to the animal's hands and feet. 20 seconds after receiving the shock, the animal was removed from the apparatus and transferred to its cage. After 2 minutes, the animal was placed in the light compartment for the second time, and after 10 seconds, the valve was opened. If the animal did not enter the dark compartment after 100 seconds, its training was complete. In other words, successful learning was recorded for the animal. Then, the animal was immediately removed from the apparatus. Otherwise, the training and training assessment were performed two more times.

Stress induction phase

Twenty-four hours after training, to induce stress before the test, the rats were placed on an elevated platform and stressed for 15 or 20 minutes.

Memory test

Immediately after stress, to measure the ability to retrieve a memory, the animal was placed in a lighted house with its back to the guillotine door, the guillotine door was opened, and the delay time of the animal entering the dark section and the time spent in the darkroom were recorded as test data. The test completion time was set to 300 seconds. An increase in the animal's delay in entering the long-term memory test phase indicated memory enhancement.

Animal grouping

The animals were divided into the following groups: 7 days of gavage without stress, including saline recipients, *C. rotundus* 2.5, 5, and 10 mg/kg; 7 days of gavage with elevated platform stress, including saline recipients, *C. rotundus* 2.5, 5, 10, 20, and 50 mg/kg; 21 days of gavage without stress, including saline recipients, *C. rotundus* 1.25 and 2.5 mg/kg; 21 days of gavage with elevated platform stress, including saline recipients, *C. rotundus* 1.25 and 2.5 mg/kg. The number of mice in each group was 7.

Statistical analysis

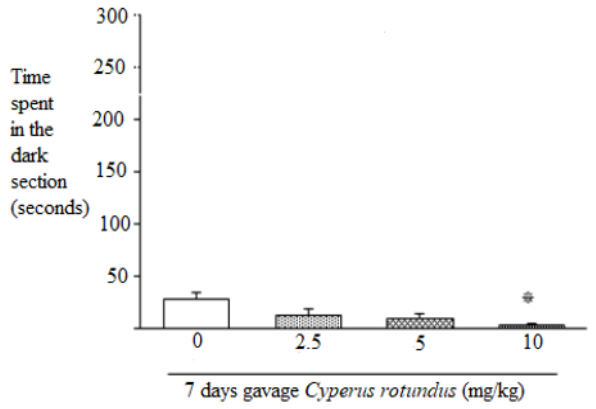
All results of the passive avoidance test and locomotor activity were described with the mean ± standard deviation from the mean, and one-way analysis of variance and Tukey's post hoc test were used. In all calculations, the significance level of the difference was considered to be $p < 0.05$. These tests were done in SPSS version 23 and Instant 3 software. The graphs were drawn using Excel software.

RESULTS AND DISCUSSION

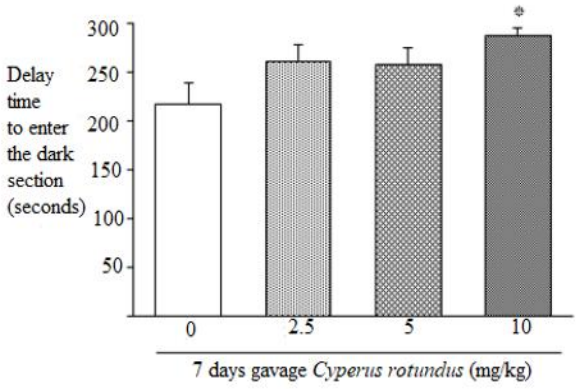
Study of the effect of 7 days of gavage of different concentrations of C. rotundus rhizome extract alone and combined with 15 minutes of stress before training on memory recall and motor activity

Figure 1 shows that in the 7-day gavage without stress group, only in the group receiving *C. rotundus* rhizome extract at a concentration of 10 mg/kg compared to the group receiving saline, an increase in the latency time to enter the dark section of the step-through apparatus ($P < 0.05$, $F_{3,24} = 3.383$) and a reduce in the time spent in it were observed ($P < 0.05$, $F_{3,24} = 4.321$) **(Figures 1a and 1b)**.

Figures 1c and 1d show that stress 15 minutes and 20 minutes before the test in the group that received saline by gavage for 7 days caused a decrease in the latency to enter the dark compartment of the step-through ($P < 0.001$, $P < 0.01$, and $F_{2,88} = 11.857$, respectively) and an increase in the time spent in this compartment ($P < 0.01$, $P < 0.05$, and $F_{2,88} = 0.796$, respectively) compared to the unstressed group. In the groups receiving 10, 20, and 50 mg/kg of the extract, compared to the saline group, an increase in the latency to enter the dark compartment of the shuttle box apparatus ($P < 0.001$, $P < 0.01$, $P < 0.05$, and $F_{5,26} = 4.109$, respectively) and a reduce in the time spent in it ($P < 0.001$, $P < 0.01$, $P < 0.05$, and $F_{5,36} = 5.265$, respectively) **(Figures 1c and 1d)**.



a)



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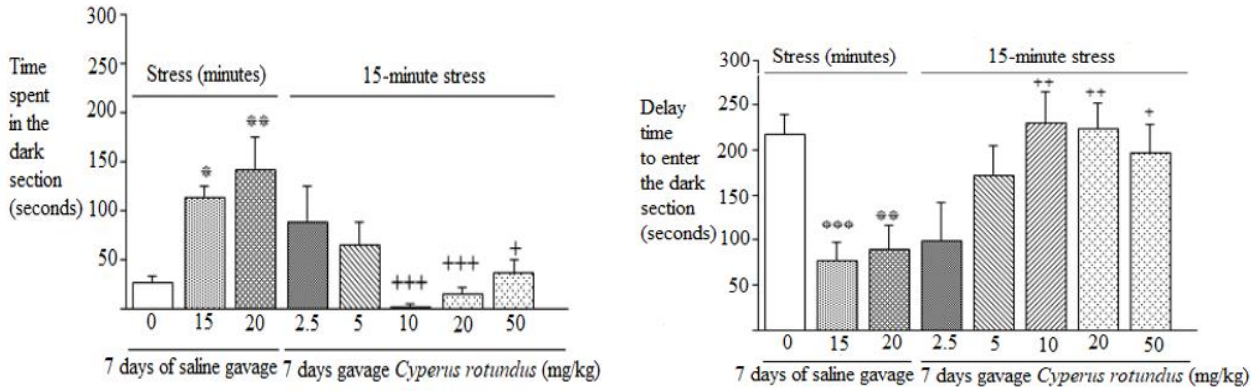

c) d)

Figure 1. The effect of seven days of gavage of different concentrations of hydroalcoholic extract of *C. rotundus* rhizome alone and in combination with stress on memory recall. * P < 0.05, ** P < 0.01, and *** P < 0.001 significant difference compared to the no-stress + saline group. + P < 0.05, ++ P < 0.01, and +++ P < 0.001 significant difference compared to the 15-minute stress + saline group. Columns indicate the mean ± standard deviation from the mean.

Table 1 shows that there was no significant difference in locomotor activity between the groups receiving different concentrations of *C. rotundus* rhizome extract for seven days alone ($P < 0.05$, $F_{3,24} = 1.183$) and combined with 15-minute stress ($P < 0.05$, $F_{5,35} = 0.4689$) as well as the 15- and 20-minute stress groups combined with 7-day saline gavage compared to the control group ($P < 0.05$, $F_{2,18} = 0.5430$).

Table 1. Motor activity in the open field test.

Groups			Mean + Standard Error of Mean (Number of times the animal crossed the lines)
7-day gavage	Saline (10 ml/kg)	No stress	38 ± 6.8
		15-minute stress	30.6 ± 0.8
		20-minute stress	33.1 ± 5.7
	C. rotundus (mg/kg)	5.2	32.6 ± 1.7
		5	35 ± 1.6
		10	37.1 ± 2.3
21-day gavage	Saline (10 ml/kg)	No stress	32 ± 2
		15-minute stress	36.9 ± 3
		20-minute stress	32.7 ± 1.5
	C. rotundus (mg/kg)	25.1	33 ± 1.7
		5.2	35.3 ± 3.3
***C. rotundus* gavage (mg/kg)**	7 days + 15 minutes stress	5.2	89.9 ± 35.7
		5	66 ± 22.1
		10	3.7 ± 2.2
		20	15.4 ± 7
		50	36.4 ± 14.9
	21 days + 20 minutes stress	25.1	34.1 ± 2.1
		5.2	32.9 ± 1.5

Study of the effect of 21 days of gavage of different concentrations of C. rotundus rhizome extract alone and with 20-minute stress before training on memory recall and motor activity

Figure 2 shows that although in the 21-day gavage without stress groups, none of the concentrations of hydroalcoholic extract of *C. rotundus* rhizome (1.25 and 2.5 mg/kg) alone could improve memory recall (latency time to enter the dark compartment ($P < 0.05$, $F_{2,18} = 1.883$) and time to stay in the dark compartment ($P < 0.05$, $F_{2,18} = 1.262$), **(Figures 1a and 1b)**.

Figures 2c and 2d show that in the groups that received saline by gavage for 21 days, 20 minutes of stress before the test significantly reduced the latency to enter the dark compartment of the shuttle box apparatus ($P < 0.001$, $F_{2,18} = 14.787$) and increased the time spent in this compartment ($P < 0.001$, $F_{2,18} = 16.797$); therefore, 20 minutes of stress before the test was considered to impair the memory of these groups.

In the 21-day gavage group with 20-minute stress, administration of *C. rotundus* rhizome extract at a concentration of 2.5 mg significantly increased the latency to enter the dark compartment ($P < 0.01$, $F_{2,18} = 49.228$) **(Figure 2c)** and reduced the time spent in this compartment ($P < 0.01$, $F_{2,18} = 22.752$) **(Figure 2d)**.

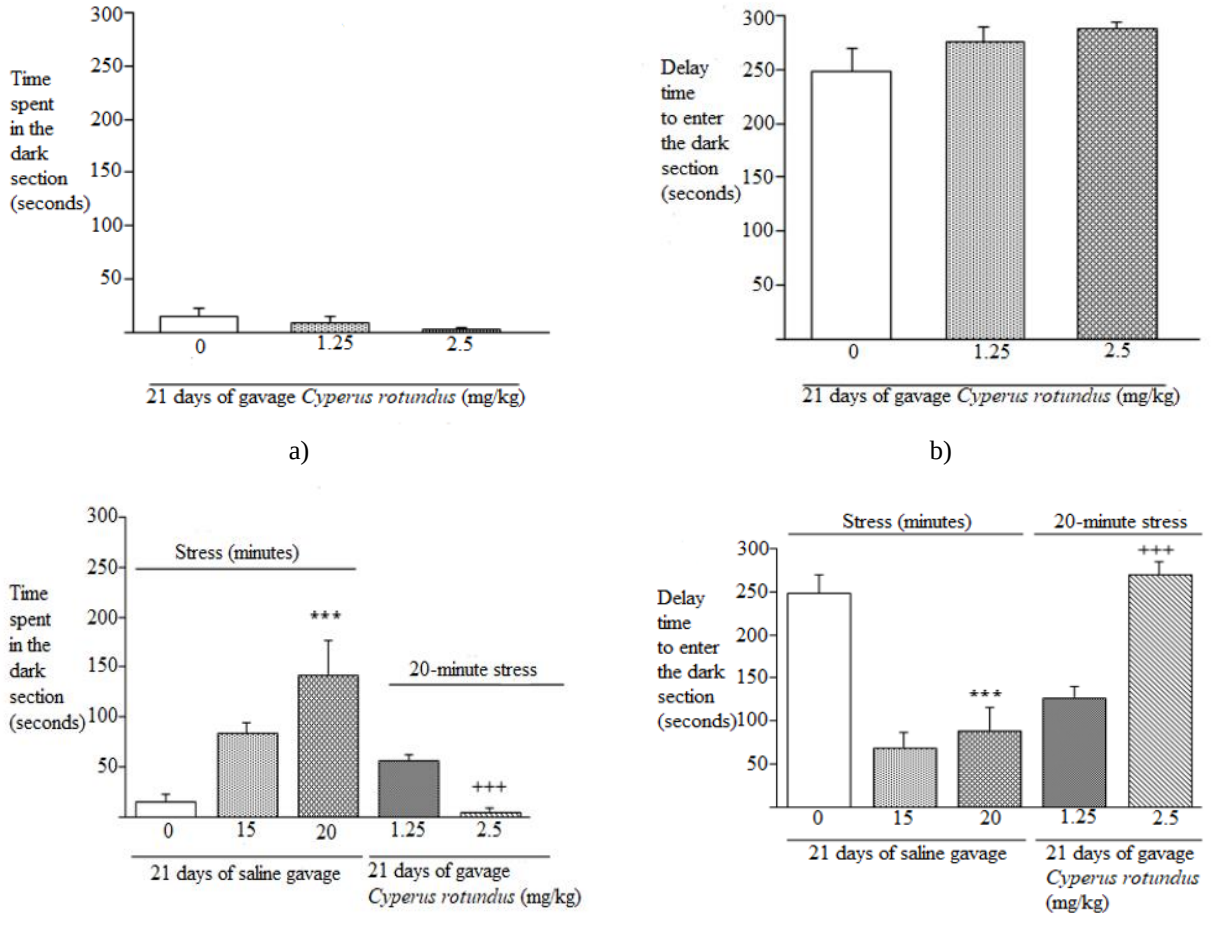

Figure 2. Effect of 21 days of gavage of different concentrations of hydroalcoholic extract of *C. rotundus* rhizome alone and in combination with stress on memory recall. *** $P < 0.001$ significant difference compared to the no-stress + saline group. +++ $P < 0.001$ significant difference compared to the 20-minute stress + saline group. Columns show mean ± standard deviation from the mean.

Table 1 shows that there was no significant difference in locomotor activity between groups receiving different concentrations of *C. rotundus* rhizome extract for 21 days alone ($P < 0.05$, $F_{2,18} = 0.3008$) and combined with 20-minute stress ($P < 0.05$, $F_{2,18} = 0.2090$), as well as the 15- and 20-minute stress groups combined with 21-day saline gavage, compared to the control group ($P < 0.05$, $F_{2,18} = 1.057$).

In this study, the effect of 7 days of continuous gavage of different amounts of hydroalcoholic extract of *C. rotundus* on memory and the improvement of impaired memory caused by 15-minute elevated platform stress was investigated. It was found that gavage of *C. rotundus*

rhizome extract before training in non-stressed and stressed groups was able to improve memory recall in non-stressed conditions and with acute stress before the test **(Figure 1)**. Next, the ineffective concentrations in the 7 days were examined over 21 days. The results showed that although these amounts did not show a significant effect on improving memory retrieval in non-stressed conditions, they significantly reduced the destructive effect of acute stress before the test on information retrieval **(Figure 2)**.

C. rotundus contains phytochemicals with various and diverse therapeutic properties [15]. In the Ayurvedic medical system, *C. rotundus* was used as a nootropic and nerve tonic [18]. *C. rotundus* rhizomes have nootropic effects [19]. The rhizomes of *C. rotundus* have medicinal properties and simple chemical analysis of the rhizomes has shown the presence of compounds that are active in the central nervous system [20, 21]. In traditional Indian medicine, the rhizomes of *C. rotundus* were recommended for increasing intelligence [22]. Therefore, the extract of this plant can be used as a memory and learning enhancer.

When an individual experiences acute stress, the autonomic system is activated, causing the release of adrenaline and symptoms such as increased heart rate, sweating, and blood pressure. In addition to stimulating the autonomic system, stress also activates the hypothalamic-pituitary-adrenal axis. This activation causes the release of glucocorticoids [23, 24]. On the one hand, the increase in these hormones causes oxidative damage to brain tissue, including the hippocampus, and on the other hand, oxidative stress occurs due to an imbalance between the formation and destruction of prooxidants and a decrease in protective mechanisms and cellular antioxidants, which may lead to increased cellular damage and apoptosis, resulting in memory loss [22]. Therefore, the prevalence of oxidative stress in the environment around neurons not only induces neuronal apoptosis, but it also seems that the cerebral hippocampus and cortex, which are interconnected to control cognitive and motor functions, are sensitive to oxidative stress and require antioxidants [25, 26].

Antioxidant compounds play an important role in maintaining health. Antioxidants such as ascorbic acid, phenolic acid, polyphenols, and flavonoids can prevent oxidative damage that leads to high-risk diseases by scavenging peroxide and hydroperoxide radicals [27, 28]. *C. rotundus* rhizome extract is rich in natural antioxidants that can be of great importance in the treatment of free radical-related diseases, including neurodegenerative diseases, and this plant can improve memory and learning [15, 27, 28]. Several phytochemical studies on *C. rotundus* root extracts have reported the presence of alkaloids, tannins, phenols, glycosides, steroids, polyphenols, sesquiterpenoids, flavonoids, b-sitosterol, cyprien, cyprol, and ascorbic acid [15], which alkaloids, terpenes, and flavonoids have antioxidant properties, and flavonoids can enhance the activity of antioxidant enzymes and increase antioxidants in the body [17]. Treatment with oligomeric flavonoids from the rhizome extract of *C. rotundus* has been shown to significantly reduce brain damage in ischemic rats by reducing malondialdehyde (the end product of lipid peroxidation) and increasing brain superoxide dismutase and glutathione [29]. Superoxide dismutase has been shown to play a key role in cellular defense against oxidative damage. The enzyme superoxide dismutase catalyzes the dismutation of O_2 to H_2O_2. H_2O_2 can be converted to O_2 and H_2O by the glutathione peroxidase and enzyme catalase.

The rhizome extract of *C. rotundus* affects and protects against the pathogenic pathways of oxido-nitrosative stress. This extract has anti-apoptotic effects; therefore, it can prevent nerve damage [15]. On the other hand, *C. rotundus* contains a potent acetylcholinesterase inhibitor. Cholinesterase inhibitors are the main drugs for the treatment of Alzheimer's. Preventing the breakdown of acetylcholine by inhibiting the enzyme cholinesterase can likely be of great importance in stabilizing memory and thinking power [30, 31].

It seems that *C. rotundus* can prevent stress-induced memory impairment due to its properties such as antioxidant effects, scavenging of free radicals in the nervous system, and interference in various neurotransmitter systems, especially cholinergic. It also seems that the use of smaller amounts of this extract over a longer period can have greater improvement effects. The notable point in the present study is that in addition to preventing the impairment in memory recall caused by stress, the hydroalcoholic extract of *C. rotundus* also significantly prevented the impairment in memory recall caused by a longer duration of stress by increasing the duration of gavage **(Figure 2)**.

Although in the acute toxicity assessment of *C. rotundus* ethanolic extract, no mortality was observed after oral administration of up to 2000 mg/kg for 5 hours after administration, and no signs of delayed toxicity or mortality were observed for 14 days [32]; however, considering that the use of high doses of medicinal plants can cause drug poisoning and subsequent problems [27, 33] and also that many plants require long-term use for therapeutic response, and this is due to their slow effect. Therefore, it seems that reducing the dose by increasing the duration of use can improve memory damaged by acute stress, and also prevent toxic effects.

CONCLUSION

In the current study, the possible ameliorating effects of *C. rotundus* hydroalcoholic extract on stress-induced memory retrieval impairment were investigated. According to the

results of this study, it appears that *C. rotundus* consumption increases the ability to retrieve information and reduces the destructive effect of stress on memory. Also, doses that are ineffective in the short term become effective if consumed over a long period.

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REFERENCES

[1] Vorhees CV, Williams MT. Tests for learning and memory in rodent regulatory studies. Curr Res Toxicol. 2024;6:100151. doi:10.1016/j.crtox.2024.100151

[2] Dalkiran B, Açıkgöz B, Dayı A. Behavioral tests used in the evaluation of learning and memory in experimental animals. JBACHS. 2022;6(3):938-45. doi:10.30621/jbachs.1017172

[3] Lang B, Kahnau P, Hohlbaum K, Mieske P, Andresen NP, Boon MN, et al. Challenges and advanced concepts for the assessment of learning and memory function in mice. Front Behav Neurosci. 2023;17:1230082. doi:10.3389/fnbeh.2023.1230082

[4] Abraham WC, Jones OD, Glanzman DL. Is plasticity of synapses the mechanism of long-term memory storage? NPJ Sci Learn. 2019;4:9.

[5] Sheynikhovich D, Otani S, Bai J, Arleo A. Long-term memory, synaptic plasticity and dopamine in rodent medial prefrontal cortex: Role in executive functions. Front Behav Neurosci. 2023;16:1068271. doi:10.3389/fnbeh.2022.1068271

[6] Tyng CM, Amin HU, Saad MNM, Malik AS. The influences of emotion on learning and memory. Front Psychol. 2017;8:235933.

[7] Yin Y, Shanks DR, Li B, Fan T, Hu X, Yang C, et al. The effects of emotion on judgments of learning and memory: A meta-analytic review. Metacognition Learning. 2023;18(2):425-47. doi:10.1007/s11409-023-09335-0

[8] Khajehpour L, Rezayof A, Zarrindast MR. Involvement of dorsal hippocampal nicotinic receptors in the effect of morphine on memory retrieval in passive avoidance task. Eur J Pharmacol. 2008;584(2-3):343-51.

[9] Zarrindast MR, Khakpai F. State-dependent memory and its modulation by different brain areas and neurotransmitters. EXCLI J. 2020;19:1081-99. doi:10.17179/excli2020-2612

[10] Tehranipour M, Pakjame R, Zafar Balanezhad S. The effect of hydroalcoholic extract of Perovskia abrotanoides on neuronal density of rats under chronic immobility stress. J Shahid Sadoughi Univ Med Sci. 2020;28:2781-93.

[11] Bailoo JD, Bergeson SE, Ponomarev I, Willms JO, Kisby BR, Cornwall GA, et al. A bespoke water T–maze apparatus and protocol: An optimized, reliable, and repeatable method for screening learning, memory, and executive functioning in laboratory mice. Front Behav Neurosci. 2024;18:1492327. doi:10.3389/fnbeh.2024.1492327

[12] Marr C, Sauerland M, Otgaar H, Quaedflieg CW, Hope L. Mitigating the negative effects of retrieval stress on memory: An arousal reappraisal intervention. Memory. 2021;29(3):330-44.

[13] Bosshard M, Gomez P. Effectiveness of stress arousal reappraisal and stress-is-enhancing mindset interventions on task performance outcomes: A meta-analysis of randomized controlled trials. Sci Rep. 2024;14(1):7923. doi:10.1038/s41598-024-58408-w

[14] Dang GK, Parekar RR, Kamat SK, Scindia AM, Rege NN. Antiinflammatory activity of Phyllanthus emblica, Plumbago zeylanica and Cyperus rotundus in acute models of inflammation. Phytother Res. 2011;25(6):904-8.

[15] Kamala A, Middha SK, Karigar CS. Plants in traditional medicine with special reference to Cyperus rotundus L.: A review. 3 Biotech. 2018;8:1-1.

[16] Kandikattu HK, Amruta N, Khanum F, Narayana VV, Srinivasulu D. A review on cyperus rotundus: Ancient weed to modern elixir of life phytochemistry and therapeutic uses of cyperus rotundus (Mustaka). Pharm Biomed Res. 2021;7(4):221-50. doi:10.18502/pbr.v7i4.9369

[17] Naseri MG, Heidari A. Antispasmodic effect of Anethum graveolens fruit extract on rat ileum. Int J Pharmacol. 2007;3(3):260-4.

[18] Entezari M, Sharifi ZN, Movassaghi S, Atabi F, Jamali Z, Salimi A. Neuroprotective effects of cyperus rotundus rhizome extract on ıschemic brain injury: Expression profile of Bax, Bcl2, Bad and Bclxl Genes. Drug Advanced Sci J. 2019;1(1):25-30.

[19] Shakerin Z, Esfandiari E, Ghanadian M, Razavi S, Alaei H, Dashti G. Therapeutic effects of cyperus rotundus rhizome extract on memory impairment, neurogenesis and mitochondria in beta-amyloid rat model of Alzheimer's disease. Metab Brain Dis. 2020;35:451-61.

[20] Xue BX, He RS, Lai JX, Mireku-Gyimah NA, Zhang LH, Wu HH. Phytochemistry, data mining, pharmacology, toxicology and the analytical methods of Cyperus rotundus L.(Cyperaceae): A comprehensive review. Phytochem Rev.

2023;22(5):1353-98. doi:10.1007/s11101-023-09870-3

[21] Mehdizadeh M, Hashem Dabaghian F, Shojaee A, Molavi N, Taslimi Z, Shabani R, et al. Short communication: Protective effects of cyperus rotundus extract on amyloid β-Peptide (1-40)-induced memory impairment in male rats: A behavioral study. Basic Clin Neurosci. 2017;8(3):249-54.

[22] Mohammadzadeh M, Babaeifar F, Babaei F. Combination thrapy of hydroalcoholic extract of Pistacia atlantica kurdica and fluvoxamine on spatial memory of immobilization rat. J Gorgan Univ Med Sci. 2017;19(3):24-31.

[23] Quaedflieg CWEM, Schwabe L. Memory dynamics under stress. Memory. 2018;26:364-76.

[24] Sadeghzadeh Z, Bagheri F. Comparison of behavioral activation/inhibition systems, emotional regulation difficulties, and selective attention in adolescents with and without parents. Front Psychol. 2023;14:1212187. doi:10.3389/fpsyg.2023.1212187

[25] Shields GS, Sazma MA, McCullough AM, Yonelinas AP. The effects of acute stress on episodic memory: A meta-analysis and integrative review. Psychol Bull. 2017;143:636-75.

[26] Marr C, Sauerland M, Otgaar H, Quaedflieg CW, Hope L. The effects of acute stress on eyewitness memory: An integrative review for eyewitness researchers. Memory. 2021;29(8):1091-100. doi:10.1080/09658211.2021.1955935

[27] Faridzadeh A, Salimi Y, Ghasemirad H, Kargar M, Rashtchian A, Mahmoudvand G, et al. Neuroprotective potential of aromatic herbs: rosemary, sage, and lavender. Front Neurosci. 2022;16:909833. doi:10.3389/fnins.2022.909833

[28] Shahmohamadi S, Hajizadeh Moghaddam A, Khosravi M. Effect of hydroalcoholic extract of Salvia officinalis L. on the activity of catalase and superoxide dismutase in an oxidative stress model created by intracerebroventricular STZ injection in male rats. Physiol Pharmacol. 2013;17(2):176-84.

[29] Sunil AG, Kesavanarayanan KS, Kalaivani P, Sathiya S, Ranju V, Priya RJ, et al. Total oligomeric flavonoids of Cyperus rotundus ameliorates neurological deficits, excitotoxicity and behavioral alterations induced by cerebral ischemic-reperfusion injury in rats. Brain Res Bull. 2011;84(6):394-405.

[30] Sharma R, Gupta R. Cyperus rotundus extract inhibits acetylcholinesterase activity from animal and plants as well as inhibits germination and seedling growth in wheat and tomato. Life Sci. 2007;80(24-25):2389-92.

[31] Babiaka SB, Ekayen DE, Njimoh DL, Abuga KO. Bioactive compounds and biological activities of cyperus rotundus L.(Cyperaceae). In: Murthy HN, Paek KY, Park SY, eds. Bioactive compounds in the storage organs of plants. Reference series in phytochemistry. Cham: Springer. doi:10.1007/978-3-031-44746-4_36

[32] Sheik HS, Vedhaiyan N, Singaravel S. Evaluation of central nervous system activities of Citrus maxima leaf extract on rodents. J Appl Pharm Sci. 2014;4:77-82.

[33] Ekor M. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. Front Pharmacol. 2014;4:177.