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Neuroprotective Effects of Aloin in Alzheimer's Disease Rat Model

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ABSTRACT

Alzheimer's disease (AD), characterized by amyloid plaques and neuronal death, is the main cause of dementia worldwide. Using natural therapies has always been a great concern for AD. Herein, Aloin, as a natural anthraquinone, was applied to examine its protective and therapeutic effects on a rat model of AD. Fifty six Wistar, male rats were randomly assigned to 7 groups (n = 8 rats/group), including control group with no Aβ42 injections, group 2 with Aβ42 injection into rats' hippocampus, group 3 with injection of phosphate buffer saline, as Aβ buffer, into rats' hippocampus, group 4 and 5 that received Aloin at 50 and 100 µg kg^{-1} in a treatment mode, respectively, after being injected with Aβ42, and group 6 that received Aloin (100 µg kg^{-1}) in a protective mode before Aβ injection. Behavioral, biochemical, and histological parameters were evaluated in all groups. Alzheimer's-induced group showed impairment in lipid profile, antioxidant enzyme level, long-term memory, along with loss of amyloid plaque formation. Treatment with Aloin improved the lipid profile, antioxidant enzyme activity, number of amyloid plaques, and memory function. Protection with Aloin also demonstrated similar improvements against AD. Hence, Aloin has shown capability of improving the deficiency of both memory and antioxidant enzyme activity as well as brain plaque formation associated with AD.

Keywords: Alzheimer's disease, Aβ42, Aloin, Amyloid plaques, Memory

INTRODUCTION

Alzheimer's disease (AD) is a progressive and irreversible neurodegenerative condition destroying memory and thinking skills and it is the most common cause of dementia. It is characterized by the presence of aggregates of amyloid β (Aβ) peptide inside the brain [1]. It has been proposed that synaptic loss, neuronal death, and cognitive dysfunction are caused by Aβ accumulation in the brain [2]. Aβ42 peptide is present in cerebrospinal fluid and is considered a toxic specie engaged in AD pathophysiology [3]. In order to study Aβ aggregation *in vivo*, intra-cerebroventricular administration of Aβ peptide into rodent brain has been used to stimulate AD. This injection could induce histological and biochemical changes, oxidative damage, and inflammatory responses resulting in memory deficits [3,4]. With this animal model, *in vivo* studies could be performed to test potential new candidates for AD therapy.

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With respect to AD therapy, pharmaceutical agents have been used to either prevent AD or restore AD-related symptoms. As chemical agents, they have shown undesired side-effects and researchers have tried to substitute them with natural compounds possessing effectiveness on cognitive functioning [5].

Aloin is an anthraquinone isolated from the plants *Aloe vera* L. used for its pharmaceutical and curative properties [6,7]. Traditionally, *Aloe vera* gel is used topical treatment of wounds, minor burns and skin irritations. Also, internal applications of *Aloe vera* for constipation, coughs, ulcers, diabetes, headaches, arthritis and immune-system deficiencies have been reported [8]. In various African and Asian countries, the Aloe extract is often used to treat infectious and inflammatory diseases [9]. Aloin, with the empirical formula of $C_{21}H_{22}O_9$, has shown antioxidant [10] and neuroprotective effects [11] along with anti-inflammatory activity [12]. In addition, Aloin has been reported to inhibit proliferation and induce the apoptosis of various tumour cells [13,14]. Beside numerous therapeutic properties, Aloin has extensively been used as ingredients in

a variety of food and cosmetic products [15]. However, the putative neuroprotective effects of Aloin is unknown. Therefore, the objective of this study was to assess the effects of Aloin, as a natural compound, on amyloid-β plaque accumulation and the subsequent changes in biochemical parameters in Alzheimer's disease rat models.

MATERIALS AND METHODS

Compounds

Aβ42 and Aloin were obtained from Sigma (St. Louis, MO, USA). Aβ1-42 (5 μg μl^{-1}) was prepared in PBS and placed in an incubator at 37 °C for 1 week before use [16]. Aloin doses (50 and 100 μg kg^{-1}) were prepared in distilled water. The maximum dose of Aloin was selected based on the European Food Safety Authority (EFSA) [17]. Commercial kits used for the evaluation of low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), cholesterol, malondialdehyde (MDA), and superoxide dismutase (SOD) were purchased from Zist Shimi Company, Iran.

Animals

The experiments were conducted on thirty six male Wistar rats (200 ± 5 g; Pasteur Institute, Tehran, Iran). The animals were kept in an animal room that was maintained at 20-25 °C with 50-70% relative humidity under a 12-h light-dark cycle. The rats had free access to food (rodent pellets) and water. To induce Alzheimer's disease (AD), animals were anesthetized by ketamine and xylasin injection and placed within the stereotactic device. Using stereotaxy and brain atlas, 2 μl of Aβ1-42 (5 μg μl^{-1}) solution was injected with a hamilton syringe in the ventricle of the animal's brain. Injection was slowly carried out in the CA region on both sides of the hippocampus. After surgery, animals recovered for one hour in a warm box before they were returned to their cages. The animals were given 7 days of recovery. After one week, amyloid plaques were formed in the animal's brain which were visible by the use of histological method described below. All experiments were performed in accordance with the international guidelines set in the *Guide for the Care and Use of Laboratory Animals* (Institute of Laboratory Animal Resources, 1996) and approved by the Research and Ethics Committee of Science and Research Branch, Islamic Azad University with the Ethics No. IR.IAU.SRB.REC.1398.130.

Experimental Design

The rats were allowed to acclimate for seven days prior to their use in the studies. The rats were randomly assigned to six groups (n = 6 rats/group) as follows:

1. Control group: Rats received regular water and food and no Aβ42 injection was performed.
2. PBS group (PBS): Rats underwent surgery and PBS (Aβ42 solvent) was injected into their brains' ventricles for four weeks.
3. Alzheimer's group (AD): Rats underwent surgery and Aβ42 solution was injected into their brains' ventricles.
4. Experimental group 1 (AD + Aloin 50 μg kg^{-1}): Alzheimer's-induced rats were treated with Aloin 50 μg/kg intraperitoneally for four weeks.
5. Experimental group 2 (AD + Aloin 100 μg kg^{-1}): Alzheimer's-induced rats were treated with Aloin 100 μg kg^{-1} intraperitoneally for four weeks.
6. Experimental group 3 (Aloin 100 μg kg^{-1} + AD): Rats received Aloin 100 μg kg^{-1} in a protective mode for four weeks and then underwent Aβ injection (induction of AD).

Behavioral Study

A shuttle-cage consisting of two compartments of equal size (26 × 26 cm), including the starting and shock compartments, separated by a sliding door (8 × 8 cm) was used. The starting compartment was light whereas the shock compartment was dark. Each experiment started with a pre-training trial: the rat was first placed in the starting compartment for 5 s, after which the sliding door was raised and the rat was allowed to stay in the dark compartment for 10 s. The rat was then put back in its cage and stayed there for 30 min after which it was again put into the shuttle cage. At this time, after entering the dark compartment, a footshock (50 Hz, 1 mA, and 5 s) was delivered to the rat. The rat was then put back into cage and stayed there for 120 s. When put back in the shuttle cage, if a latency (in the order of 120 s) was observed before entering the dark compartment, successful acquisition of passive avoidance learning was recorded. A similar procedure was used 24 h after training sessions to make a retention test for evaluating long-term memory. Higher or lower latencies are taken as

indicative of increase or decrease in memory retention [18].

Biochemical Evaluation

Animals were anesthetized by inhalation of mild diethyl ether and their blood was taken. The blood samples were allowed to clot for 30 min at room temperature and centrifuged at 1000 g at 37 °C for 10 min to separate the serum. Levels of HDL, LDL, TG, cholesterol, and MDA and the activity of SOD were determined. SOD activity measurement is made based on the enzyme ability to inhibit the auto-oxidation of pyrogallol, which is checked at 420 nm [19], while MDA reacts with thiobarbituric acid (TBA) in serum to produce a state of MDA-TBA, which is then measured by colorimetric (OD = 532) method [20].

Histological Study

At the end of experiment, the rats were decapitated under anesthesia and their brain were removed for histological assessments. The brains were fixed in 10% formalin and consequently embedded with paraffin. Serial sections of 6 μm-thickness were then prepared. Thioflavin-S method was applied for staining of amyloid plaques in hippocampus cells [21] and amyloid plaques were counted using ImageJ 1.8.0-112 software. The images were observed by a fluorescence microscope.

Statistical Analysis

SPSS software V.22 was used with ANOVA and TUKEY analysis of variance in order to investigate the significant differences between the groups. Data is reported as MEAN ± SEM with significance levels of $p < 0.05$, $p < 0.01$, and $p < 0.001$ for groups.

RESULTS

Effect of Aloin on Body Weight Changes

Body weight was monitored in all groups throughout the period of the study for four weeks as shown in Table 1. At the beginning of the experiment, body weights were not significantly different among the groups. Also, throughout the experiment (weeks 2 and 3) and also at the end of the study period (week 4), no significant difference was observed in the body weights between different groups.

Passive Avoidance Test

Alzheimer's-induced group showed loss of long-term memory by entering the dark chamber on an average time of 70 s. Among the experimental groups being treated with Aloin, only the group treated with the higher dose of Aloin (100 μg kg^{-1}) showed significantly longer step-through latency compared to the Alzheimer's group ($p < 0.01$) in the test day (Fig. 1). The group that received Aloin in a protective mode exhibited improved long-term memory compared to the Alzheimer's group ($p < 0.05$).

Effects of Aloin Treatment and Protection on Biochemical Factors

The level of MDA and SOD activity were assessed before and after treatment with Aloin in blood serum of different groups. The AD-induced group demonstrated a notable reduction in the SOD activity compared to the

Table 1. The Body Weight of Rats in Different Groups. n = 6/Group

Groups	Week 1 (g)	Week 2 (g)	Week 3 (g)	Week 4 (g)
Control	264.47 ± 5.70	266.50 ± 4.89	270.67 ± 6.06	274.83 ± 7.93
PBS	271.40 ± 6.24	273.33 ± 7.50	275.33 ± 8.96	278.00 ± 11.61
AD	272.35 ± 6.59	274.50 ± 10.49	274.17 ± 7.15	276.83 ± 12.21
AD + Aloin (50 μg kg^{-1})	271.37 ± 8.12	273.33 ± 9.19	274.17 ± 11.19	275.33 ± 9.54
AD + Aloin (100 μg kg^{-1})	269.98 ± 7.29	271.17 ± 8.27	273.50 ± 9.29	277.00 ± 5.86
Aloin (100 μg kg^{-1}) + AD	273.47 ± 7.03	275.83 ± 6.46	278.83 ± 5.83	279.33 ± 12.47

Note: Data are expressed as Mean ± SEM.

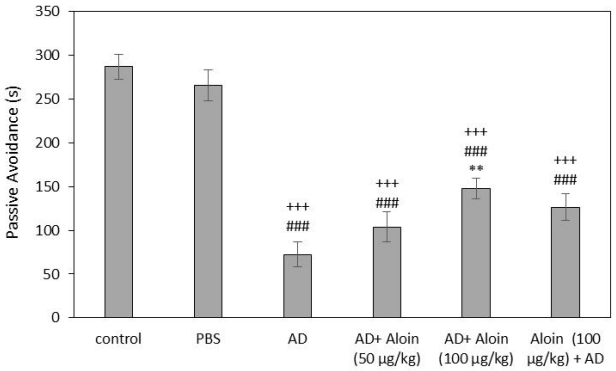

Fig. 1. The mean latency to enter the dark chamber on the test day. Control: rats received only regular water and food; PBS: rats underwent surgery with PBS being injected into brain; AD: Aβ1-42 was injected into brain to induce Alzheimer's disease (AD); AD + Aloin 50 µg kg^{-1}: Alzheimer's-induced group treated with 50 µg kg^{-1} Aloin; AD + Aloin 100 µg kg^{-1}: Alzheimer's-induced group treated with 100 µg kg^{-1} Aloin; Aloin 100 µg kg^{-1} + AD: rats received Aloin 100 µg kg^{-1} in a protective mode before induction of AD. +++: $p < 0.001$ and ++: $p < 0.01$ compared with the control group. ###: $p < 0.001$ and ##: $p < 0.01$ compared with the PBS group. **: $p < 0.01$ and *: $p < 0.05$ compared with the Alzheimer's disease (AD) group.

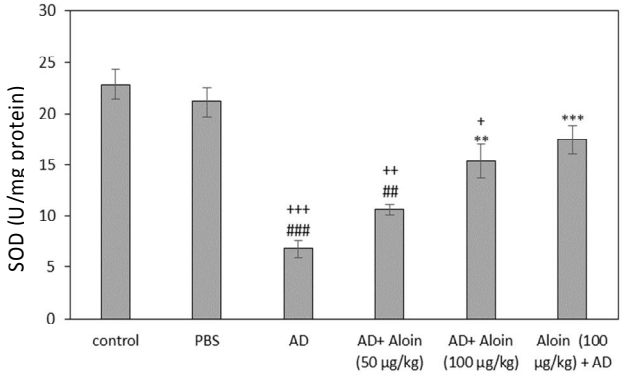

Fig. 2. Overall serum level of SOD in different groups. Control: rats received only regular water and food; PBS: rats underwent surgery with PBS being injected into brain; AD: Aβ1-42 was injected into brain to induce Alzheimer's disease (AD); AD + Aloin 50 µg kg^{-1}: Alzheimer's-induced group treated with 50 µg kg^{-1} Aloin; AD + Aloin 100 µg kg^{-1}: Alzheimer's-induced group treated with 100 µg kg^{-1} Aloin; Aloin 100 µg kg^{-1} + AD: rats received Aloin 100 µg kg^{-1} in a protective mode before induction of AD. +: $p < 0.05$ and +++: $p < 0.001$ compared with the control group. ###: $p < 0.001$ compared with the PBS group. **: $p < 0.01$ and ***: $p < 0.001$ compared with the Alzheimer's disease group.

control group ($p < 0.001$) (Fig. 2). However, groups receiving Aloin 100 µg kg^{-1} in both therapeutic ($p < 0.01$) and protective ($p < 0.001$) modes showed significant increase in SOD activity compared to the AD-induced group. On the other hand, serum level of MDA was increased in the disease-induced group compared with the control group ($p < 0.001$), while the MDA levels of the Aloin-treated groups at 100 µg kg^{-1} were significantly decreased ($p < 0.01$) compared to the Alzheimer's-induced group (Fig. 3). Moreover, the group receiving Aloin (100 µg kg^{-1}) in protective mode showed a notable decrease in MDA level compared to the AD group ($p < 0.01$).

Effects of Aloin Treatment and Protection on Lipid Profiles

A few factors of lipid profile, including cholesterol, triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were evaluated. As shown in Fig. 4A, the level of cholesterol was significantly high in the disease-induced group, injected with β-amyloid, compared to the control group ($p < 0.001$). However, when the disease group received 100 µg kg^{-1} of Aloin in both treatment and protective modes, the amount of cholesterol was significantly lowered ($p < 0.001$).

The serum level of TG was also considerably higher in the AD-induced group compared to the control group ($p < 0.001$). On the other hand, as compared to the disease group, TG level was notably improved in the group treated with 100 µg kg^{-1} of Aloin ($p < 0.001$) (Fig. 4B). The improvement of TG in the protective group was also notable compare with the disease group ($p < 0.01$).

With respect to HDL, only the group receiving 100 µg kg^{-1} Aloin in the protective mode showed the most increase in the HDL level ($p < 0.001$) compared to the

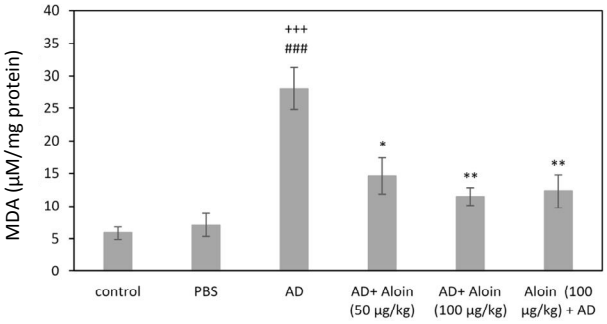

Fig. 3. Overall serum level of MDA in different groups. Control: rats received only regular water and food; PBS: rats underwent surgery with PBS being injected into brain; AD: Aβ1-42 was injected into brain to induce Alzheimer's disease (AD); AD + Aloin 50 µg kg^{-1}: Alzheimer's-induced group treated with 50 µg kg^{-1} Aloin; AD + Aloin 100 µg kg^{-1}: Alzheimer's-induced group treated with 100 µg kg^{-1} Aloin; Aloin 100 µg kg^{-1} + AD: rats received Aloin 100 µg kg^{-1} in a protective mode before induction of AD. +++: $p < 0.001$ compared with the control group. ###: $p < 0.001$ compared with the PBS group. *: $p < 0.05$ and **$p < 0.01$ compared with the Alzheimer's disease group.

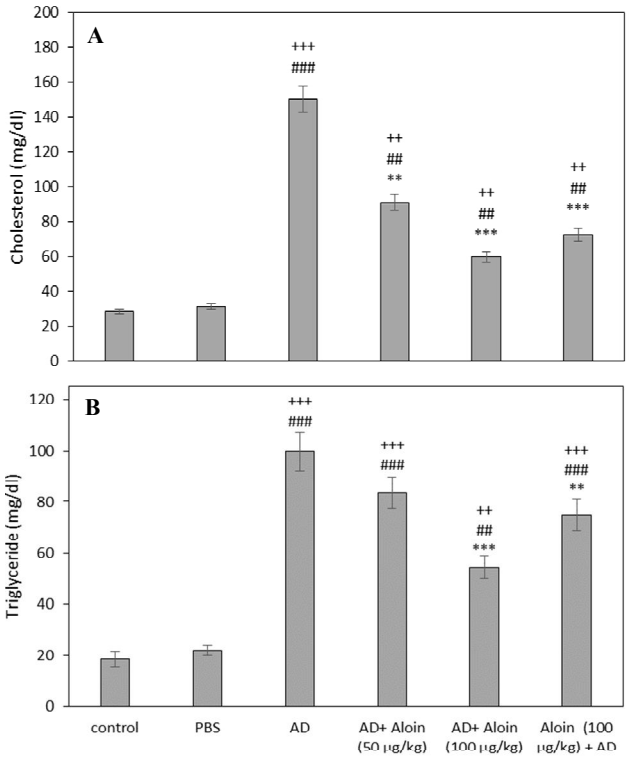

Fig. 4. Overall serum levels of cholesterol and TG in different groups. Control: rats received only regular water and food; PBS: rats underwent surgery with PBS being injected into brain; AD: Aβ1-42 was injected into brain to induce Alzheimer's disease (AD); AD + Aloin 50 µg kg^{-1}: Alzheimer's-induced group treated with 50 µg kg^{-1} Aloin; AD + Aloin 100 µg kg^{-1}: Alzheimer's-induced group treated with 100 µg kg^{-1} Aloin; Aloin 100 µg kg^{-1} + AD: rats received Aloin 100 µg kg^{-1} in a protective mode before induction of AD. ++: $p < 0.01$ and +++: $p < 0.001$ compared with the control group. ##: $p < 0.01$ and ###: $p < 0.001$ compared with the PBS group. **: $p < 0.01$ and ***: $p < 0.001$ compared with the Alzheimer's disease group.

disease-induced group, in which the HDL level was notably lower than the control group ($p < 0.001$). The group treated with both doses of Aloin also demonstrated an increase in HDL level ($p < 0.01$) (Fig. 5A).

Regarding the serum level of LDL, it was high in the disease-induced group compared to the control group ($p < 0.001$). Meanwhile, the level of LDL was notably lowered in the groups treated with 100 µg kg^{-1} of Aloin as well as the group receiving 100 µg kg^{-1} Aloin in the protective mode compared to the AD-induced group ($p < 0.01$) (Fig. 5B).

Amyloid Plaque Formation

Amyloid plaques were investigated by Thioflavin S staining, which results into a fluorescence in amyloid plaques that could be distinguished as bright spots (Fig. 6). Upon intra-hippocampal injection of Aβ42, a high number of plaques formed in the brain tissue of disease-induced group compared with the control group ($p < 0.001$) (Fig. 7C). Aloin consumption at 100 µg kg^{-1} in both treatment ($p < 0.001$) and protective ($p < 0.01$) modes caused a significant reduction in the plaque numbers compared to the AD-induced group (Figs. 6 and 7).

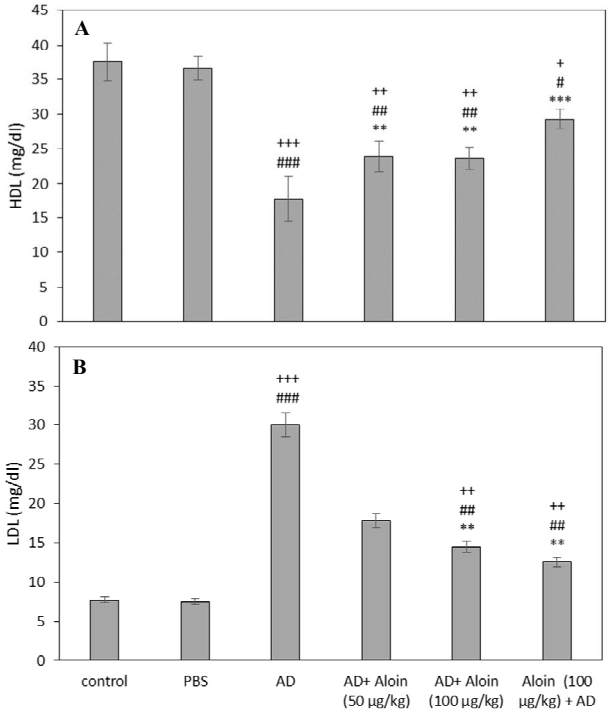

Fig. 5. Overall serum levels of LDL and HDL in different groups. Control: rats received only regular water and food; PBS: rats underwent surgery with PBS being injected into brain; AD: Aβ1-42 was injected into brain to induce Alzheimer's disease (AD); AD + Aloin 50 µg kg^{-1}: Alzheimer's-induced group treated with 50 µg kg^{-1} Aloin; AD + Aloin 100 µg kg^{-1}: Alzheimer's-induced group treated with 100 µg kg^{-1} Aloin; Aloin 100 µg kg^{-1} + AD: rats received Aloin 100 µg kg^{-1} in a protective mode before induction of AD. ++: $p < 0.01$ and +++: $p < 0.001$ compared with the control group. ##: $p < 0.01$ and ###: $p < 0.001$ compared with the PBS group. **: $p < 0.01$ and ***: $p < 0.001$ compared with the Alzheimer's disease group.

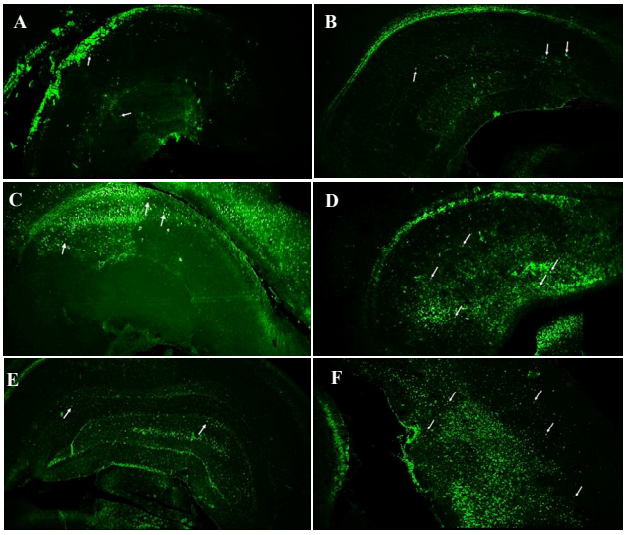

Fig. 6. Thioflavin S staining of amyloid plaques in the hippocampus CA1 region. A: (Control group) rats received only regular water and food; B: (PBS) rats underwent surgery with PBS being injected into brain; C: (AD) Aβ1-42 was injected into brain to induce Alzheimer's disease (AD); D: (AD + Aloin 50 µg kg^{-1}) Alzheimer's-induced group treated with 50 µg kg^{-1} Aloin; E: (AD + Aloin 100 µg kg^{-1}) Alzheimer's-induced group treated with 100 µg kg^{-1} Aloin; F: (Aloin 100 µg kg^{-1} + AD) rats received Aloin 100 µg kg^{-1} in a protective mode before induction of AD. White arrows represent amyloid plaques in the tissue. Images are magnified at X100.

DISCUSSION

While the exact pathogenesis of AD is still unclear, several investigations have proved that Aβ aggregation plays an important role in the pathophysiology and the neurodegeneration process of AD [2] resulting in oxidative toxicity on neuronal cells as a principal event in AD [22]. Alzheimer's disease has shown to affect memory, thinking, and behavior by disturbing brain cells [23,24]. In agreement with the present study, it has been reported that Aβ41 injection in rat's hippocampus can lead to neuronal degeneration [25]. Meanwhile, several studies have worked on the inhibitory effects of small natural molecules and their antioxidative properties on Aβ fibril formation [26,27]. Aloin is the major anthraquinone glycosyl of the *Aloe* species [28] and has been used for their curative and therapeutic properties [29,30]. Aloin has shown to significantly improve cognitive dysfunction in rat models [31] and also recover histopathological damage in the hippocampus in old mice [32]. In the present study, injection of Aβ42 into the rat's hippocampus also resulted in

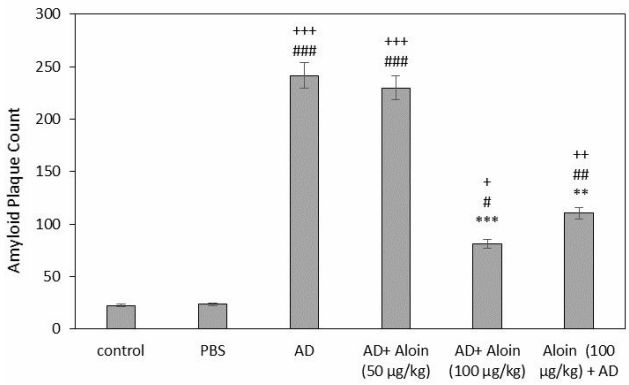

Fig. 7. Number of amyloid plaques in the ippocampus CA1 region in different groups. Control: rats received only regular water and food; PBS: rats underwent surgery with PBS being injected into brain; AD: Aβ1-42 was injected into brain to induce Alzheimer's disease (AD); AD + Aloin 50 µg kg^{-1}: Alzheimer's-induced group treated with 50 µg kg^{-1} Aloin; AD + Aloin 100 µg kg^{-1}: Alzheimer's-induced group treated with 100 µg kg^{-1} Aloin; Aloin 100 µg kg^{-1} + AD: rats received Aloin 100 µg kg^{-1} in a protective mode before induction of AD. +++: $p < 0.001$, ++: $p < 0.01$ and +: $p < 0.05$ compared with the control group. ###: $p < 0.001$, ##: $p < 0.01$ and #: $p < 0.05$ compared with the PBS group. ***: $p < 0.001$ and **: $p < 0.01$ compared with the Alzheimer's disease (AD) group.

amyloid plaque formation and reduction of antioxidant strength. Applying Aloin to AD-induced rats, in both treated and protective modes, exhibited a significant reduction in the number of amyloid plaques leading to significant improvement of learning and memory impairment, proven by the histopathological assessment and behavioral test. Same with Aloin, some natural anthraquinones, including Emodin, have shown neuroprotective properties in the treatment of neurodegenerative disease by specifically preventing β-amyloid-induced neuronal death *in vitro* [33]. Furthermore, pre-treatment with Emodin has prevented death of cortical neurons [34]. The anti-aggregation activity of Emodin has been observed in other anthraquinones with the capability of intercalating with β-amyloid sheets and efficiently preventing aggregation of toxic Aβ40 [35]. Furthermore, mitoxantrone and pixantrone, two anthraquinones, can prevent aggregation of toxic (soluble) Aβ42 [36].

In the present study, the SOD activity was decreased in AD-induced rats. SOD is an active antioxidant enzyme whose activity is sufficient for inactivation of superoxide anions produced during oxidative stress in cells [37]. It has been reported that after entering the nerve cells, beta amyloid produces oxygen free radicals which eventually leads to oxidation of proteins and lipid peroxidation [38]. The accumulation of oxidative damage to lipids, proteins, and nucleic acids have shown cognitive impairment in both aged humans and rodents [39]. In aging brain, oxidative stress causes memory impairment [40] and ultimately progression of Alzheimer's disease [41]. Moreover, it has been shown that injection of intra-hippocampal Aβ leads to reduced antioxidant activity [42]. Herein, Aloin demonstrated the ability of increasing SOD activity and therefore could offer protection against Aβ-induced oxidative stress in the hippocampus. In support with our study, Aloin has shown to significantly suppress the level of ROS and to increase antioxidant enzymes activities in the aging mice [32]. Emodin, an Aloin analog, has also shown the capability of increasing SOD activity [43]. It seems that AKT plays an important role in the Emodin-induced protection [33]. Similarly, a synthetic anthraquinone, AQ2S, has shown neuroprotective property by caspase inhibition and AKT activation [44].

One way to directly measure the free radicals *in vivo* is to quantify the cellular components reacting with the free radicals, such as lipids [45]. One of the final products of polyunsaturated fatty acids peroxidation in the cells is malondialdehyde (MDA) [46]. An increase in free radicals causes overproduction of MDA whose level is commonly known as a marker of both oxidative stress [46] cell membrane injury [45]. In the present study, decreased activity of SOD was consistent with an increase in the level of MDA in the Alzheimer's-induced rats. Herein, applying Aloin in both treated and protective modes exhibited a considerable increase in SOD activity leading to a notable decrease in MDA level. In accordance with our study, different studies have also demonstrated a great potential for Aloin to increase the SOD activity and decrease lipid peroxidation and MDA level [11,47-49]. Furthermore,

reduction of lipid peroxidation has been reported by applying Emodin, an Aloin analog [43].

Lipid profile, including levels of TG, LDL, and cholesterol were elevated in the AD rats. As it has been reported, high serum levels of TG, cholesterol and LDL could be involved in the progress of AD and the dementia itself modifies lipid levels due to the changes in metabolism [50]. Shepardson *et al.* also reported high cholesterol levels leads to the development of AD neuropathology. Regarding the possible mechanism, they have suggested that cholesterol may increase the activity of the β- or γ-secretase enzymes that generate Aβ from APP [51]. Another study has suggested that under low-cholesterol conditions, Aβ interacts with the cell membrane leading to Aβ internalization and degradation; on the contrary, high levels of cholesterol could cause Aβ dissociation from the cell surface leading to Aβ aggregation in the extracellular space [52]. Reed *at al.* also reported high level of LDL and low level of HDL in association with brain amyloid. They have suggested that one possible mechanism could be the fact that there is minimal or no exchange of HDL and LDL particles, respectively, across the blood-brain barrier [53]. Herein, Aloin showed capability of improving the lipid profile in AD-induced rats. In accordance with our study, Aloin has shown improvement in serum lipid profile of aluminium sulphate-induced male albino rats [54]. Similarly, it has been shown that Aloin administration to rats with ulcerative colitis significantly reduced elevated serum total cholesterol and TG concentrations, and markedly increased the reduced HDL level [55].

Quinones are one of the largest and most diverse groups of secondary metabolites in plants. They possess antioxidant, anti-inflammatory, and antibacterial activities, along with neuroprotective effects [56]. Therefore, they can play an important role in the creation of new biologically active compounds including drugs.

CONCLUSIONS

It has been demonstrated that the intra-hippocampal injection of Aβ42 induced significant learning deficits and Aloin administration, in a dose-dependent mode, significantly improved long-term memory. Antioxidant and anti-plaque activities may be the mechanisms contributing toward Aloin beneficial effects. In this case, valuable therapeutic and protective potential for Aloin have been shown in counteracting memory, amyloid plaque formation, and imbalances of antioxidant system and lipid profile associated with AD, and this compound seems interesting enough to be further investigated.

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