IJP (2016), Vol. 3, Issue 3 **(Research Article)**

Received on 30 January 2016; received in revised form, 27 February 2016; accepted, 26 March 2016; published 31 March 2016

ORAL ADMINISTRATION OF AN ALCOHOLIC EXTRACT OF *CARDARIA DRABA* PREVENTED SCOPOLAMINE-, ZINC CHLORIDE - AND SODIUM METAVANADATE – INDUCED AVOIDANCE MEMORY RETENTION IMPAIRMENTS IN STEP-THROUGH PASSIVE AVOIDANCE TASK IN MICE

A. Akbari [*1], K. Tabrizian [1], A. Miri [2] and M. Shafiei [3]

Department of Pharmacology and Toxicology, Faculty of Pharmacy [1], Medicinal Plants Research Center [2], Department of Pharmaceutical Sciences, School of Pharmacy [3], Zabol University of Medical Sciences, Zabol, Iran.

Keywords:

Cardaria draba, Zinc chloride, Sodium metavanadate, Scopolamine, Step-through, Avoidance memory

Correspondence to Author:
Atefeh Akbari

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Zabol University of Medical Sciences, Zabol, Iran.

E-mail: ati.akbari68@gmail.com

ABSTRACT: *Cardaria draba* commonly known as whitetop or hoary cress is a perennial herb that is native to Eastern Europe and eastern Asia, including Iran. In this study, the effects of alcoholic extract of *Cardaria draba* (25, 50 and 100 mg/kg) *via* oral gavage for 2 weeks alone and on scopolamine (1 mg /kg/d, 4 days, i.p.) - zinc chloride (75 mg/kg/d, 2 weeks oral gavage) - and sodium metavanadate (22.5 mg/kg/d, 2 weeks oral gavage) - induced avoidance memory retention alterations were investigated in the step-through passive avoidance task. Zinc chloride and scopolamine were dissolved in saline and sodium metavanadate were dissolved in animal's drinking water. At the end of each part of studies, animals were trained for one day in a step-through task. The avoidance memory retention alterations were evaluated 24 h, 48 h, 96 h and 168 h later to the training session. Zinc chloride and sodium metavanadate oral gavage for 2 weeks decreased latencies compared to control animals. Also, four days intra-peritoneal injection of scopolamine decreased latency compared to control animals. Finally, findings of this research showed that 2 weeks oral gavage of alcoholic extract of *Cardaria draba* (100 mg/kg) prevented scopolamine-, zinc chloride- and sodium metavanadate- induced avoidance memory retention impairments.

INTRODUCTION: *Cardaria draba* (Hoary cress, Lepidium draba or whitetop), is a perennial herb in the mustard family that can grow up to 2 ft. (0.6 m) tall. The leaves are soft, gray-green, 1.5-3 in. (3.7-7.6 cm) long with fine hairs and heart-shaped bases[1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.IJP.3(3).131-39

Article can be accessed online on: www.ijpjournal.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.3(3).131-39

Hoary cress is native to Central Europe and Western Asia including Iran and was first introduced into the United States in the early 20th century. Expectorant, laxative, anti-inflammatory, diuretic, antiscorbutic, and appetitive effects of *Cardaria draba* were described in previous studies [2-5].

The pathophysiology of Alzheimer's disease (AD) is complex and involves several different biochemical pathways such as cholinergic system dysfunctions in the basal forebrain and hippocampus [6, 7]. It is known that acetylcholine (ACh) is an important neurotransmitter related to

memory and learning processes. Excessive acetylcholine esterase (AChE) activity leads to constant ACh deficiency, memory and cognitive impairments [8].

It has been demonstrated that there is a specific deficiency in Ach, choline acetyltransferase, and an increase in AchE in autopsy material from patients with Alzheimer's disease [9]. Muscarinic cholinergic receptor antagonists are known to induce impairments in learning and memory. Scopolamine and atropine, competitive muscarinic receptor antagonists, have been shown to impair the learning and memory of rodents in a variety of behavioral tasks, such as the passive avoidance response test and water maze test [10, 11].

Zinc is the most abundant and the most soluble of the transition metals in natural systems. Zinc is an essential micronutrient involved in numerous physiological functions. Zinc deficiency has been shown to impair cognitive functioning, but little work has been done on the effects of elevated zinc. There are reports about the memory impairments, apoptosis, and cytotoxicity induced by an excess level of zinc consumption. Therefore, its balanced concentration is required for normal behavior, CNS development and preventing of neurological disorders such as Alzheimer's disease [12-15]. Vanadium (V), a metalloid which is widely distributed in the environment, has been shown to exert toxic effects on a variety of biological systems including the nervous system [16].

This experimental study was designed to evaluate the effects of oral administration of an alcoholic extract of *Cardaria draba* on avoidance memory retention alterations induced by scopolamine, zinc chloride, and sodium metavanadate in step-through passive avoidance learning the task in male mice.

MATERIALS AND METHODS:

Animals: In this experimental study, all animal manipulations were carried out according to the guidelines of the declaration of Helsinki. Mice (20-25 g) from the Faculty of Pharmacy, Zabol University of Medical Sciences were used in this study. All animals were maintained under controlled conditions (12-h light/12-h dark cycle) at room temperature (20-22^{o}C). They were housed in groups of five per each cage, having free access to food and water. All animal experiments were done during the light cycle.

Preparation of Alcoholic Extract of *Cardaria draba*: *Cardaria draba* in Zabol medicinal plants Research Center was collected in February 2013, chopped, dried in the open air and stored in 4-8 ^{o}C in dark well-closed container**.** The extraction was done by maceration method in ethanol 80% at room temperature. After filtration, the ethanol was evaporated to dryness under vacuum.

Drugs: Zinc chloride ($ZnCl_2$) was purchased from Merck Company (Germany) and dissolved in saline. Scopolamine and sodium metavanadate were purchased from Sigma (USA) and dissolved in saline and drinking water, respectively.

Step-Through Passive Avoidance Task: The details of the passive avoidance apparatus were described in previous studies [17]. In this study, each animal was gently placed in the light chamber, the door was opened after 10 sec and the time that animal waited before crossing to the dark chamber was recorded as the latency (300 s was determined as a cut-off point of study). Electric shocks (0.2 mA intensity for 2 s), were delivered to the grid floor of the dark compartment. All training and testing trials were carried out at a similar time each day. During the retention test sessions, no electric shock was applied.

Experiments:

Experiment 1:

Part A: Alcoholic extract solution of *Cardaria draba* was prepared daily. Different concentrations of C*ardaria draba* (25, 50 and 100 mg/kg) were administered via oral gavage needles once a day for two weeks. On day 14th, one training trial was done in step-through avoidance inhibitory learning task. Avoidance memory retentions were evaluated 24 h, 48 h, 96 h and 168 h later to training trials. Control animals received a vehicle of *Cardaria draba* via oral gavage needles for the same period.

Part B: This experiment aimed to assess the effects of 4 days intra-peritoneal injections of scopolamine (1 mg/kg) on avoidance memory retention. On the final day of this part of the study (after the last injection), one training trial was done. Avoidance memory retentions were tested 24 h, 48 h, 96 h, and

168 h later to training trials. Control animals received saline.

Part C and Part D: Fresh solutions of zinc chloride and sodium metavanadate (SMV) in normal saline and animal's drinking water respectively were prepared daily. Zinc chloride (75 mg/kg) and SMV (22.5 mg/kg) were administered *via* oral gavage needles once a day for two weeks. On day 14th, one training trial was done in step-through avoidance inhibitory learning task. Avoidance memory retentions were evaluated 24 h, 48 h, 96 h and 168 h later to training trials. Control animals received saline and drinking water respectively *via* oral gavage needles for the same period.

Experiment 2: The aim of this experiment was to assess the effects of *Cardaria draba* (100 mg/kg, orally for 2 weeks) on scopolamine - (1 mg/kg, i.p. for 4 days), $ZnCl_2$- (75 mg/kg, oral gavage for 2 weeks) and SMV- (22.5 mg/kg, oral gavage for 2 weeks) induced avoidance memory retention alterations in step-through passive avoidance task. The 4-days intra-peritoneal injections of scopolamine were started on day 11th of *Cardaria draba* oral administration. On the final day of each study (after the last treatments), one training trial was done. Avoidance memory retentions were tested 24 h, 48 h, 96 h, and 168 h later to training trials.

Statistical Analysis: One-way analysis of variance (ANOVA) and unpaired t-test were used to compare the findings of this study. A Newman–Keuls multiple comparison posts–hoc test was carried out to analyze differences between groups. A P-value of 0.05 or less was considered statistically significant.

RESULTS:

Effects of C*ardaria draba* Alcoholic Extract on Passive Avoidance Memory Retention in Step-Through Task: Pre-training oral administration of *Cardaria draba* alcoholic extract (100 mg/kg) for 14 consecutive days caused a significant increase **Fig. 1A-D** in step-through latency during the retention tests (**p<0.01 for 24 h and 48 h and *p<0.05 for 96 h and 168 h) compared to control animals.

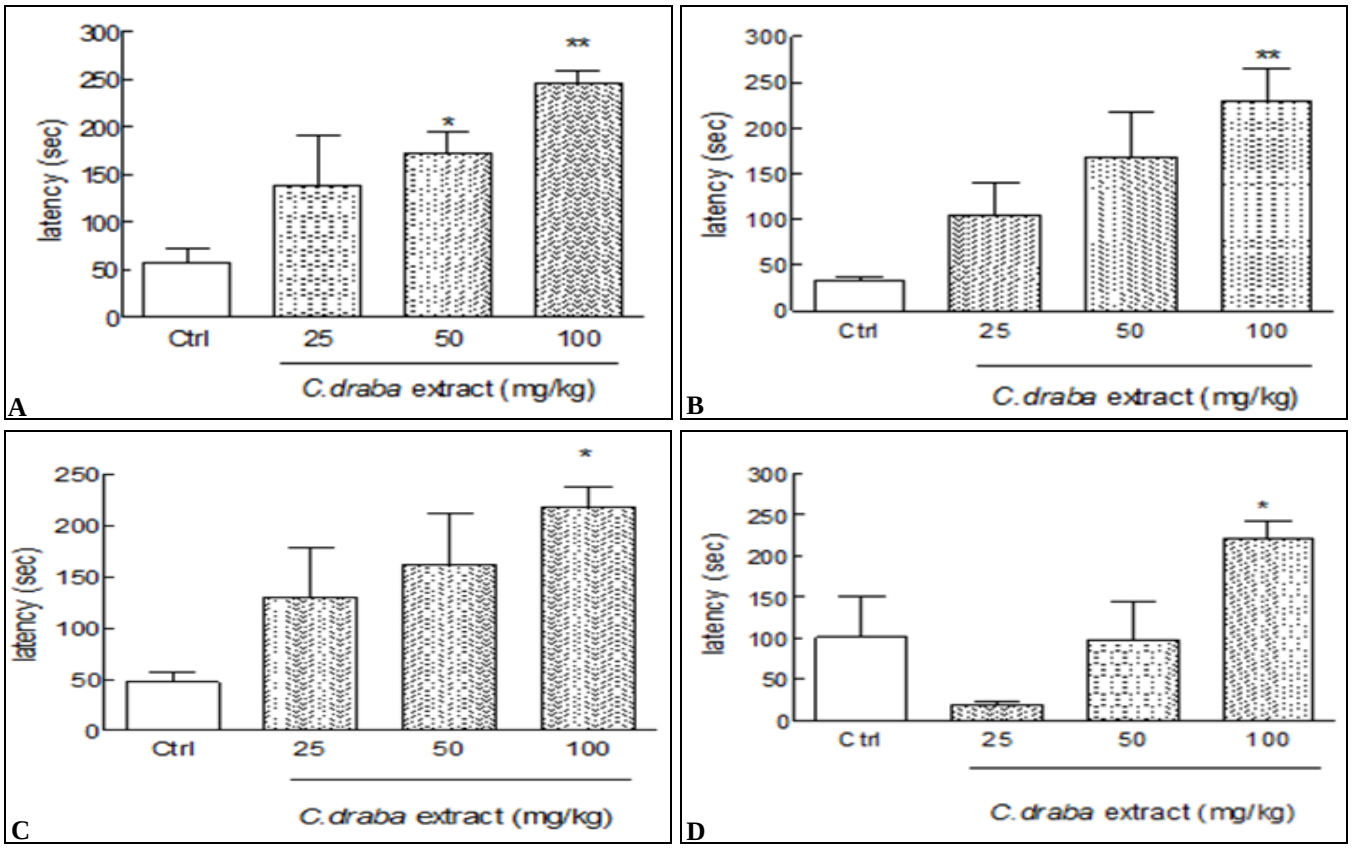

FIG. 1A – D: EFFECTS OF ALCOHOLIC EXTRACT OF *CARDARIA DRABA* ON AVOIDANCE MEMORY RETENTION IN STEP-THROUGH PASSIVE AVOIDANCE TASK. Each value represents the Mean ± S.E.M. of 7 Mice. *p<0.05 and **p<0.01 significantly different from the control group.

Cardaria draba alcoholic extract (50 mg/kg) caused significant retention improvements (*p<0.05) only at 24 h compared to the control group **Fig. 1A**. Thus, the greatest avoidance memory retention improvement was obtained with 100 mg/kg of *Cardaria draba* alcoholic extract.

Effects of Scopolamine on Passive Avoidance Memory Retention in Step-Through Task: Four days intra-peritoneal injection of scopolamine (**Table 1**: 1 mg/kg) caused a significant decrease in step-through latency during the retention tests after 24 h (****p<0.0001), 48h (**p<0.01), 96 h (*p<0.05) and 168 h (**p<0.01) compared to control (saline-treated) animals **Table 1**. Effects of zinc chloride and sodium metavanadate (SMV) oral administration on passive avoidance memory retention in step-through task: Pre-training oral administration of zinc chloride (75 mg/kg) for 14 consecutive days caused a significant decrease in step-through latency during the retention tests **Table 2**, ****p<0.001 for all designed retention tests) compared to control animals. Also, pre-training oral administration of SMV in animals drinking water impaired avoidance memory retention **Table 3** after 24 h (****p<0.0001), 48 h (***p<0.001), 96 h (***p<0.001) and 168 h (***p<0.001) significantly compared to their related control group.

TABLE 1: EFFECTS OF SCOPOLAMINE ON AVOIDANCE MEMORY RETENTION IN STEP-THROUGH PASSIVE AVOIDANCE TASK

Time Treatment	24h	48h	96h	168h
Ctrl	246.6±26.61	228.1±33.5	212.4±48.48	181.6±35.39
Scopolamine	47.04±11.26****	87.75±31.61 **	56.89±28.11*	38.59±9.094**

Each value represents the mean ± S.E.M. of 7 mice. *p<0.05, **p<0.01 and ****p<0.0001 significantly different from control (saline) group.

TABLE 2: EFFECTS OF ZINC CHLORIDE ON AVOIDANCE MEMORY RETENTION IN STEP-THROUGH PASSIVE AVOIDANCE TASK

Time Treatment	24h	48h	96h	168h
Ctrl	299.4±0.6250	270.0±30.03	257.7±42.28	272.8±27.23
Scopolamine	21.12±3.436****	29.93±10.13****	11.60±3.605****	20.62±6.893****

Each value represents the mean ± S.E.M. of 7 mice. ****p<0.0001 significantly different from the control (saline) group.

TABLE 3: EFFECTS OF SODIUM METAVANADATE ON AVOIDANCE MEMORY RETENTION IN STEP-THROUGH PASSIVE AVOIDANCE TASK

Time Treatment	24h	48h	96h	168h
Ctrl	296.3±1.886	257.2±41.16	258.1±41.89	255.9±41.03
Scopolamine	37.67±9.669****	31.76±10.74***	37.57±13.89***	50.51±23.20***

Each value represents the mean ± S.E.M. of 7 mice. ***p<0.001 and ****p<0.0001 significantly different from control group.

Effects of *Cardaria draba* Alcoholic Extract (100 mg/kg) on Scopolamine-Induced Avoidance Memory Retention Deficits in Step-Through Task: 14 days oral administration of an alcoholic extract of C*ardaria draba* prevented scopolamine- (1 mg/kg, i.p. for 4 days) induced avoidance memory retention impairments, significantly in step-through passive avoidance task (##p<0.01 for 96 h and ####p<0.0001 for 168 h) compared to scopolamine – treated animals **Fig. 2C** and **D**.

Effects of *Cardaria draba* Alcoholic Extract (100 mg/kg) on Zinc Chloride – Induced Avoidance Memory Retention Impairment in Step-Through Task: 14 days oral administration of an alcoholic extract of *Cardaria draba* prevented zinc chloride- (75 mg/kg, oral gavage for 14 days) induced avoidance memory retention impairments, significantly in step-through passive avoidance task (##p<0.01 for 168 h) compared to zinc chloride – treated animals **Fig. 3 D**.

Effects of *Cardaria draba* Alcoholic Extract (100 mg/kg) on SMV – Induced Avoidance Memory Retention Impairment in Step-Through Task: 14 days oral administration of an alcoholic extract of *Cardaria draba* prevented SMV- (22.5 mg/kg, oral gavage for 14 days) induced avoidance memory retention impairments, significantly in step-through passive avoidance task (#p<0.05 for 48 h and ##p<0.01 for 96 h and 168 h) compared to SMV– treated animals (**Fig. 4B – D**, respectively).

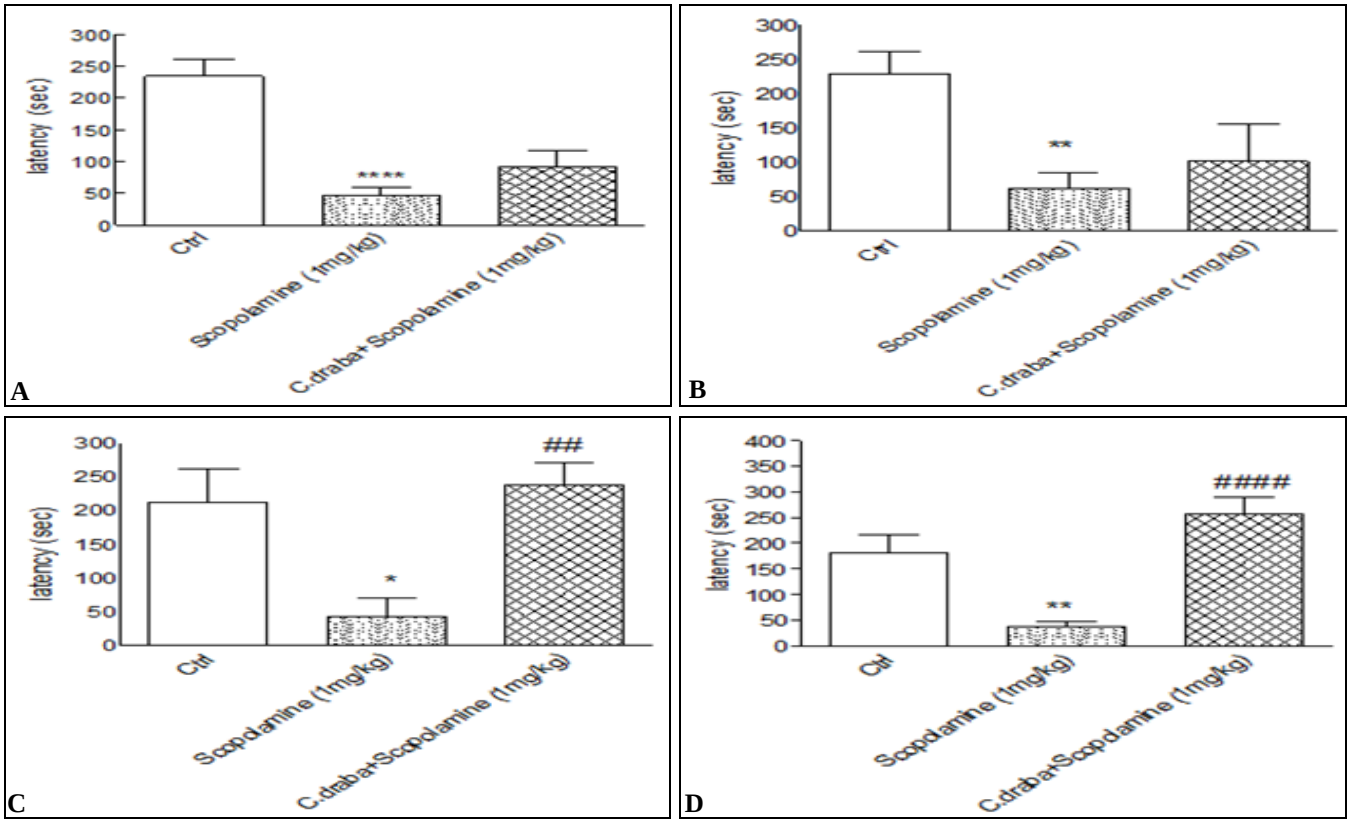

FIG. 2A – D: EFFECTS OF ALCOHOLIC EXTRACT OF *CARDARIA DRABA* (100 mg/kg, ORAL GAVAGE FOR 2 WEEKS) ON SCOPOLAMINE - INDUCED AVOIDANCE MEMORY RETENTION IMPAIRMENTS IN STEP-THROUGH PASSIVE AVOIDANCE TASK. EACH VALUE REPRESENTS The mean ± S.E.M. of 7 mice. *p<0.05, **p<0.01 and ****p<0.0001 significantly different from control group. ##p<0.01 and ###p<0.001 significantly different from scopolamine - treated group**.**

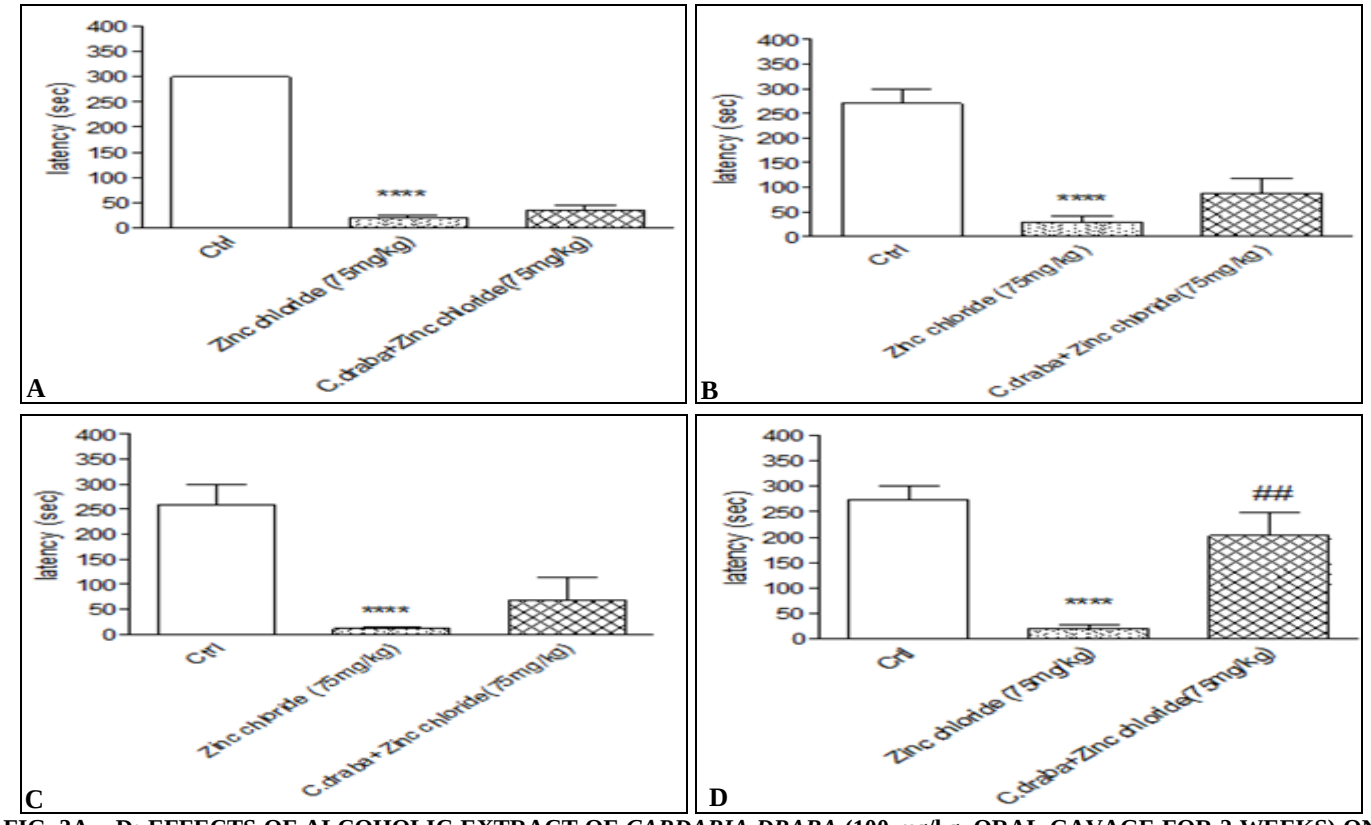

FIG. 3A – D: EFFECTS OF ALCOHOLIC EXTRACT OF *CARDARIA DRABA* (100 mg/kg, ORAL GAVAGE FOR 2 WEEKS) ON ZINC CHLORIDE - INDUCED AVOIDANCE MEMORY RETENTION IMPAIRMENTS IN STEP-THROUGH PASSIVE AVOIDANCE TASK. Each value represents the mean ± S.E.M. of 7 mice. ****p<0.0001 significantly different from the control group. ##p<0.01 significantly different from zinc chloride - treated group

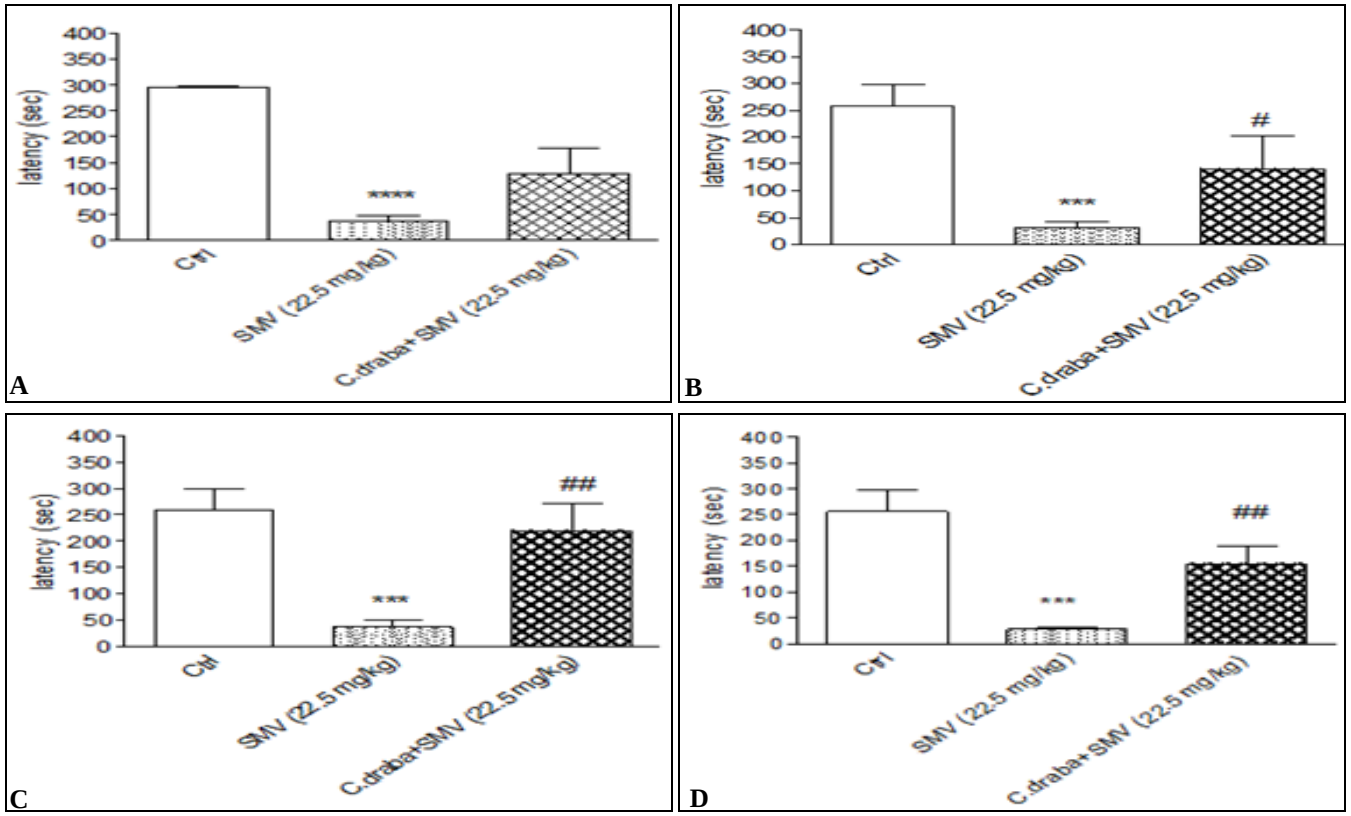

FIG. 4A – D: EFFECTS OF ALCOHOLIC EXTRACT OF *CARDARIA DRABA* (100 mg/kg, ORAL GAVAGE FOR 2 WEEKS) ON SODIUM METAVANADATE (SMV) - INDUCED AVOIDANCE MEMORY RETENTION IMPAIRMENTS IN STEP-THROUGH PASSIVE AVOIDANCE TASK. Each value represents the mean ± S.E.M. of 7 mice. ***p<0.001 and ****p<0.0001 significantly different from control group. #p<0.05 and ##p<0.01 significantly different from SMV - treated group.

DISCUSSION: One of the significant findings of this study is that 2 weeks oral administration of *Cardaria draba* alcoholic extract (100 mg/kg) caused a significant avoidance memory retention improvement in step-through passive avoidance task. Other results of this study showed that *Cardaria draba* could prevent avoidance memory retention impairments induced by scopolamine, zinc chloride and sodium metavanadate in combination treatments.

It has been suggested for a long time that the cholinergic system has important role in learning and memory especially acquisition. Scopolamine is a nonselective anticholinergic that induces senile and Alzheimer-type dementia. Administration of scopolamine (1mg/kg i.p) for 4 consecutive days induced impairment of passive avoidance memory retention along to 168 h which can impair learning and retention memory processes [18, 19]. In recent times, more studies paid attentions on the probable adverse effects of elevated levels of zinc, which can plays as a toxic compound in cognitive processes [20] and may be a risk factor in Alzheimer's disease [9]. Administration of the adequate concentration of zinc during diet indicates the effectiveness of this proper level of zinc in memory processes, cognitive behaviors, and alleviation of oxidative stress [21]. Moreover, the harmful effects of zinc on formation of neurotic plaques and cerebrovascular amyloid deposits in Alzheimer's disease (AD) have been reported by other investigators [12].

In fact, zinc in pathologic condition by induction of oxidative stress and promoting amyloid plaque formation has a key role in memory loss [12]. It has previously demonstrated that proper zinc treatment results in elevation of the cyclic nucleotide cGMP by inhibiting phosphodiesterase (PDE) activity. It has been suggested that this zinc-induced cGMP elevation may lead to activation of protein kinase A [22]. In some other cellular studies, only significant elevation of cGMP was observed in adequate zinc-treated cells [23]. It has been realized that different factors like kind of experimental task, employed protocol, stage of memory formation, concentration of zinc, facilitation of specific neurotransmitter and modified neurochemicals are involved in zinc activity on memory functions.

Previously we demonstrated that pre-training oral administration of sodium metavanadate (SMV;25 mg/kg) impaired spatial memory acquisition in Morris water maze and decreased ChAT and VAChT protein expression as cholinergic system markers in the CA1 region of the hippocampus and medial septal area (MSA). Experimental and histochemical studies have shown that in sodium metavanadate ($NaVO_3$) treated rats, formation of reactive oxygen species (ROS) and oxidative system alterations may be observed [24].

It has been reported that administration of peroxovanadium (pV) compounds may induce the expression of inducible nitric oxide synthase (iNOS) in mice livers and aminoguanidine (AG) as a selective iNOS inhibitor reversed this pV-induced iNOS expression [25]. The widespread belief that oxidative damage plays a major role in cancer, ageing, and in a number of chronic diseases has focused scientific and public attention on the possibility that antioxidants could prevent or at least retard these processes [26].

Flavonoids are a group of polyphenolic compounds [27]. A main subgroup of the flavonoids is the flavonols, of which quercetin and kaempferol are the major representatives [28]. Quercetin, one of the major flavonoids in some fruits and vegetables, has much stronger antioxidative and anticarcinogenic activities than Vitamin C [29, 30]. Recently, it has been reported that quercetin can pass through the blood-brain barrier of *in-situ* models [31]. In addition, quercetin exerts the protective effect in a stroke model induced by transient global ischemia [32].

Previous study showed that the EGb761, a standardized extract from the herbal medicine *Ginkgo biloba*, contains a high amount of quercetin and exhibits the neuroprotective effect against oxidative damage induced by 6-OHDA [33]. Quercetin in a high dose significantly decreased AChE activity in the hippocampal homogenate, which indicates that there is the increase of available acetylcholine at the synaptic terminal resulting in the improvement of cognitive performance by the animals [34]. It has been suggested that potential neuroprotective ability of *Ginkgo biloba* is determined by inhibition of monoamine oxidase (MAO)-A and –B in the presence of kaempferol [35].

CONCLUSION: In conclusion, regarding to the findings of this research, it is reasonable to deduce that because of the presence of quercetin and kaempferol in this plant (*Cardaria draba*) it may be useful as a novel treatment or protective agent against Alzheimer's disease.

ACKNOWLEDGEMENT: This work was supported by Medicinal Plants Research Center in Zabol University of Medical Sciences of Iran.

CONFLICT OF INTEREST: The authors declare that they have no conflict of interest.

REFERENCES:

1. Miri A, Sharifirad J, Sharifirad M and Teixeira de Silva JA: Allelopathic activity of medical plant, C. draba. Ann Biologic Res 2013; 4(6): 76-79.
2. Francis A and Warwik SI: The biology of Canadian weeds. 3. *Lepidium draba* L., L. chalepense L., L. appelianum Al-Shehbaz (updated). Can J Plant Sci 2008; 88: 379-401.
3. Haghighi M and Mozafariyan M: The introduction of extinct endemic vegetables of Iran. J Med Plants Res 2011; 5(33): 7085-7107.
4. Mojab F: phytochemical screening of some species of Iranian Plants. Iran J Pharm Res. 2003; 2(2): 77-82.
5. Kamkar A: Study of antioxidant functional of the water, methanol, and ethanol extracts of endemic *Cuminum cyminum* L. and *Cardaria draba* L. in the *in-vitro* systems. J Ofogh-e-Danesh 2010; 3(16): 212-220
6. Kang SY, Lee KY, Koo KA, Yoon JS, Lim SW, Kim YC and Sung SH: ESP-102, a standardized combined extract of *Angelica gigas*, Saururus *chinensis* and *Schizandra chinensis*, significantly improved scopolamine-induced memory impairment in mice. Life Sci 2005: 76: 1691-1705.
7. Wang R, Yan H and Tang XC: Progress in studies of huperzine A, a natural cholinesterase inhibitor from Chinese herbal medicine. Acta Pharmacol Sin 2006; 27: 1-26.
8. Yamada N, Hattori A, Hayashi T, Nishikawa T, Fukuda H and Fujino T: Improvement of scopolamine-induced memory impairment by Z-ajoene in the water maze in mice. Pharmacol Biochem Behav 2004; 78: 787-791.
9. Cuajungco MP, Goldstein LE, Nunomura A, Smith MA, Lim JT and Atwood CS: Evidence that the Aβ plaques of Alzheimer's represent the redox silencing

and entombment of Aβ by zinc. J Biol Chem 2000; 275: 19439-19442.

10. Lee KY, Sung SH, Kim SH, Jang YP, Oh TH and Kim YC: Cognitive enhancing activity of loganin isolated from *Cornus officinalis* in scopolamine induced amnesic mice. Arch Pharm Res 2009; 32: 677-683.
11. von Linstow, Roloff E, Harbaran D, Micheau J, Platt B and Riedel G: Dissociation of cholinergic function in spatial and procedural learning in rats. Neurosci 2007; 146: 875-889.
12. Bitanihirwe BKY and Cunningham MG: Zinc: The Brain's Dark Horse. Synapse 2009; 63: 1029-1049.
13. Hamadani JD, Fuchs GJ, Osendarp SJ, Huda SN and Grantham-MacGregor SM: Zinc supplementation during pregnancy and effects on mental development and behavior of infants: a follow-up study. Lancet. 2002; 360: 290-294.
14. Tamura T, Goldenberg RL, Ramey SL, Nelson KG and Chapman VR: Effect of zinc supplementation of pregnant women on the mental and psychomotor development of their children at 5y of age. Am J Clin Nutr 2003; 77: 1512-1516.
15. Flinn JM, Hunter D, Linkous DH, Lanzirotti A, Smith LN, Brightwell J and Jones BF: Enhanced zinc consumption causes memory deficits and increased brain levels of zinc. Physiol Behav 2005; 83: 793-803.
16. Azami K: Nicotine attenuates spatial learning deficits induced by sodium metavanadate. Neuro Toxicol 2011; 33: 44-52.
17. Ader R, Weijnen JAWM and Molemen P: Retention of a passive avoidance as a function of the intensity and duration of electric shock. Pscychonom Sci 1972; 26: 125-128.
18. Azami NS: Involvement of dorsal hippocampal α-adrenergic receptors in the effect of scopolamine on memory retrieval in inhibitory avoidance task. Neurobiol Learn Mem 2010; 93(4): 455-462.
19. Klinkenberg I and Blokland A: comparison of scopolamine and biperiden as a rodent model for cholinergic cognitive impairment. Psychopharmacol 2011; 215(3): 549-566
20. Hamadani JD, Fuchs GJ, Osendarp SJ, Huda SN and Grantham-MacGregor SM: Zinc supplementation during pregnancy and effects on mental development and behavior of infants: a follow-up study. Lancet. 2002; 360: 290-294.
21. Ebuehi OAT and Akande GAL Effect of zinc deficiency on memory, oxidative stress and blood chemistry in rats. Adv Med Dent Sci. 2008; 2: 74-82
22. Bulow VV, Dubben S, Engelhardt G, Hebel S, Pulmakers B, Heine H, Rink L and Haase H: Zinc-dependent suppression of TNF-α production is mediated by protein kinase A- induced inhibition of Raf-1, IκB Kinase β, and NFκB. J Immunol 2007; 179: 4180-4186.
23. Hönscheid A, Dubben S, Rink L and Haase H: Zinc differentially regulates mitogen-activated protein kinases in human T cells. J Nutr Biochem 2012; 23: 18-26.
24. Cuesta S, Francés D and García GB: ROS formation and antioxidant status in brain areas of rats exposed to sodium metavanadate. Neurotoxicol Teratol 2011; 33(2): 297-302.
25. Matte C, Marquis JF, Blanchette J, Gros P, Faure R, Posner BI and Olivier M: Peroxovanadium-mediated protection against murine leishmaniasis: role of the modulation of nitric oxide. Eur J Immunol 2000; 30(9): 2555-2564.
26. Fahey JW and Talalay P: Antioxidant functions of sulforaphane: a potent inducer of phase II detoxication enzymes. Food and Chem Toxicol 1999; 37: 973-979.
27. Hertog MGL, Hollman PCH and Van De Putte B: Content of potentially anticarcinogenic flavonoids of tea infusions, wines, and fruit juices. J Agric Food Chem.1993; 41: 1242-1246.
28. Rimm EB, Katan MB, Ascherio A, Stampfer MJ and Willett WC: Relation between intake of flavonoids and risk for coronary heart disease in male health professionals. Ann Intern Med 1996; 125: 384-389.
29. Takahama U: Scavenging of active oxygen by flavonoids. Tanpakushitsu Kakusan Koso 1988; 16(33): 2994-2999.
30. Heo HJ and Lee CY: Protective effects of quercetin and vitamin C against oxidative stress-induced neurodegeneration. J Agric food Chem 2004; 52(25): 7514-7517.
31. Youdim KA, Qaiser MZ, Begley DJ, Rice-Evans CA and Abbott NG: Flavonoid permeability across an in situ model of the blood-brain barrier. Free Radical Biol Medi. 2004; 5(36): 592-604.
32. Cho JY, Kim IS, Jang YH, Kim AR, and Lee SR: Protective effect of quercetin, a natural flavonoid against neuronal damage after transient global cerebral ischemia. Neurosci Lett 2006; 3(404): 330-335.
33. Kim MS, Lee JI, Lee WY and Kim SE: Neuroprotective effect of *Ginkgo biloba* L. extract in a rat model of parkinson's disease. Phytother Res 2004; 8(18): 663-666.
34. Sriraksa N, Wattanathorn J, Muchimapura S, Tiamkao S, Brown K and Chaisiwamongkol K: Cognitive-enhancing effect of quercetin in a rat model of Parkinson's disease induced by 6-

hydroxydopamine. Evid-Based Complement Alternat Med 2011; 2012: 87-97.

35. Sloley BD, Urichuk LJ, Morley P, Durkin J, Shan JJ, Pang PK and Coutts RT: Identification of kaempferol as a monoamine oxidase inhibitor and potential neuroprotectant in extracts of *Ginkgo biloba* leaves. J Pharm Pharmacol 2000; 52: 451-459.

How to cite this article:
Akbari A, Tabrizian K, Miri A and Shafiei M: Oral administration of an alcoholic extract of *Cardaria draba* prevented scopolamine-, zinc chloride - and sodium metavanadate - induced avoidance memory retention impairments in step-through passive avoidance task in mice. Int J Pharmacognosy 2016; 3(3): 131-39. doi link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.3(3).131-39.