The Potential Effect of Epigallocatechin-3-Gallate alone or in Combination with Vitamin E and Selenium on Alzheimer’s Disease Induced by Aluminum in Rats

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Introduction

Alzheimer’s disease (AD) is a progressive neurodegenerative disease that leads to nerve cell death and tissue loss throughout the brain. Over time, the brain shrinks dramatically, affecting nearly all its functions [1]. AD disrupts both the way electrical charges travel within cells and the activity of neurotransmitters. It affects a person’s ability to remember things, think clearly, and use good judgment [2,3]. In AD brain, plaques form when protein pieces called β-amyloid (Aβ) clump together. Plaques are deposits of a protein fragment called Aβ that builds up in the spaces between nerve cells. Tangles are twisted fibers of another protein called tau that build up inside cells and destroy a vital cell [4]. Strong evidence of oxidative damage in AD brain exists; Aβ and its sequelae may be associated with this oxidative stress [5]. The prevalence of AD varies among many different factors, including age, co-morbidities, genetics, and education level. There is no cure for AD, however promising research and development for early detection and treatment is underway [6].

Aluminum (Al) is the third most abundant element with the global industrialization and consequent pollution. It is increasingly taken into our bodies through food, air, water, and even drugs [7]. Al is also added as alum in drinking water for purification [8].

Abstract

Background: Alzheimer’s disease (AD) is the most common cause of dementia. Epigallocatechin-3-gallate (EGCG) is the most abundant catechin in green tea; it is a natural chelator and can reduce iron-accumulation in instances of neurodegenerative diseases. Vitamin E (VE) and Selenium (Se) are antioxidant and have ability to counteract free radicals which contribute to pathological process in AD.

Objective: To evaluate the possible protective effects of EGCG and/or vitamin E & selenium against aluminium-induced AD in rats.

Methods: Five groups were used; one group served as control and four groups were injected daily with AlCl3 70 mg/kg I.P for six weeks, one of them served as AD model group while the other three groups were treated with EGCG (10 mg/kg, I.P), VE (100 mg/kg, P.O) & Se (1 mg/kg, P.O) or with their combination together with AlCl3 during six weeks of AD induction. After 6 weeks all rats were examined in the behavioural tests (Morris water maze and Conditioned avoidance test). Histopathological changes in different brain regions were determined and biochemical parameters (Aβ, ACHE, SOD, TAC, and MDA) were also estimated.

Results: The results showed significant increase in Aβ, ACHE and MDA as well as significant decrease in SOD and TAC in untreated AD model group; in addition to increase in learning time and trial number in the behavioural tests. Hippocampus neuronal degeneration and pyknosis were also detected. EGCG and/or VE & Se minimized the deteriorating effects of aluminium on biochemical parameters as well as on memory and learning impairment. Moreover, intact hippocampus had been also shown especially in the combination treatments; however some plaques were detected in VE & Se group.

Conclusion: EGCG is more effective in minimizing the hazards of aluminium-induced AD than VE & Se. However, the combination treatment has more pronounced protective effects than EGCG alone.

Keywords: Alzheimer’s disease, Aluminium, EGCG, Vitamin E, Selenium
Excessive Al intake might lead to deposition of Aβ in central nerve cells and over expression of its precursor protein [9,10]. It is considered as a potential etiological factor in neurodegenerative disorder like AD [11].

Epigallocatechin-3-gallate (EGCG) is the most abundant and active compound responsible for most of green tea’s role in promoting good health by acting through different pathways; as antioxidant, anti-inflammatory, antiatherogenic and also showing gene expression activity, functioning through growth factor-mediated pathways [12]. EGCG as an antioxidant is more effective in protecting cells than vitamin C and vitamin E [13,14]. It has COX-2 inhibiting property [15] and has been found to attenuate peroxide production in glial cells by either inhibiting the deamination of monamines or acting as a free radical scavenger [16].

Vitamin E (VE) and selenium (Se) are antioxidant and have ability to counteract free radicals. Animal and tissue culture studies suggested that they can protect brain cells from damage [17]. Marginal or deficient Se concentrations might be associated with age-related declines in brain function, possibly due to decreases in its antioxidant activity [18,19].

Because AD is a disease of aging which directly linked to repeated oxidative stress and chronic inflammation [20], therapies that diminish such effects have become an important tool in seeking more effective treatments for AD [21]. In the light of what was mentioned, the aim of this study was to evaluate the possible protective effects of EGCG and/or VE and Se against aluminum-induced AD in rats.

Materials and Methods

Animals

The study was conducted in accordance with ethical guidelines of Faculty of Pharmacy, Al-Azhar University, Egypt. Fifty male Sprague Dawley rats, weighing 250–280 g were used. Rats were obtained from The Nile Co. for Pharmaceuticals and Chemical Industries, Cairo, Egypt. They were housed in stainless-steel cages, three to four per cage, at a temperature of 25 ± 1°C with alternatively 12 hour light and dark cycles. Rats were kept under the same adequate conditions and provided with their daily dietary requirements of standard diet pellets (El-Nasr, Abu Zaabal, Cairo, Egypt) contained not less than 20% protein, 5% fiber, 3.5% fat, 6.5% ash and a vitamin mixture, water was given ad libitum. Rats were taken to test situation one hour before each experiment for adaptation and after removing food and water from the cages. Experiments were usually carried out at a fixed time around 9 AM: 2 PM.

Drugs and chemicals

Aluminum chloride - hydrated (AlCl3.6H2O), EGCG and Se (Sodium selenite: Na2SeO3) were purchased from Sigma Chemical Co. (St. Louis, MO, USA). All were freshly dissolved in distilled water. VE was obtained from Kahira Pharmaceutical and Chemicals Ind. Co., Cairo, Egypt. It was freshly dissolved in corn oil. All other chemicals and solvents were of highest grade-commercially available.

Experimental design

Animals were randomly assigned to five groups (10 rats per group) and treated for six weeks as follows; the first group served as control and was given saline daily. The other four groups were injected daily with AlCl3.6H2O (70 mg/kg IP) [22]. One of them served as AD model group while the other three groups were treated with EGCG (10 mg/kg, IP every other day) [23], VE (100 mg/kg, P.O daily) & Se (1 mg/kg, P.O daily) [24] or with their combination together with AlCl3 during the six weeks of AD induction. All drugs were administered at a dose volume not exceeding 0.5 ml/200 g body weight. At the end of the six weeks, two behavioral tests; Morris water maze test and Conditioned avoidance test were carried out (2 days’ time interval between them). Rats were sacrificed 24 h after the last test and the brain tissues were dissected and washed with ice-cold saline. All of the brain tissues were either subjected for analysis immediately or kept frozen at -80°C till the time of analysis. They were homogenized in saline; the homogenates were used to assess oxidative stress markers (lipid peroxides expressed as malondialdehyde (MDA), superoxide dismutase (SOD), and total antioxidant capacity (TAC) as well as acetylcholine esterase (ACHE) activity and Aβ content. In additions, specimens from the whole brain areas from different treated groups were taken for histopathological examination.

Behavioral experiments

Two experiments of behavioural assessments with different degree of stressfulness were selected to formulate an integrative testing battery. The chosen battery of tests allows measuring the most behavioral changes and responses to the different treatments.

Morris water maze (MWM) test: It is a hippocampus dependent spatial learning task as previously described [25]. Animal are required to learn to locate an escape platform in a pool of water, using visual cues surrounding the maze. The MWM tank was 150 cm in diameter; 62.5 cm in height, painted black, and filled to a depth of 40 cm with water maintained at a temperature of 20 ± 1°C. Around the room, numerous visual cues (e.g. bookcase and tables) were present which remained constant throughout the experiment. The maze was divided geographically into four quadrants northeast (NE), northwest (NW), southeast (SE), southwest (SW), and starting positions, north (N), south (S), east (E), west (W) that were equally spaced around the perimeter of the pool, a hidden circular platform (diameter: 13 cm) was located in the center of the NW quadrant. 1 cm below the surface of the water. The position of the escape platform remained the same for all the animals across the training trials. After six weeks treatment, rats were trained to find a submerged escape platform located in a fixed position during four consecutive daily sessions. Each session consisted of four trials. Four different starting positions, equally spaced around the perimeter of the pool, were used in a fixed order. Each trial had a maximum duration of 60 sec begin with releasing the rats in MWM then calculated escape latency which is the time in seconds taken to escape on to the submerged platform, rats not finding the platform within these 60 sec were placed on it. At the end of each trial the rats were allowed to remain on the platform for 20 sec in order to recognize the place well. For the training trials, escape latency was averaged per rat (four different positions) then calculated the averages of the groups. Two hours after the last training trial (the fourth trial of the fourth day), rats were subjected to a memory probe trial during which they swam for 60 sec in the absence of the training platform. All rats started from the same position, opposite to the
target quadrant (the quadrant where the escape platform had been positioned). The time of probe trial (time in seconds spent in the target quadrant) was calculated. A video camera (Nikon, Melville, NY, USA) linked to a computer was mounted directly above the MWM pool to record the time taken by each rat to reach the hidden platform (escape latency) indicating learning ability. Memory trial measured as the time spent in the target quadrant.

**Conditioned avoidance (CA) test:** All rats were alternatively trained in the apparatus of the conditioned avoidance test which was previously described [26,27] and modified [28]. The use of this test was extended and the parameters were manipulated for evaluating learning ability and memory consolidation in high stressful conditions. The apparatus consists of five interconnected chambers; four of them can be electrified using a laboratory DC power supply, model GPR-6060 D to deliver the foot shock (unconditioned stimulus, 50 volts, 25 pulse /sec) through their stainless steel grid floor. The fifth chamber represents the safety area (glass floor). Training was conducted by pairing of auditory stimulus (conditioned stimulus, electric bell) for 5 sec., followed by 5 sec. of foot shock. Number of trials to avoid the electric shock and reach the safety area during 5 sec. of the conditioned stimulus was calculated for each rat at the 1st and the 2nd day of training indicating learning ability and memory retention (short term memory).

**Biochemical parameters:**

1. **Protein estimation:** The protein content was measured in the brain homogenates according to Bradford method [29] using bovine serum albumin as a standard.

2. **Assessment of oxidative stress markers:** TAC, MDA and SOD were measured in the brain homogenate for each rat. The determination of the TAC is performed by the reaction of antioxidants in the serum sample with a defined amount of exogenously provide H$_2$O$_2$. The residual H$_2$O$_2$ is determined colorimetrically by an enzymatic reaction which involves the conversion of 3, 5-dichloro-2-hydroxybenzene sulphonate to a colored product [30]. Lipid peroxidation was determined by estimating the level of thiobarbituric acid reactive substances (TBARS) measured as MDA [31]. SOD activity was assessed relying on the ability of the enzyme to inhibit the phenazine methosulphate mediated reduction of nitroblue tetrazolium dye [32]. The increase in absorbance at 560 nm for 5 min is measured.

3. **Determination of ACHE activity:** It was assessed in brain tissue homogenate using ELISA Kits (Ray Biotech, Inc., USA) according to the manufacturer’s instructions.

4. **Determination of Aβ content:** It was assessed in brain tissue homogenate by determination of Aβ using ELISA Kits (USCN Life Science, Inc., Product Number MBS702915) according to the manufacturer’s instructions.

**Histopathological examination of the brain:** Brain specimens were fixed in 10% formalin for 24 h then washed with tap water. For light microscopy, the specimens were prepared and stained [33]. Serial dilutions of alcohol (methyl, ethyl and absolute ethyl) were used for dehydration. Specimens were cleared in xylene embedded in paraffin at 56°C in hot air oven for 24 h. Paraffin bees wax tissue blocs were prepared for sectioning at 4 microns thickness by microtome. The obtained tissue sections were collected on glass slides and deparaffinized, then sections were stained with Hematoxylin & Eosin stain for routine histological examination.

**Statistical analysis:** Data are presented as mean ± SEM. Multiple comparisons were performed using one-way ANOVA followed by Tukey Kramer as a post hoc test. The 0.05 level of probability was used as the criterion for significance. All statistical analyses were performed using Instat (version 3) software package. Graphs were sketched using GraphPad Prism (ISI®, USA) software (version 5).

**Results**

**Behavioral changes in Morris Water Maze test**

As shown in Figure 1a, learning ability of rats treated with EGCG or VE & Se either alone or in combination was increased as indicated by the significant decrease in escape latency (sec) from the first to the fourth day of training in MWM test as compared to AD model group (AlCl3) by approximately 44.11%, 47.64%, 50.31% and 47.58% respectively with EGCG and by 46.79%, 59.62%, 52.86% and 58.08% respectively with VE & Se or by 40.40%, 50.75%, 45.85% and 41.93% respectively for the combination treatment. The changes in the time spent in target quadrant (sec), indicating memory is shown in Figure 1b. Rats treated with EGCG, VE & Se or their
combination significantly increased the time spent in target quadrant reached to approximately 204.47%, 171.64% or 230.47% respectively as compared to AD model group (Figure 1a and 1b).

Behavioral changes in the Conditioned Avoidance test

Rats treated with EGCG, VE & Se and the combination of both showed marked decrease in the number of trials to avoid the electric shock at the 1st day of the experiment, which represents enhancement of learning ability, amounted to 27.27%, 35.06% and 23.37% respectively with respect to AD model group (Figure 2a). Administration of EGCG, VE & Se and their combination caused marked decrease in the number of trials to avoid the electric shock at the 2nd day of the experiment amounted to 34.26%, 50.00% and 26.31% respectively with respect to AD model group (Figure 2b) indicating memory enhancement (Figure 2a and 2b).

Brain oxidative stress biomarkers (MDA, SOD and TAC)

Results are shown in Figure 3a, b and c, administration of EGCG or VE & Se alone or in combination during induction and progression of AD showed marked decrease in MDA activity amounted to 35.02%, 44.25% and 25.45% respectively with respect to AD model group.

On the other hand, administration of EGCG or VE & Se alone or in combination during induction and progression of AD showed marked increase in SOD activity reached to 582.1%, 406% and 712.3% respectively and in TAC activity reached to 309.1%, 233.7% and 395.3 % respectively as compared to AD model group (Figure 3a-3c).

Brain acetylcholine esterase (ACHE) activity

The results are shown in Figure 4, administration EGCG, VE & Se and the combination of both during induction and progression of AD produced marked decrease in ACHE activity amounted to 35.02%, 44.25% and 25.45% respectively with respect to AD model group.

On the other hand, administration of EGCG or VE & Se alone or in combination during induction and progression of AD showed marked decrease in MDA activity amounted to 35.02%, 44.25% and 25.45% respectively with respect to AD model group.

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Brain β-amyloid (Aβ) content

Rats treated with EGCG, VE & Se or their combination during induction and progression of AD showed marked decrease in Aβ content amounted to 37.34%, 43.48% or 27.49% respectively with respect to AD model group (Figure 5).

Histopathological alterations in the brain

Histopathological alterations in brain specimens from different treated groups are shown in Figure 6. Brain specimens from control rats showed normal histological structure of meninges, cerebral cortex, hippocampus and striatum in the cerebrum. While, in brain specimens of rats injected with AlCl₃, focal gliosis in the cerebral cortex, neuronal degeneration and pyknosis in the hippocampus were shown. The meninges and striatum showed also congestion in the blood vessels with edema. Haemorrhages in the medulla oblongata and in the brain fissures at the cerebellum also appeared. On the other hand, treatment of rats with EGCG markedly ameliorated the pathological changes induced by AlCl₃, where the hippocampus and the meninges with the underlying cerebral cortex were histological intact. Treatment with VE & Se showed focal gliosis in the cerebral cortex and focal eosinophilic plagues in the striatum, while the hippocampus was histological intact. Additionally, combined administration of EGCG and both VE & Se showed no histopathological alteration in the hippocampus and in the cerebral cortex (Figure 6A-6P) (Table 1).

Discussion

Alzheimer’s disease (AD) is a neurodegenerative disorder that leads to impairment of memory and cognitive ability and represents one of the most financially draining diseases to society [34]. In the present study, AD was induced in rats by injection of AlCl₃ (70 mg/kg, IP) daily for consecutive six weeks. Results indicated that, it caused progressive deterioration of learning ability and spatial memory as evidenced by Morris water maze task (MWM). Experimentally, it was demonstrated that administration of AlCl₃ caused learning deficits in the MWM task in rats [24] and rabbits [35]. It also caused marked elevation in the number of trials to avoid the electric shock in the 1st and 2nd days of the conditioned avoidance test. These results could

![Figure 6](image-url)
Figure 6 (D–I): Representative photomicrographs of brain sections stained by Hematoxylin–Eosin stain (magnification 40 X): Sections taken from brain of AD model rats showing focal gliosis in the cerebral cortex (6D), neuronal degeneration and pyknosis in the hippocampus (6E). The meninges showed congestion in the blood vessels with oedema (6F), congestion in the blood vessels of the striatum (6G), hemorrhages in the medulla oblongata (6H) and in the brain fissures at the cerebellum (6I).

Figure 6 (J and K): Representative photomicrographs of brain sections stained by Hematoxylin–Eosin stain (magnification 40 X): Section taken from brain of EGCG treated group showing that the hippocampus (6J) and the meninges with the underlying cerebral cortex (6K) were histological intact.

Figure 6 (L–N): Representative photomicrographs of brain sections stained by Hematoxylin–Eosin stain (magnification 40 X): Section taken from brain of VE & Se treated group showing that the hippocampus was histological intact (6L) but there was focal gliosis in the cerebral cortex (6M) and focal esinophilic plagues in the striatum (6N).

Figure 6 (O and P): Representative photomicrographs of brain sections stained by Hematoxylin–Eosin stain (magnification 40 X): Sections taken from brain of combination treatment group (EGCG, VE & Se) showing no histopathological alteration in the hippocampus (6O) as well as in the cerebral cortex (6P).
be attributed to the deficits in learning, memory and retrieval abilities (cognitive functions); the number of trials demonstrated by the animal in the conditioned-avoidance technique is known as a valuable parameter to assess the memory and learning behaviors of animal [27]. These results could be attributed to the ability of aluminum (Al) to interfere with downstream effectors molecules involved in long-term potentiating [36]; this disruption could then explain the memory impairment and neurobehavioral deficits observed. Also Al is a well-known neurotoxicant reported to accelerate oxidative damage to biomolecules. Furthermore, Al salts have been reported to cause cell depletion in the hippocampus, isocortex [37] and degeneration of cholinergic terminals in the cortical areas. It accumulates in the cingulated bundle and thereby induces learning deficits [38].

Results also showed marked elevations in ACHE activity, Aβ content, MDA level and marked decrease in TAC, SOD content with AlCl3. A possible explanation of the previous results could depend on the hypothesis that Al is a potent cholinotoxin [39]; it has a biphasic effect on acetylcholinesterase activity, with an initial increase in the activity of this enzyme followed by a marked decrease. This biphasic effect has been attributed to the slow accumulation of Al in the brain [40]. Moreover, Al was previously found to be a potent pro-oxidant known to enhance lipid peroxides in the cortex and hippocampus [41]. Concerning the data obtained the present results revealed increased production of MDA in brain of AlCl3 - treated rats. Similar result stated that significant increase in MDA concentration in hippocampus and frontal cortex of rats administered daily AlCl3 via drinking water for six weeks [42]. The obtained data revealed also significant inhibition in activities of SOD and TAC in brain tissue of AlCl3 treated rats which was consistent with results of several investigators who revealed marked decrease in endogenous antioxidant after administration of different salts of Al [43-46] as well as increase in the level of TBARS. The activities of GST, SOD, catalase and GPX were decreased in liver, kidney and brain of rat treated with AlCl3 daily for 70 days. Parallel to the present results, it was reported that intrahippocampal injections of AlCl3 in wistar rats induced significant increase in nitric oxide and malondialdehyde concentrations as well as significant reduction of glutathione contents at 3hrs, and 30 days after treatment [47]. In addition, the neurotoxicity of Aβ in whatever form may involve the formation of reactive oxygen species and Al is a prooxidant and is known to promote the oxidation activity of Aβ in the presence of iron. Al has also been linked to Aβ production through the immune response. It is also linked to activate complement which in turn has been linked to the enhanced aggregation of Aβ [48]. Self-aggregation of Aβ due to Al administration leads to generation of hydrogen peroxide and hydroxyl radical via certain chemical reactions [49]. The production of these reactive oxygen species induces membrane lipid peroxidation, which can impair the function of the membrane ion-motive ATPase resulting in membrane depolarization and a decrease in cellular ATP levels. Consequently, histological examination of the brain in the present work which showed that AlCl3 (70 mg/kg for six weeks) produced focal gliosis in the cerebral cortex, neuronal degeneration and pyknosis in the hippocampuses can be confirmed. Meninges and strium showed also congestion in the blood vessels with edema, hemorrhages in the medulla oblongata and in the brain fissures at the cerebellum also appeared.

Results of the present study also showed that administration of EGCG induced a significant decrease in escape latency accompanied by a significant increase the time spent in target quadrant in MWM indicating improvement of learning ability and spatial memory. In the conditioned-avoidance test, EGCG treated rat also showed marked decrease in the number of trials to avoid the electric shock in the 1st and 2nd days of the experiment as compared to AlCl3 treated rats. These results could be attributed to the improvement in the learning as well as in memory and retrieval abilities (cognitive functions). These results are in agreement with the data which stated that administration of EGCG improved cognitive function and attenuated brain Aβ neuropathology in a transgenic AD mouse model [50]. In particular; EGCG inhibits the fibrillogenesis of Aβ through binding to the natively unfolded polypeptides and preventing their conversion into toxic aggregates intermediates [51]. It was also reported that, treatment with EGCG in mutant AD mice improved memory function and reducing the levels of Aβ [52]. Results of the present study also showed that administration of EGCG significantly decreased ACHE activity, MDA level and Aβ content, while significantly increased oxidative stress marker (SOD and TAC activity) in AD rat model. The current work was in accordance with the results in which EGCG increased SOD activity and protected against glycation end products induced neurotoxicity by decreasing ROS and MDA [53], and also in agreement with the results showed that EGCG treatment led to the increase of SOD activity and decrease in MDA contents in the hippocampus [54]. In addition, EGCG is able to bind Aβ [51]; it may act as an antioxidant and anti-inflammatory against Aβ aggregation in hippocampus and thus have a neuroprotective effect. Actually, Aβ neurotoxicity has been reported to be mediated by free radicals and attenuated by antioxidants and free radical scavengers [55]. Moreover, EGCG has been shown to prevent Aβ induced hippocampal neuronal cell death in cultured hippocampal neurons through its antioxidant property [56]. In the present work, histological examinations in different brain regions were in parallel with other findings where administration of EGCG to AD rat model showed no histopathological alteration in the hippocampus.

Results of the present study also showed that administration of Vitamin E (VE) and Selenium (Se) to AD model rats induced significant decrease in escape latency to reach the hidden platform accompanied by a significant increase the time spent in target quadrant in MWM which indicate improvement of learning ability and spatial memory. Also, in the CA test VE and Se treated rats showed marked decrease in the number of trials to avoid the electric shock in the 1st and 2nd days of the experiment. These resulting data could be attributed to the improvement in the learning, memory and retrieval abilities (Cognitive functions). Results of the present study also showed that VE and Se treated rats showed marked decrease in ACHE activity, MDA and Aβ content in addition to marked increase in SOD and TAC activity. The effect of VE and Se is to lesser extent than EGCG.

It is well known that antioxidants reduce oxidative radical-induced reactions. VE (α-Tocopherol) is an important antioxidant in biological systems that inhibits peroxidation of membrane lipids by scavenging lipid peroxyl radicals and is converted into a tocopheryl radical as a consequence [57]. Selenium is one of the necessary trace elements in the human body,
which has the ability to counteract free radicals and protect the structure and function of proteins, DNA and chromosomes against the injury of oxidation [58]. Because oxidative stress and cognitive dysfunction are strongly correlated, agents that modulate reactive oxygen species may be potentially useful as anti-dementia agents. Chronic administration of Se was found to improve not only the memory retention, muscle strength, and locomotion but also reduce oxidative damage induced by chronic Al administration. Se treatment was also found to attenuate the rise in MDA concentration of Al-treated rats [24]. Strong evidence of oxidative damage in AD brain exists and Aβ may be associated with this oxidative stress [5], it causes oxidative damage to and neurotoxicity of neurons. VE blocks these effects in vitro [59-62]. Data showed that the presence of VE with Al alleviated its harmful effect on several parameters and their levels which become near to the normal values [63-65]. The present results are in parallel to those which stated that VE or Se in combination with Al significantly decreased level of free radicals [66]. The protective effect of VE against the neurotoxic effect of AlCl3 may be attributed to its ability to appear as the first line of defense against peroxidation of polyunsaturated fatty acid contained in cellular and subcellular membrane phospholipids, it acts as antioxidant, breaking oxidative radical-induced reactions [67] and counteracts Al harmful effects not only by preventing free radical formation but also by favoring Al disposal [42].

The behavioral and biochemical results of the present work are confirmed by the histological examinations of different brain regions in which administration of VE & Se or Al to AD model rats showed histologically intact hippocampus despite the focal gliosis in the cerebral cortex and focal encephalophic plagues in the striatum.

As regarding the combination treatment (EGCG and VE & Se), there was significant decrease in escape latency to reach the hidden platform accompanied by a significant increase in the time spent in target quadrant in MWM indicating improvement of learning ability and spatial memory of AD model rats. Results of the present study also showed that combination treatment induced a significant decrease in the number of trials to avoid the electric shock in the 1st and 2nd days of the experiment. These resulting data could be attributed to the improvement in the cognitive functions. Results of the present study also showed that combination group treated rats showed marked decrease in ACHE and MDA activity as well as in Aβ content together with marked increase in SOD and TAC activity. The effect of the combination treatment was more pronounced than the effect of either EGCG or VE & Se alone and confirmed by the histological examination of the different brain regions. Therefore, the present study highlights that combination of EGCG and VE & Se improved all behavioral, biochemical and histological changes induced by AlCl3 in rats, an effect that could be partially correlated with their antioxidant and/or anti-inflammatory properties leading to neuroprotection. However, there is no published data regarding the effect of the combined treatments of EGCG with VE & Se on the induction and/or the progression of AD.

Conclusion

EGCG is more effective in minimizing the hazards of aluminum during induction and progression of AD than the antioxidants VE & Se. This may be attributed to its additional anti-inflammatory effect as well as to its ability to antagonize Aβ aggregation in the hippocampus. In this way EGCG have a neuroprotective effect which confirmed by biochemical, behavioral and histopathological examination. The combination treatment has more pronounced effect in minimizing the hazards of aluminum- induced AD than either EGCG or VE & Se.

References


