Evaluation of the Possible Protective and Therapeutic Influence of Coriander (Coriandum sativum L.) Seed Aqueous Extract on Hippocampal Pyramidal Cells Against Alzheimer's Disease Induced by Aluminum Chloride in Adult Male Albino Rats

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Abstract: Alzheimer's disease is a common neurodegenerative disease. The first and most severely affected brain area is hippocampus. Several studies have used aluminum chloride ($Alcl_3$) to produce an animal model of Alzheimer's disease. Coriander is a plant which has potent antioxidant ability. As well as it has a memory improving property. This investigation aims to clarify the role of coriander seed aqueous extract on hippocampus pyramidal cells against Alzheimer's disease induced by aluminum chloride in adult male albino rats. 24 Adult male albino rats were divided into 4 groups 6 for each. Control , $AlCl_3$ (300mg/kg p. o.), $AlCl_3$(300mg/kg p. o.) plus (0.5gm/kg p. o) coriander aqueous seed extract treated group for a month and (0.5gm/kg p. o.) coriander extract treated group after stopping aluminum chloride treatment each for a month. Specimens from hippocampus were processed for haematoxylin and eosin, toluidine blue and Nauta stains. Aluminum chloride treatment showed that most of the pyramidal cells were *shrunken, the cells were pale and the fibers appeared detached. A*luminum chloride and coriander treated group restore the pyramidal cells of the hippocampus to normal. The coriander treatment after stopping $AlCl_3$ treatment restores the hippocampus pyramidal cells to normal. In conclusion coriander seed aqueous extract showing protection and therapeutic action on pyramidal cells in hippocampus against Alzheimer's disease induced by aluminum chloride treatment.

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Key words: coriander, Alzheimer's disease, hippocampus, aluminum chloride, rat.

1. Introduction

Alzheimer's disease (AD) is a neurodegenerative and cause gradual memory loss. The first and most severely affected brain area is hippocampus (1, 2). Several studies have used aluminum chloride to produce an animal model of Alzheimer's disease (3-5). Chronic aluminum toxicity was achieved during four weeks by daily administration of aluminum chloride (4-7). It was evident that links neural damage with excessive generation of free radicals, which may be due to factors such as oxidative stress. In fact, oxidative stress is considered a trigger for initiation and propagation of neurodegenerative diseases. Overall, there is substantial evidence indicating that a condition of increased oxidative damage to lipids, proteins, and nucleic acids is present in both brain regions and peripheral tissues of individuals affected by one of several neurodegenerative diseases (8, 9). There has been a steady rise in the number of patients suffering from Alzheimer's disease all over the world. There are around 35 million patients suffering from Alzheimer's disease globally (10). On average, patients die within 8 years of the onset of the first symptoms. The Drugs used for treatment of AD patients only improve symptoms but not slow the progression of AD (11). In accord with this view antioxidants agents are considered a promising approach to slowing the progression and limiting the extent of neural cell loss in AD. This strategic approach may offer a chance for protection or therapies in human neurodegenerative diseases (9). In an attempt to provide low cost, highly effective and non toxic remedy for prevention and treatment of AD. Coriander is a plant belonging to family Umbelliferae. Both the leaves and seeds are used for medicinal purpose. It used to treat hypertension, cardiovascular disorders and diabetic diseases. Also it has potent antioxidant ability and antimicrobial activity. As well as it has a memory improving property (12-16). Present investigation aims to clarify the role of coriander seed aqueous extract as a protective and therapeutic agent against Alzheimer's disease was induced by $AlCl_3$ on the pyramidal cells in hippocampus of male albino rats.

2. Materials and Methods:

2.1 Animals

24 adult male albino rats weighing 150-200 gm were used. The rats were housed under good hygienic environmental condition in National Organization for Drug Control and Research at laboratory animal department El Haram-Egypt. The rats were divided into four groups 6 for each. Control, (300mg/kg p. o.) aluminum chloride treated group, (300mg/kg p. o.) aluminum chloride + (0.5g/kg p. o.) coriander seed aqueous extract, (0.5g/kg p. o.) coriander seed aqueous extract for another month after stopping (300mg/kg p. o.) aluminum chloride treatment.

2.2 Plant material

Coriander seeds were obtained from local market in Egypt. The seeds were ground. 200 ml of boiling water were added to 5g of coriander powder, covered, left for10 minutes and filtered. The filtrate was given to the rats in a dose 0.5g/kg equivalent to human therapeutic dose (17)

3 .Histological study

Specimens from hippocampus were used for histological studies fixed in neutral formalin for a week at room temperature, dehydrated, clearing and embedded in paraffin wax. The paraffin sections were cut at 20 µm thickness and stained with haematoxylin and eosin (18), others stained with toluidine blue(for Nissl's granules) (19) and with Nauta (for nerve cells and neuro fibers) (20). The histochemical interpretation was done using computer image analyzing system (Leica Model). Estimation of the optical density of thirty cells in each group was made. The data obtained were statistically analyzed according to *(21)*. Differences between the group means were assessed using T-test. $P \leq 0.05$ was considered significant.

4. Histological Results:

Control group (Group 1)

Hippocampus was identified as a C shaped structure in coronal section of the brain. Sections stained with Heamatoxlin and eosin of hippocampus of control group showed that hippocampus included four subdivisions named CA1, CA2, CA3 and CA4 (figures1, 2). The higher power examination of the area CA1 of the hippocampus revealed that it consists of three layers (polymorphic, pyramidal, and molecular layer) (figures3, 4).The pyramidal layer is the principal cell layer. This layer is formed of closely adherent pyramid-shaped neurons. The pyramidal neurons appeared with large nuclei and basophilic cytoplasm (figure5). The dentate gyrus (↑) could be detected as dark C-shaped structure surrounding area CA3 (figures1, 2). Toluidine blue stained sections showed the pyramidal cells with large vesicular nuclei and darkly stained cytoplasm containing Nissl's granules (figure 6). Nauta stained sections showed the pyramidal cells and the fibers appeared regular in thickness (figure 7).

Group II

Group received (300mg/Kg p. o.) aluminum chloride for a month. H&E stained sections showed that most of pyramidal cells were shrunken (Figures 8&9). Toluidine blue stained sections showed that most of pyramidal appeared *shrunken* within reduced Nissl's granules (figure10) .Nauta stained sections showed that most of pyramidal cells appeared degenerated ,others appeared shrunken within detached neurofibers (Figure 11).

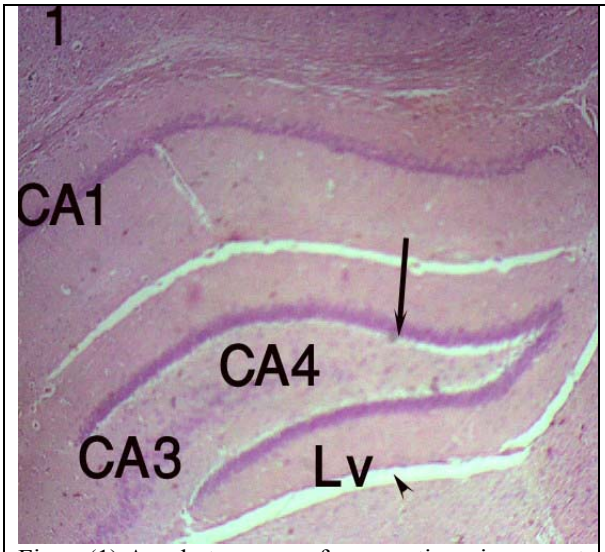
Group III:

Group received 300mg/kg p. o. aluminum chloride +0.5g/kg p. o. coriander seed aqueous extract for a month .H&E stained sections showed restoration the pyramidal cells to normal (Figure12). Toluidine blue stained sections showed restoration the pyramidal cells within Nissl's granules to normal (figure 13). Nauta stained sections showed restoration the pyramidal cells within neurofibers to normal (Figure 14).

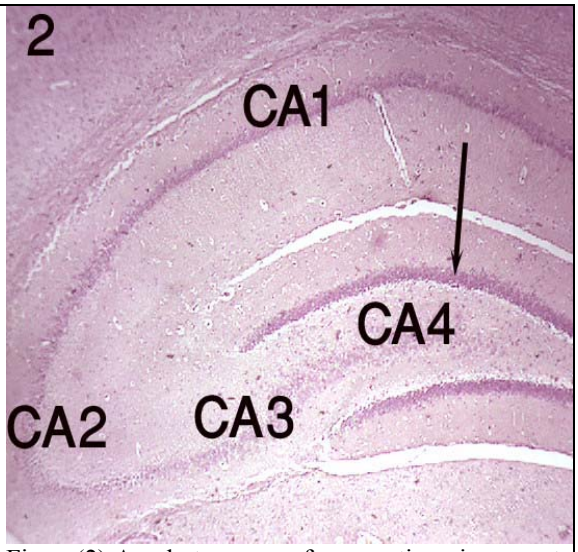
Group IV:

Group received 300mg/kg p. o. aluminum chloride for a month and administered 0.5 g/kg coriander seed aqueous extract for another month after stopping aluminum chloride treatment. H& E stained sections showed restoration the pyramidal cells to normal (Fiqure15). Toluidine blue stained sections showed restoration the pyramidal cells within Nissl's granules to normal (Figure 16). Nauta stained sections showed restoration the pyramidal cells within neurofibers to normal (Figure 17).

Statistical analysis reported that significant reduction in pyramidal cells, Nissl's granules and neurofibers in Alcl3 treated group. Meanwhile group treated with $Alcl_3$ and coriander seed aqueous extract recorded that non significant reduction in pyramidal cells, Nissl's granules and neurofibers. As well as group treated with coriander seed aqueous extract after stopping $Alcl_3$ treatment displayed non significant change in pyramidal cells, Nissl's granules and neurofibers in comparison with control group(Table1& Histogram1).



Figure(1):A photogram of a section in a rat hippocampus of control group ,showing its three regions appearing as Cornu Amonis CA1,CA3,CA4.The dentate gyrus (↑),Lateral ventricle(LV) and third ventricle(3V) can also be noticed. (H&E x 100)



Figure(2):A photogram of a section in a rat hippocampus of control group ,showing its four regions appearing as Cornu Amonis CA1,CA2,CA3&CA4.The dentate gyrus (↑) can also be noticed . (H&E x 100)

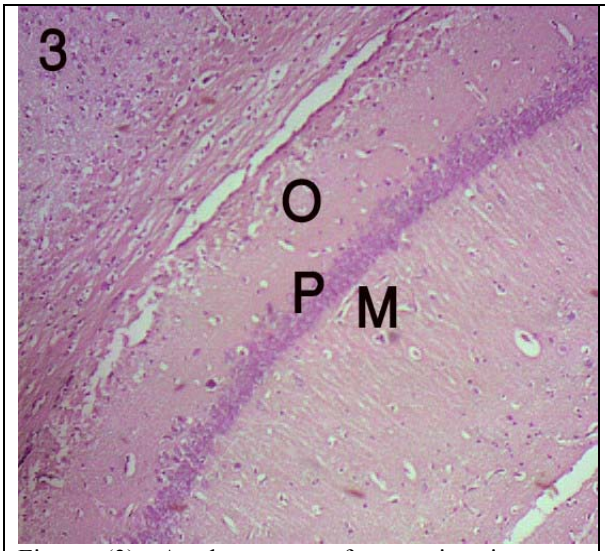


Figure (3): A photogram of a section in a rat hippocampus of control group, showing area CA1.The three layers of the hippocampus: outer polymorphic (o), middle pyramidal (p) and inner molecular (M). (H&E x200)

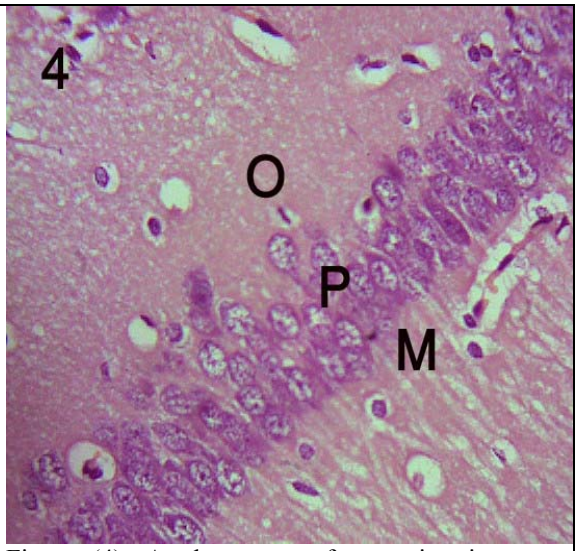


Figure (4): A photogram of a section in a rat hippocampus of control group, showing the three layers of the hippocampus: outer polymorphic (o),middle pyramidal(p) and inner molecular (M). (H&E x400)

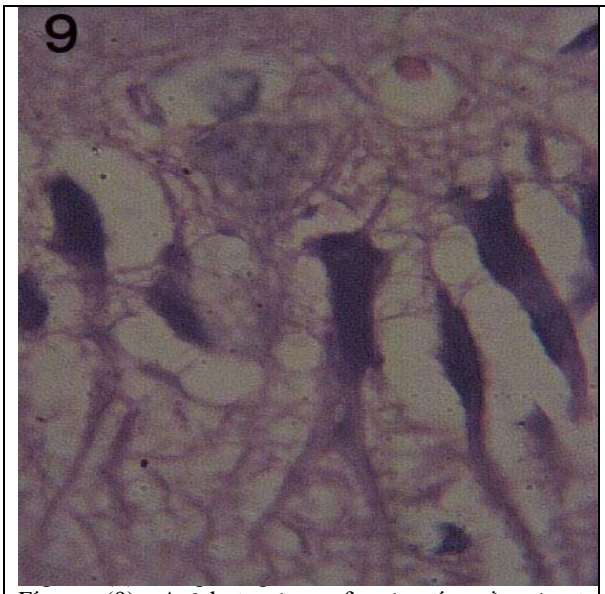


Figure (9): A photogram of a section in a rat hippocampus of control group ,showing the three layers of the hippocampus cortex (c), molecular (M), pyramidal (p) and inner molecular (M) (H&E x1000)

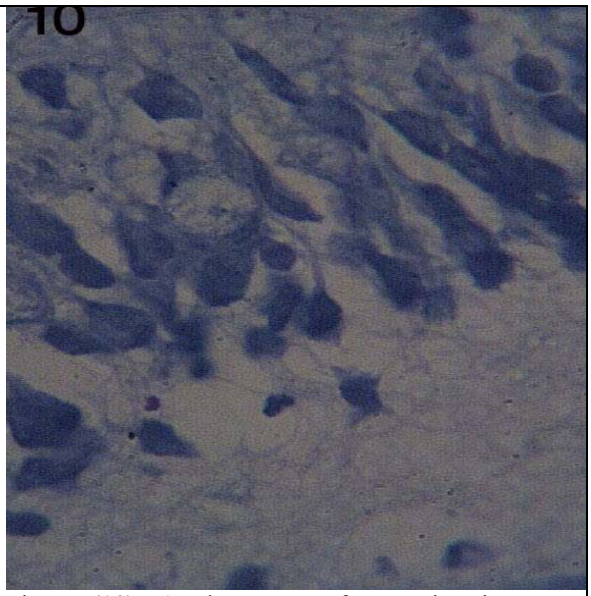


Figure (10): A photogram of a section in a rat hippocampus of aluminum chloride treated group showing most of pyramidal cells appeared shrunken and degenerated with deep stained cytoplasm and pyknotic nuclei (H&E x1000)

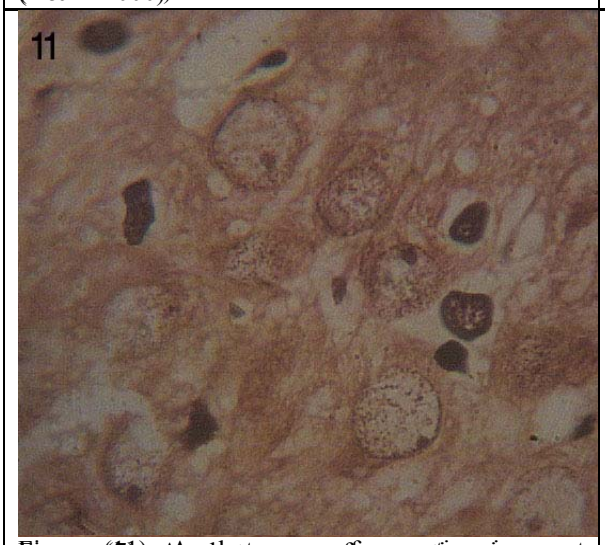


Figure (11): A photogram of a section in a rat hippocampus of aluminum chloride treated group showing most of pyramidal cells appeared shrunken and degenerated with deep stained cytoplasm and pyknotic nuclei and others appeared shrunken within detached neurofibers (Nauta stain x1000)

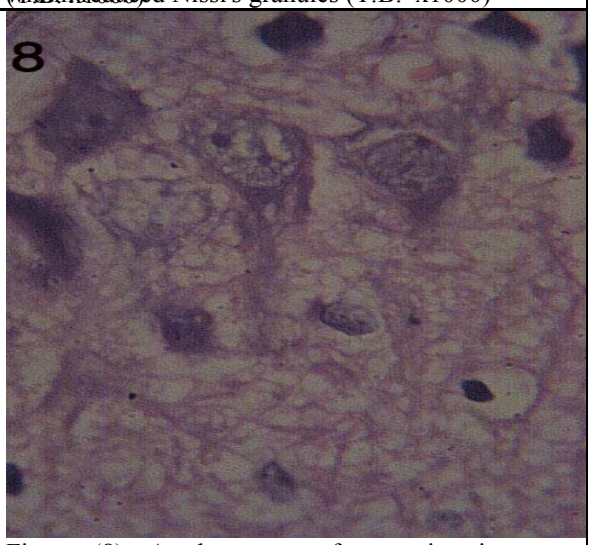


Figure (8): A photogram of a section in a rat hippocampus of aluminum chloride treated group ,showing most of the pyramidal cells appeared shrunken and degenerated (H&E x1000)

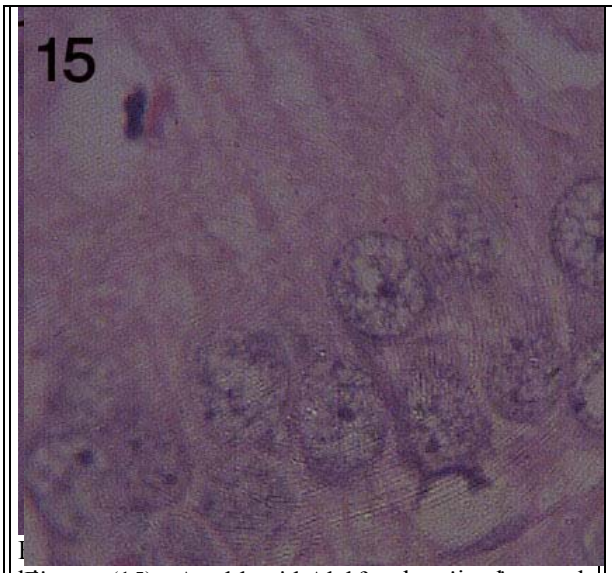


Figure (15): A photogram of a section in a rat hippocampus treated with $Alcl_3$ and coriander seed aqueous extract showing most of pyramidal cells restore to normal (H&Ex1000)

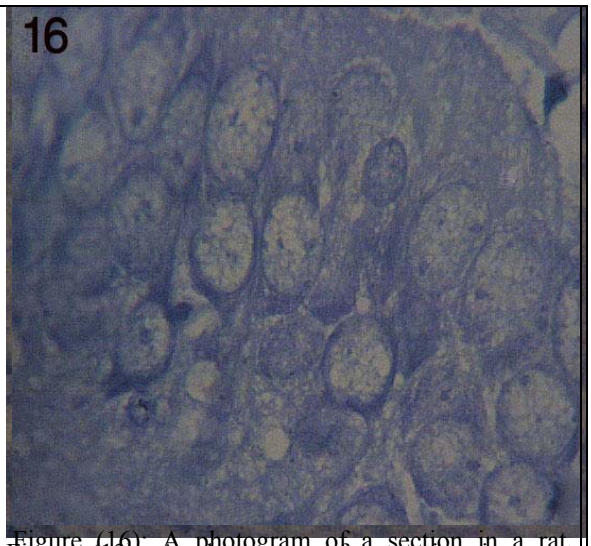


Figure (16): A photogram of a section in a rat hippocampus treated with coriander seed aqueous extract after stopping $Alcl_3$ showing most of pyramidal cells restore to normal within Nissl's granules.(T.B. x1000)

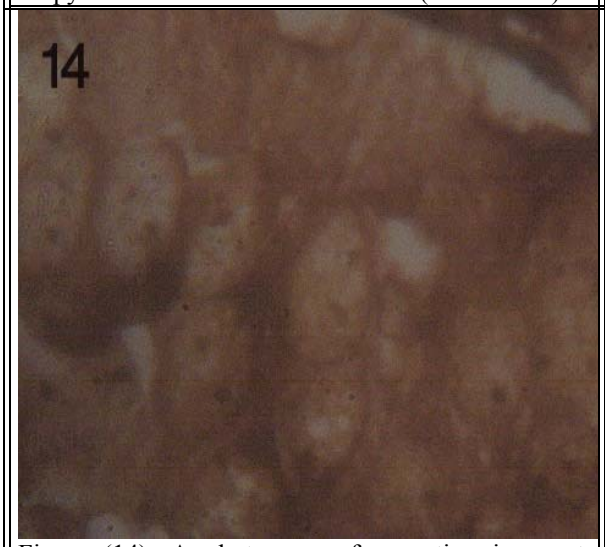


Figure (14): A photogram of a section in a rat hippocampus treated with $Alcl_3$ and coriander seed aqueous extract showing most of pyramidal cells restore to normal within neurofibers (Nauta stain x1000)

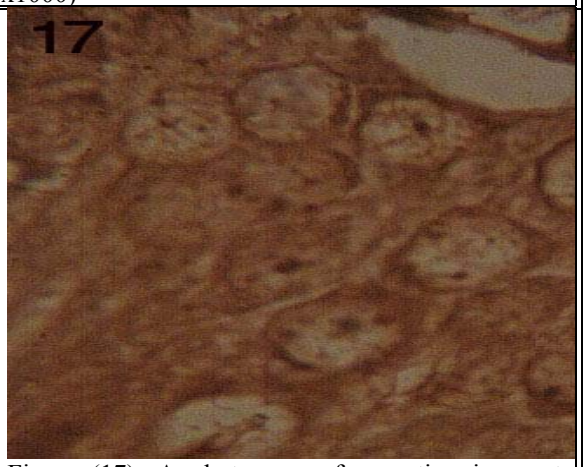
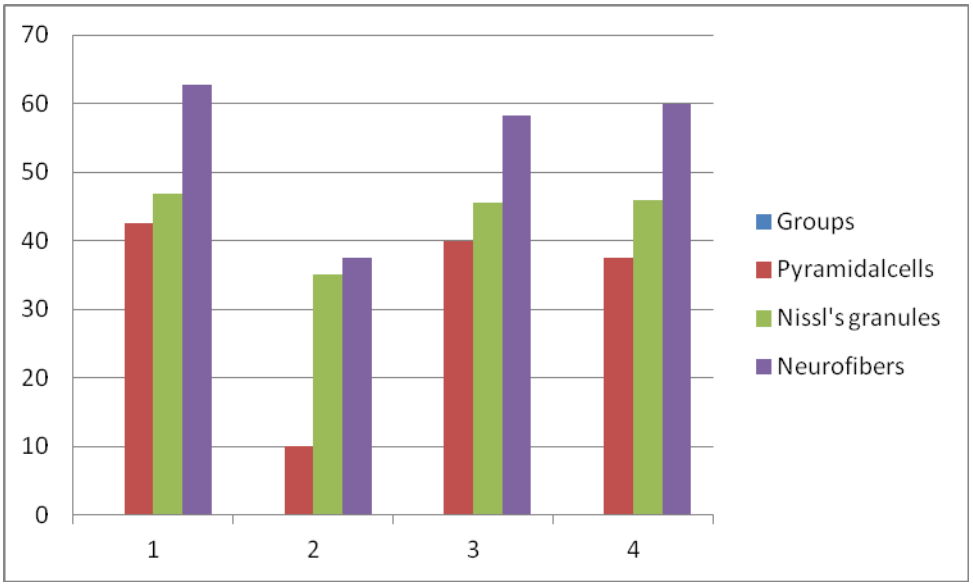


Figure (17): A photogram of a section in a rat hippocampus treated with coriander seed aqueous extract after stopping $Alcl_3$ showing most of pyramidal cells restore to normal within neurofibers (Nauta stain x1000)

Table (1): The quantitative measurements of the color density (Pixel) of pyramidal cells, collagen fibers and Nissl's granules in the hippocampus of control and treated groups of male rats.

	Statistical analysis	Control	$ALCl_3$	Protective	Therapeutic
Pyramidal cells	Average	42.5	10	40	37.5
	SD.	5.24	3.76	4.47	5.24
	Max.	50	15	45	45
	Min	35	5	35	30
	t test		5.9433	1	1.66
	Probability		Reduced	Non Sig.	Non Sig.
Nissl's granules	Average	46.83	35	44.33	46
	SD.	3.82	4.47	3.83	3.74
	Max.	50	40	50	50
	Min	40	30	40	40
	t test		4.9	1.1	1.53
	Probability		Reduced	Non Sig.	Non Sig.
Nerofibers	Average	62.66	37.5	58.33	60
	SD.	7.66	5.24	5.58	7.07
	Max.	70	45	65	70
	Min	50	30	50	50
	t test		5.5	1.09	0.6
	Probability		Reduced	Non Sig.	Non Sig.

P≥ 0.01 Highly Significant, P≥ 0.05 Significant, P< 0.05 Non significant



Histogram (1) Quantitative measurements of, pyramidal cells, Nissl's granules and neurofibers in the hippocampus of control and treated groups of male rats.

Discussion

Alzheimer's disease (AD) is a progressive disease that destroys the mind with forgetfulness in early stages, followed by the inability to communicate and provide self care. On average, patients die within 8 years of the onset of, the first symptoms. Aluminum is known toxin to the nervous system that starts the disease processes, leading to brain cell death, senile plaques and neurofibrillary tangles (22).

In the present investigation following administration of aluminum chloride for four weeks to rats results in shrunken , faintly stained cytoplasm, detached neurofibers and significant reduction in the pyramidal cells, in hippocampus. This effect was an indicator to obtain AD model. AD model is based on the generation of free radicals in the brain, which increases lipid peroxidation and decreases the antioxidant glutathione, together with causing memory impairment.(10)

Investigations in such oxidative stress show that interactions between abnormal mitochondria and disturbed aluminum cation metabolism are at least in part, the cause of such oxidative stress responsible for cytoplasmic oxidative damage observed in these susceptible neurons which could ultimately lead to their demise. The abnormal clusters of dead and dying nerve cells and protein clog up the cell. The destruction of nerve cells lead to the decrease in the substance secreted by neurons that send messages to other neurons and this appears to disconnect areas of the brain that work together. This will slow down or completely shut off the flow of blood in smaller vessels, the brain cells die without blood flow and oxygen (23).

It has been observed that the use of antioxidants and neuroprotective agents may decrease the risk of memory deficits associated with Alzheimer diseases (9). In an attempt to provide low cost, highly effective, non toxic remedy for prevention and treatment of AD.

Coriander has been reported to scavenge free radicals and inhibit lipid peroxidation .It has also shown to preserved the endogenous antioxidant system ,which are normaly consumed ,when tissues or cells are exposed to oxidative damage.

The potent antioxidant activity of coriander could prevent oxidative damage resulted from interaction between aluminum cation and unstable oxygen from abnormal mitochondrial and could protect pyramidal cells in the hippocampus against damage was induced by $Alcl_3$ overload. As well as coriander could provide therapeutic action after stopping $Alcl_3$ treatment.

In conclusion coriander seed aqueous extract showing protection and an improvement in the therapeutic action. Coriander with low or no side effect could be considered a good remedy for treatment AD.

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