

# Study the Possible Protective and Therapeutic Influence of Coriander (*Coriandrum sativum* L.) Against Neurodegenerative Disorders and Alzheimer's disease Induced by Aluminum Chloride in Cerebral Cortex of Male Albino Rats

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**Abstract:** Several studies reported many neurodegenerative disorders and Alzheimer's disease induced by aluminum chloride on cerebral cortex of male rats. Coriander (*Coriandrum sativum* L.) is a plant among others which improve blood circulation to the head, impart mental concentration and memory capabilities. Coriander, both its leaves and its seeds are grown as spice group all over the world. The present investigation aims to clarify the role of coriander seed aqueous extract as a protective and therapeutic agent against neurodegenerative disorders and Alzheimer's disease induced by  $AlCl_3$  on the pyramidal cells in cerebral cortex of male albino rats. 24 Adult male albino rats were divided into four groups 6 for each, control, (300mg/kg p.o)  $AlCl_3$  treated group for a month, (300mg/kg p. o.) $AlCl_3$  plus (0.5gm/kg p. o) aqueous seed coriander extract treated group for a month and (0.5gm/kg p. o.) aqueous seed coriander extract treated group after stopping aluminum chloride treatment each for a month. Specimens from cerebral cortex were processed for haematoxylin and eosin, toluidine blue and Nauta stains. Aluminum chloride treatment showed dilatation of blood capillaries and presence of many shrunken pyramidal cells, the cells are pale and chromatolytic, the fibers appear detached and irregular in thickness. Aluminum chloride and coriander treated group restore the pyramidal cells of the cerebral cortex to normal. The treatment with coriander for a month after stopping  $AlCl_3$  treatment restores the pyramidal cells to nearly normal. In conclusion coriander seedaqueous extract showing protection and an improvement in therapeutic action on pyramidal cells in cerebral cortex against neurodegenerative disorders and Alzheimer' disease induced by aluminum chloride treatment. [Enas, A..Khalil Study the Possible Protective and Therapeutic Influence of Coriander (*Coriandrum sativum* L.) Against Neurodegenerative Disorders and Alzheimer's disease Induced by Aluminum Chloride in Cerebral Cortex of Male Albino Rats. Nature and Science 2010;8(11):202-213] (ISSN: 1545-0740).

**Key words:** coriander, Alzheimer's disease, cerebral cortex, aluminum chloride, rat.

## 1. Introduction

Several studies have used aluminum to produce an animal model of neurotoxicity and Alzheimer's disease (1-3). Increased amounts of aluminum have been reported in brain of subjects suffering from Alzheimer's disease (4). Alzheimer's disease is a neurodegenerative and cause gradual memory loss (5). Aluminum might be gained from tap water either naturally, or through the treatment process as aluminum sulphate (1), from using aluminum containers and from aluminum – containing products (antacids, dialysis fluid and antiperspirants) (6,7). The repeated aluminum administration remarkably induced neurobehavioral changes (3).

Coriander (*Coriandrum sativum* L.) is a plant among others which improve blood circulation to the head, impart mental concentration and memory capabilities. Coriander, both its leaves and its seeds are grown as spice group all over the world. It has

hypotensive, hypolipidemic, hypoglycemic, anticancer, antioxidant and antiinflammation properties (8-11). The seeds contain an essential oil linalool. It is considered safe as an added food ingredient and has a potent antioxidant property (12, 13).

The present investigation aims to clarify the role of coriander seed aqueous extract as a protective and therapeutic agent against neurodegenerative disorders and Alzheimer's disease induced by  $AlCl_3$  on the pyramidal cells in cerebral cortex 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 for each. Control, (300mg/kg p. o.) aluminum chloride treated group, (300mg/kg p. o.) aluminum chloride + (0.5g/kg p. o.) coriander aqueous seed extract for another month after stopping 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 for 10 minutes and filtered. The filtrate was given to the rats in a dose 0.5g/kg equivalent to human therapeutic dose (14).

## 3. Histological study

Specimens from cerebral cortex 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  $\mu$ m thickness and stained with haematoxylin and eosin (15), others stained with toluidine blue (for Nissl's granules) (16) and with Nauta (for nerve cells and neuro fibers) (17).

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 (18). Differences between the group means were assessed using T-test.  $P \leq 0.05$  was considered significant and the percentage of change was calculated as follows:

$$\% = \frac{\text{Percentage of change} = \frac{\text{Data of treated} - \text{Data of control}}{\text{Data of control}} \times 100$$

## 4. Histological Results:

### Control group (Group 1)

Haematoxylin and eosin stained sections of the cerebral cortex showed the general histological structure of the cerebral cortex layers, the outer molecular layer (Mol), the outer granular layer (OGr), the outer pyramidal layer (OP), the inner granular layer (IG), the inner pyramidal with the large sized pyramidal cells (IP) and the polymorphic layer (MG) (Figure 1). In the inner pyramidal layer the neurons

appeared with large nuclei and basophilic cytoplasm ( $\uparrow$ ). The intercellular area (neuropil) ( $\uparrow\uparrow$ ) is occupied by glia cells ( $\leftrightarrow$ ) and blood vessels (arrow head) (Figure 2). Toluidine blue stained semithin sections showed the pyramidal cells with large vesicular nuclei and darkly stained cytoplasm containing Nissl's granules (Figure 3). Nauta stained semithin sections showed the cells and the fibers of the pyramidal layer. The fibers appear regular in thickness (Figure 4).

### Group II:

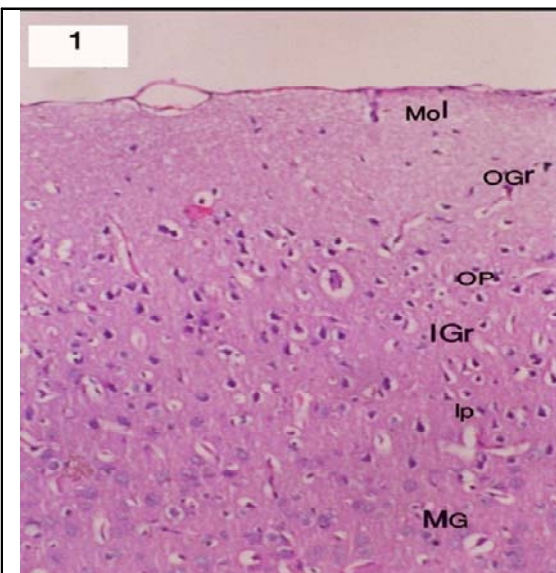
Group received orally 300mg/kg aluminum chloride for a month. H&E stained sections showed dilatation of blood capillary ( $\uparrow$ ) and shrunken many of the pyramidal cells ( $\leftrightarrow$ ) (Figure 5). Toluidine blue stained semithin sections showed displayed most of the nuclei of the pyramidal cells ill-defined chromatin and faintly stained cytoplasm without clear Nissl's granules (chromatolysis) ( $\uparrow$ ) with vacuolated neuropil (Figure 6). Nauta stained sections revealed reduced the number of pyramidal cells with detached neurofibers (Figure 7), disappearance of pyramidal cells with irregular in fibers thickness (Figure 8).

### Group III:

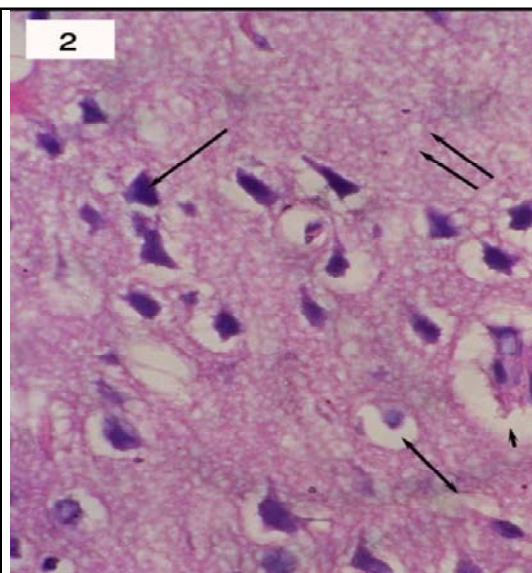
Group received 300mg/kg aluminum chloride + 0.5g/kg coriander seed aqueous extract for a month. H&E stained sections displayed restore the pyramidal cells to their normal structure (Figure 9). Toluidine blue stained semithin sections showed restore the pyramidal cells to their darkly stained cytoplasm containing Nissl's granules (Figure 10). Nauta stained sections revealed restore the pyramidal cells within neurofibers to normal (Figure 11).

### Group IV:

Group received 300mg/kg aluminum chloride for a month and administered 0.5 g/kg coriander seed aqueous extract for another month after stopping  $\text{AlCl}_3$  treatment. H&E stained sections displayed restore the pyramidal cells to nearly their normal structure (Figure 12). Toluidine blue stained semithin sections showed restore most of pyramidal cells to nearly their darkly stained cytoplasm containing Nissl's granules (Figure 13). Nauta stained sections revealed restore of the pyramidal cells within neurofibers nearly to normal (Figure 14).



Figure(1):A photomicrograph of a paraffin section from a control rat showing the general histological structure of the cerebral cortex layers, the outer molecular layer(Mol), the outer granular layer(OGr), the outer pyramidal layer(OP), the inner granular layer (IG),the inner pyramidal with the large sized pyramidal cells(IP) and the polymorphic layer(MG).H&E X200



Figure(2):A photomicrograph of a paraffin section from a control rat cerebral cortex showing the cells in the inner pyramidal layer the neurons appeared with large nuclei and basophilic cytoplasm (↑) . The intercellular area (neuropil)(↑↑) is occupied by glia cells (↔) and blood vessels (arrow head).H&EX1000

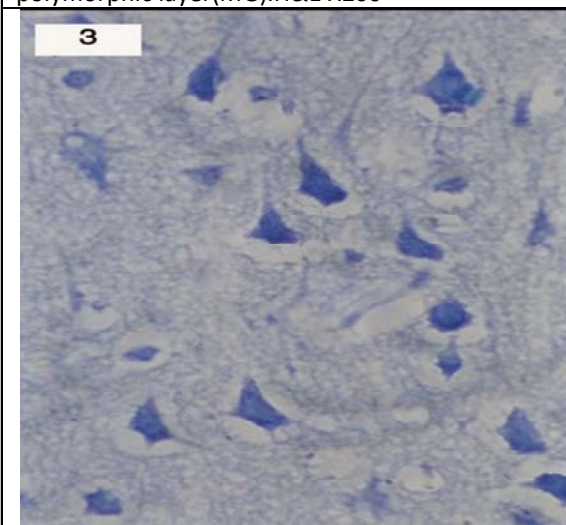


Figure3:A photomicrograph of a paraffin section from a control rat cerebral cortex showing the pyramidal cells with large vesicular nuclei and darkly stained cytoplasm containing Nissl's granules (T. B. X1000).

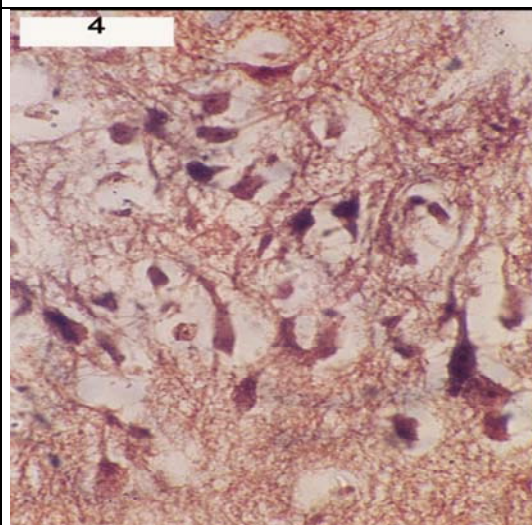


Figure4:A photomicrograph of a paraffin section from a control rat showing the cells and the fibers of the pyramidal layer. The fibers appear regular in thickness (Nauta stainX1000).

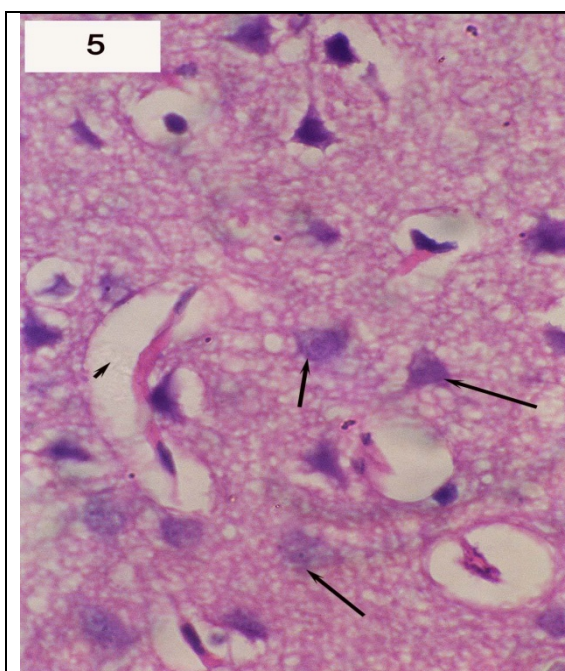


Figure 5: A photomicrograph of a paraffin section from a rat pyramidal layer administered 300mg/kg aluminum chloride for a month showing dilatation of blood capillary (↑) and shrunken many of the pyramidal cells (↔). (H&E X1000)

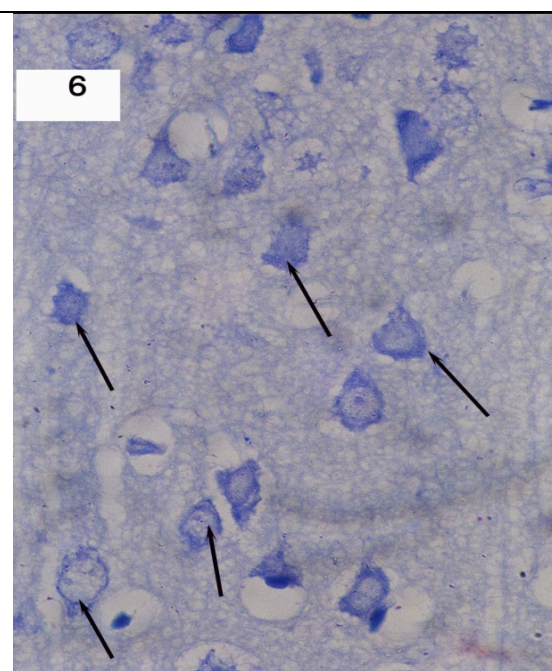


Figure 6: A photomicrograph of a paraffin section from a rat administered 300mg/kg aluminum chloride for a month showing most the nuclei of the pyramidal cells ill-defined chromatin and faintly stained cytoplasm without clear Nissl's granules (chromatolysis) (↑) with vacuolated neuropil. (T. B. X1000)

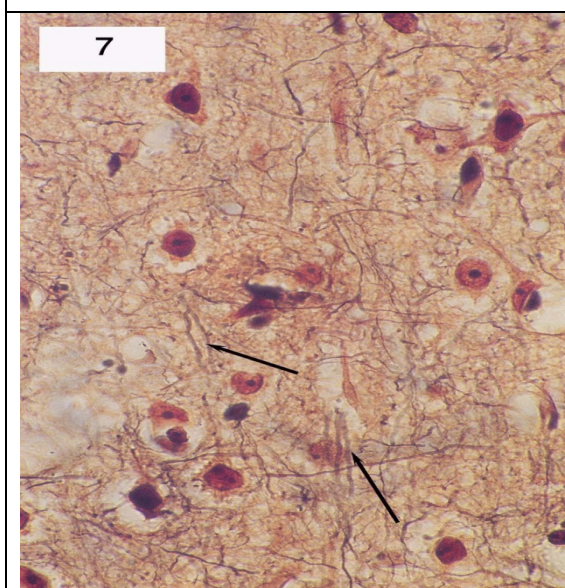


Figure 7: A photomicrograph of a paraffin section administered 300mg/kg aluminum chloride for a month showing less number of pyramidal cells, detached neurofibers with vacuolated neuropil. (Nauta stain X1000).

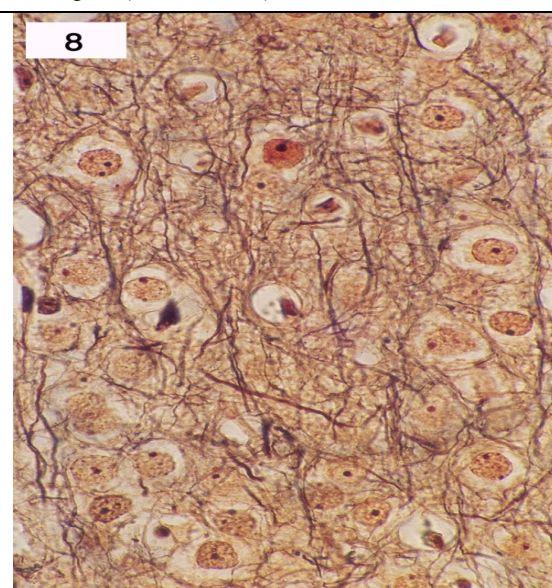


Figure 8: : Group received orally 300mg/kg aluminum chloride for a month showing disappearance of pyramidal cells with detached & irregular in fibers thickness. (Nauta stain X1000).

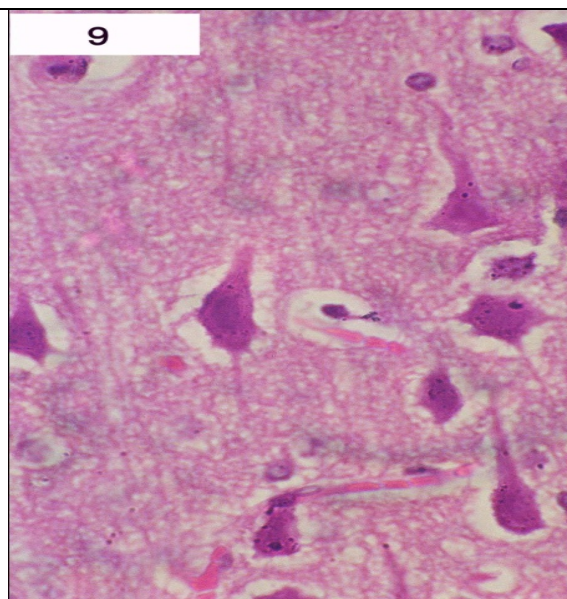


Figure9: A photomicrograph of a paraffin section from a rat pyramidal layer in cerebral cortex administered 300mg  $\text{AlCl}_3$  /Kg plus 0.5 gm Of coriander seed aqueous extract for a month showing restore the pyramidal cells to normal structure. (H&E X1000)

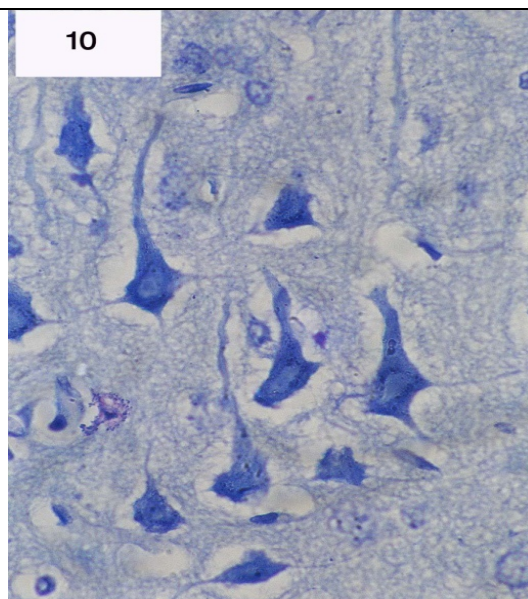


Figure10: A photomicrograph of a paraffin section from a rat pyramidal layer in cerebral cortex administered 300mg  $\text{AlCl}_3$  /Kg plus 0.5 gm of coriander seed aqueous extract for a month showing restore the Nissl's granules to normal. (T.B.X1000)

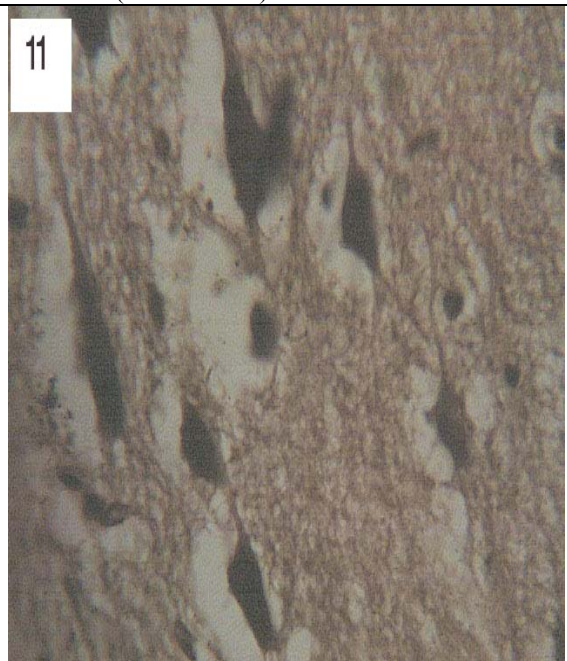


Figure11: A photomicrograph of a paraffin section from a rat pyramidal layer in cerebral cortex administered 300mg  $\text{AlCl}_3$  /Kg plus 0.5 gm Of coriander seed aqueous extract for a month showing restore the pyramidal cells within neurofibers nearly to normal. (H&E X1000)

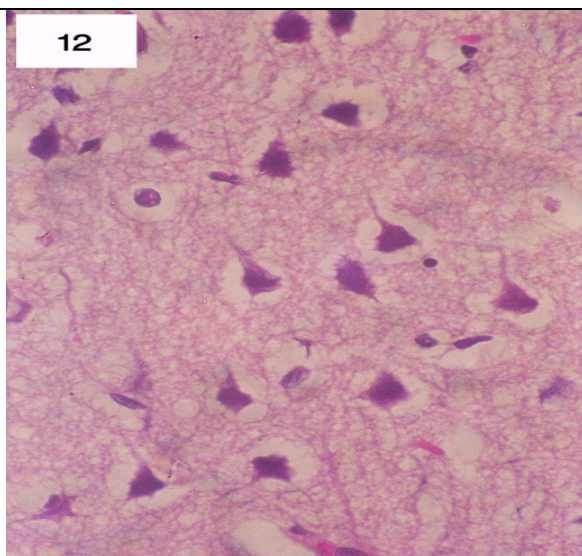


Figure12: A photomicrograph of a paraffin section from a rat pyramidal layer in cerebral cortex administered 0.5 gm of coriander seed aqueous extract for a month after stopping  $\text{AlCl}_3$  treatment showing restores most of the pyramidal cells to normal structure. (H&E X1000)

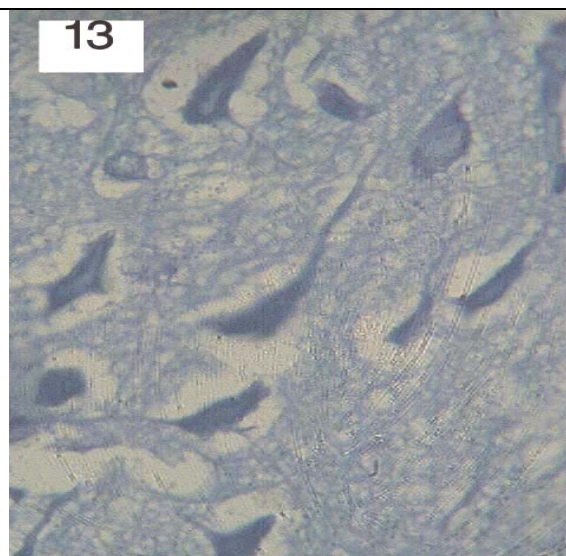


Figure13: A photomicrograph of a paraffin section from a rat pyramidal layer in cerebral cortex administered 0.5 gm of coriander seed aqueous extract for a month after stopping  $\text{AlCl}_3$  treatment showing restore most of the Nissl's granules to normal. (H&E X1000)

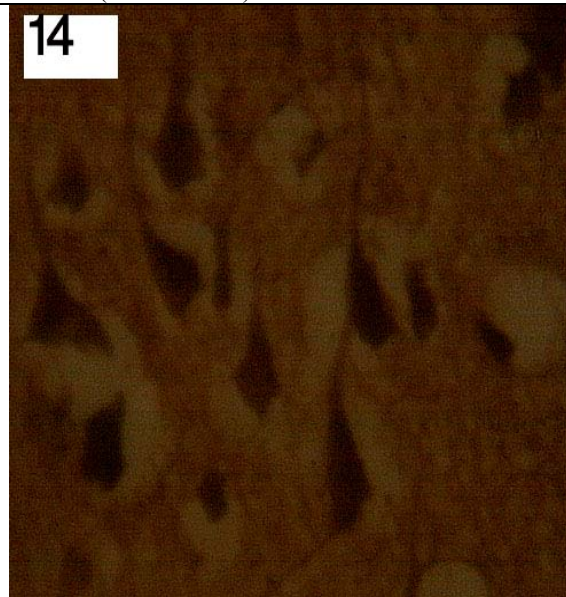
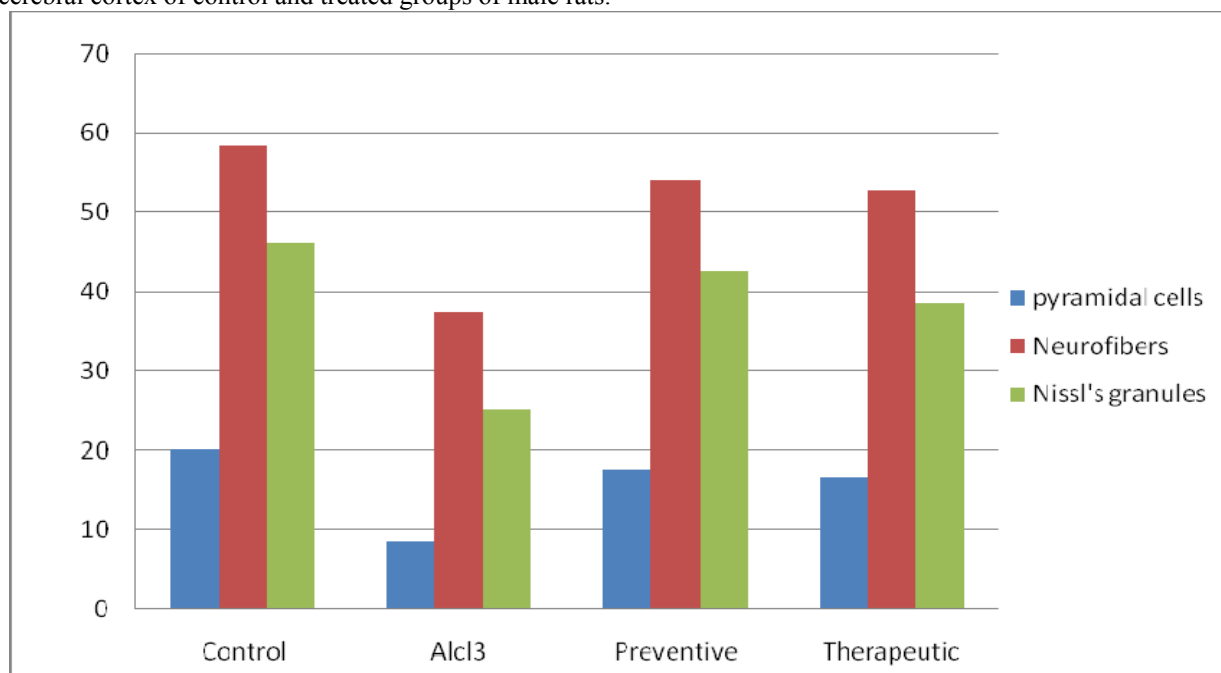


Figure14: A photomicrograph of a paraffin section from a rat pyramidal layer in cerebral cortex administered 0.5 gm of coriander seed aqueous extract for a month after stopping  $\text{AlCl}_3$  treatment showing restore many of the pyramidal cells within neurofibers nearly to normal. (H&E X1000)

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

	Statistical analysis	Control	Al Cl <sub>3</sub>	Protective	Therapeutic
Pyramidal cells	Average	20	8.5	17.5	16.67
	SD.	3.16	4.2	2.74	2.58
	Max.	25	15	20	20
	Min	15	3	15	12
	t test		5..27	1.43	1.95
	Probability		Highly reduced.	Non Sig.	Non Sig.
Neurofibers	Average	58.5	37.5	54	52.7
	SD.	4.73	5.24	3.74	3.88
	Max.	60	45	60	55
	Min	50	30	50	45
	t test		7.29	1.83	1.84
	Probability		Highly reduced	Non Sig	Non sig
Nissl' s granules	Average	46	25	42	40.33
	SD.	3.8	6.33	3.74	1.39
	Max	50	35	50	45
	Min	40	20	40	36
	T test		7	1.57	1.88
	Probability			Non Sig	Non Sig

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



$P \geq 0.01$  Highly Significant,  $P \geq 0.05$  Significant,  $P < 0.05$  Non significant

Analytical analysis referred that aluminum chloride treated group displayed marked decrease in pyramidal cells, Nissl's granules and neurofibers. Meanwhile preventive and therapeutic groups revealed non significant decrease in pyramidal cells, Nissl's granules and neurofibers compared to control group.

## Discussion

Alzheimer's disease is characterized by progressive pathological changes in the brain that translate into clinical signs of decline in cognitive abilities (memory, concentration, orientation), functional abilities (shopping, preparing meals, getting dressed), mood, behavior, and finally physical

changes (stiffness, loss of the ability to walk, or smile). The pathological changes in the Alzheimer's brain include deterioration and loss of neurons (nerve cells) leading to brain atrophy (shrinkage). Aluminum toxicity and its symptoms mimic those of Alzheimer's disease (19, 20).

Aluminum is present in water as municipal water supplies treated with both aluminum sulphate and aluminum chloride. As well as in food as cans used for beverages, like colas and fruits drinks, beside aluminum containers increase the amount of toxic metal in food. Also in medications as antidiarrhea, eye drops used for treatment of glaucoma, vaccines and intravenous solution and in air born aluminum come from industrial sources or

increasing the frequency of use of antiperspirants(21-23,6,7).

In this investigation the over load of aluminum chloride to rats lead to neurotoxicity and Alzheimer's disease appeared as shrunken of pyramidal cells ,reduced number of the pyramidal cells, faintly stained cytoplasm (chromatolysis) indicated decreased mental concentration ,with detached neurofibers and irregular in thickness. These brain changes inducing by aluminum chloride administration were due to oxidative damage which contribute to disease pathogenesis and were in accordance with (24, 4, and 2).

Free radicals are normally held in balance by the body antioxidant defense system, but with an excessive amount of free radicals oxidative cell damage can occur. This oxidative damage may be due to immobilize reactive molecules in the brain cells and increases rate of lipid peroxidation with the release of free radicals inside the neurons (25, 26). As well as it was reported that oxidative stress is an early event in Alzheimer's disease, proximal to the development of hallmark pathologies; it likely plays an important role in the pathogenesis of the disease. Investigations into the cause of such oxidative stress show that interactions between abnormal mitochondria and disturbed aluminum cation metabolism are, at least in part, 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 leads to the decrease in the substance secreted by neurons that send messages to other neurons and this appears to disconnected areas of the brain that normally 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 (27).

Dietary antioxidants cooperate with the body enzymes to protect the brain from free radical damage. Coriander (*Coriandrum sativum*) is a plant among others which improve blood circulation to the head, impart mental concentration and memory capabilities. It has free radical scavenging and lipid peroxidation activities (28). Also it has a potent antioxidant and low or no side effects, increase antioxidant enzymes, hypoglycemic, antibacterial and antifungal (29-33). As well as the antioxidant activity of coriander could protect liver from oxidative damage induced by  $\text{CCl}_4$  (34), and from lead induced testis oxidative damage (35).

The potent antioxidant activity of coriander seed aqueous extract, its ability to increase antioxidant enzymes and to promote oxygen to the brain could prevent oxidative damage caused by interaction between aluminum cation and unstable oxygen from abnormal mitochondria and protect pyramidal cells in cerebral cortex against damage induced by aluminum chloride overload. Meanwhile coriander seed aqueous extract could provide some protective mechanism after stopping aluminum chloride and proved an improvement in the therapeutic action.

In conclusion coriander seed aqueous extract showing protection and an improvement in therapeutic action on pyramidal cells in cerebral cortex against neurodegenerative disorders and Alzheimer's disease induced by aluminum chloride treatment.

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