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**RESEARCH ARTICLE**

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# ALUMINIUM-INDUCED BRAIN OXIDATIVE STRESS IN MALE RATS AND THE POSSIBLE AMELIORATING ROLE OF OMEGA-3

**ABSTRACT:**

The present study was designed to investigate oxidative stress of aluminium (Al)-induced brain toxicity in rats and extended to investigate the possible ameliorating role of Omega -3 fatty acids. Forty eight male albino rats weighing 130 ± 10 g BW were assigned to 8 groups (6 each) as follows: normal control group; $AlCl_3$ group (100 mg /kg BW); wheat germ oil group, Omega-3 low or high doses. The three other groups were given $AlCl_3$ in addition to wheat germ oil, Omega -3 low dose or Omega -3 high dose respectively. Rats were administered their respective dose daily, for 90 days (6 days a week). The results revealed that the levels of thiobarbituric acid reactive substances (TBARS) and protein carbonyl (PC) were significantly increased, while the activities of superoxide dismutase (SOD) and catalase (CAT), as well as the reduced glutathione (GSH) content were significantly decreased in the cerebral cortex (Co) and hippocampus (Hip) of rats intoxicated with $AlCl_3$. Moreover, the lipid profile; total lipids (TL), total cholesterol (TC) and triglycerides (TG) were significantly increased in serum and the mentioned brain regions, while the levels of phospholipids (PL), total protein (TP) and serum HDL-C were significantly decreased in $AlCl_3$ group. Additionally, serum and brain alkaline phosphatase (ALP) and acid phosphatase (ACP) activities were significantly increased. On the other hand, the results exhibited that, Omega -3 when given in low or high dose along with $AlCl_3$ was able to ameliorate the mentioned parameters in dose relating manner approaching them to the normal ranges. It can be concluded that Al neurotoxicity may be attributed to Al-induced oxidative stress and inhibition of the antioxidant system, and consequently to the impaired lipid profile, total protein and enzyme activities. Furthermore, the results suggested that the Omega-3 in particular the high dose could be able to antagonize Al neurotoxicity perhaps by its antioxidant properties.

**KEY WORDS:**

Aluminium chloride, Alzheimer's disease, Omega-3, oxidative stress, Antioxidants.

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## INTRODUCTION:

Aluminium metal is abundantly present in the earth's crust. From the environment it gets access to the human body via the gastrointestinal and the respiratory tracts (Yokel, 2000). Despite Al abundant presence and wide exposure, the metal has no known biological role. Investigations show that Al compounds can reach systemic circulation via different routes such as through ingestion (Yokel and McNamara, 2001), dermal absorption (Flarend *et al*., 2001) resulting in a continuous exposure of the metal to the biological system (Flarend *et al*., 1997).

Aluminium is a highly neurotoxic element and has been reported to play a role

in degeneration of nerve cells in the brain of human and experimental animals (Linton et al., 1987) and proposed as an environmental factor that may contribute to some neurodegenerative diseases, and affects several enzymes and other biomolecules relevant to Alzheimer's disease (Domingo, 2006). Indeed, the brain is a target of Al toxicity which can alter blood-brain barrier (BBB) mediating its transport to the brain (Zatta *et al*., 2002) and gets deposited in the cortex (Platt *et al*., 2001) and hippocampus (Struys-Ponsar *et al*., 1997) by altering the physiological ligands present at these barriers (Yokel and McNamara, 2001).

High aluminium exposure leads to increased central nervous system (CNS) Al concentrations that altered CNS concentrations of the essential trace elements; iron and manganese and increased the susceptibility of CNS to lipid peroxidation (LPO) (Fraga *et al*., 1990; Oteiza *et al*., 1993b) and increased lipid peroxidation and protein carbonyl group content in synaptosomal membranes of rats (Albendea *et al*., 2007). Moreover, Newairy *et al*. (2009) and Yousef (2004) reported that Al-induced changes in biochemical parameters, increased lipid peroxidation and decreased the activities of the antioxidant enzymes in rat plasma and rabbit brain.

Actually, the brain and other neural tissues are particularly rich in long-chain poly unsaturated fatty acids (PUFAs), which serve as specific precursors for eicosanoids that play important roles in normal CNS cells development and function (Gendron *et al*., 2005; Heird and Lapillone, 2005; Matsuoka *et al*., 2005). Omega-3 fatty acids are central components of glial and neuronal membrane phospholipids, and take part in brain membrane remodeling and synthesis, and in signal transduction (Rapoport, 2001). Fontani *et al*. (2005) have examined the effects of Omega-3 supplementation on some cognitive and physiological parameters in healthy subjects, and have found that Omega-3 supplementation is associated with an improvement of attentional and physiological functions, particularly those involving complex cortical processing. Raghu and Venkatesan (2008) reported that fish oil supplementation significantly reduced fasting serum concentrations of total cholesterol (10%), triacylglycerols (25%), VLDL-C was an increase in HDL cholesterol concentration (14%, $P < 0.01$). A number of epidemiologic studies suggest that a higher intake of fish oils is associated with a reduced risk of dementia later in life (Huang *et al*., 2005). The reduced risk is thought to be more specifically a result of the n-3 fatty acids, docosahexaenoic acid (DHA) or eicosapentaenoic acid (EPA), which are highly concentrated in fish (Schaefer *et al*., 2006). Kalmijn *et al*. (1997) initially reported that fish consumption was inversely related to incidence of dementia/AD. DHA administration exerts antioxidant activity as shown by increasing glutathione reductase activity and decreasing accumulation of lipid peroxide and ROS in the cortex and hippocampus of Alzheimer Disease (AD) model rats (Hashimoto *et al*., 2002).

## MATERIAL AND METHODS:

### Chemical:

Aluminium Chloride ($AlCl_3$) was obtained from agents of Sigma Chemicals (St. Louis, MO, USA). Omega-3 capsules (each capsule has 300 mg EPA, 700 mg DHA and 100mg wheat germ oil) and wheat germ oil were obtained from pharmacy in mansoura city. All other chemicals were purchased locally and were of analytical reagent grade.

This study was carried out on 48 adult male albino rats weighing 130 ± 10 g BW, supplied by The Urology and Nephrology Center; Mansoura University. The rats were maintained under controlled humidity; temperature (25 ± 2˚C) and light (12h light/ 12h dark). They were fed standard commercial rodent pellet diet and water *ad libitum* (free access to water and food).

### Experimental Protocol:

After one week of acclimatization, the rats were divided into 8 groups consisting of 6 animals each. All treatments were continued for 90 days as follows:

1- Normal control group (no treatment).
2- Wheat germ oil group.
3- Omega -3 fatty acids low dose (given orally by stomach tube as 0.4 g/kg BW) (Songur *et al*., 2004)
4- Omega -3 fatty acids high dose (given orally by stomach tube as 0.8 g/kg BW)
5- Aluminium (Al) group (mixed with diet as 100 mg $AlCl_3$/ kg BW) (Bilkei-Gorzó, 1993).
6- Al and Wheat germ oil group (treated as in groups 5 and 2, respectively).
7- Al and Omega-3 low dose extract group (treated as in groups 5 and 3, respectively).
8- Al and Omega-3 high dose group (treated as in groups 5 and 4, respectively).

### Sample preparation:

At the end of the experimental period, overnight-fasted animals were decapitated, blood samples were collected and sera were separated and stored at -20°C until biochemical assay. The brain was then gently removed; the cerebral cortex and hippocampus were separated on an ice-chilled glass plate as described elsewhere (Nayak and Chatterjee, 2001). The tissue samples were quickly frozen on dry ice, weighed, and stored at -80°C in refrigerator until biochemical assay. Cortex and hippocampus were chosen for the present study

because aluminium affects more severely the cortex and hippocampus regions than any other area of the central nervous system (Urano *et al*., 1997). Also, these brain regions are known to be particularly susceptible in Alzheimer's disease, and have an important role in learning and memory functions (Bihaqi *et al*., 2009).

**Biochemical analysis:**

Determination of lipid peroxidation product thiobarbituric acid reactive substances (TBARS) was carried out according to the method of (Ohkawa *et al*., 1982). Meanwhile, protein carbonyl was measured spectrophotometrically according to the method of (Smith *et al*., 1991). On the other hand, superoxide dismutase (SOD) and catalase (CAT) activities were determined following the methods of (Nishikimi *et al*., 1972) and (Bock *et al*., 1980), respectively. Additionally, reduced glutathione (GSH) content was determined spectrophotometrically according to the method of (Prins and Loose, 1969). The levels of alkaline phosphatase (ALP), acid phosphatase (ACP), total protein (TP), total lipids (TL), phospholipids (PL), triglycerides (TG), total cholesterol (TC) in serum, cortex and hippocampus and serum HDL cholesterol were determined by using commercial kits from (Biodiagnostic, 29 Tahreer St., Dokki, Giza, Egypt).

**Statistical analysis:**

Data were presented as means ± standard error (SE). The statistical analysis was performed with one-way analysis of variance (ANOVA) using SPSS (version 17) software package for Windows followed by *Dunken test*. A p-value of less than 0.05 was considered statistically significant.

## RESULTS:

As observed in table 1, the obtained results showed that the level of cortex and hippocampus TBARS was significantly increased in animals intoxicated with Al in comparison with the control value. Wheat germ oil and Omega-3 doses administration to rats intoxicated with Al caused a significant reduction in the elevated cortex and hippocampus TBARS concentration compared to Al intoxicated group. Low and high Omega-3 doses administration to rats intoxicated with Al caused a significant reduction in the elevated cortex and hippocampus TBARS concentration compared to Al and wheat germ oil group. Comparing low dose and high dose on Al treated rats, the result showed that high dose of Omega-3 caused a significant reduction in the elevated cortex and hippocampus TBARS concentration.

Table 1. Cortex (CO) and Hippocampus (Hippo) Lipid Peroxidation (LPO) concentration (n mol /g tissue), Protein Carbonyl (PC) concentration (µmol DNPH/g tissue), Catalase activities (CAT) (µmol/sec./g.), superoxide dismutase (SOD) activities (U/min/g wet tissue)and reduced glutathione (GSH) content (mg /g tissue)

| | | Animal Groups | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Con. | W | L | H | Al | Al + W | Al + L | Al + H |
| CO. LPO | Mean ±SE | 217.0 ±1.9 | 223.17 ±3.15 | 216.5 ±2.7 | 214.5 ±3.12 | 330.7[a] ±3.05 | 299[ab] ±2.93 | 274.3[abc] ±2.42 | 256.8[abcd] ±2.80 |
| Hippo. LPO | Mean ±SE | 122.1 ±2.7 | 122.2 ±2.8 | 118.5 ±3.69 | 117.8 ±2.5 | 318.1[a] ±2.7 | 281.3[ab] ±3.12 | 229.2[abc] ±5.8 | 183.5[abcd] ±4.12 |
| CO. PC. | Mean ±SE | 0.135 ±0.01 | 0.136 ±0.010 | 0.121 ±0.01 | 0.121 ±0.01 | 0.618[a] ±0.02 | 0.482[ab] ±0.019 | 0.363[abc] ±0.013 | 0.256[abcd] ±0.012 |
| Hippo. PC. | Mean ±SE | 0.23 ±0.006 | 0.23 ±0.016 | 0.22 ±0.01 | 0.21 ±0.013 | 0.66[a] ±0.016 | 0.54[ab] ±0.015 | 0.24[bc] ±0.031 | 0.22[bc] ±0.010 |
| CO. CAT | Mean ±SE | 4.2 ±0.06 | 4.13 ±0.049 | 4.23 ±0.07 | 4.27 ±0.07 | 0.83[a] ±0.049 | 1.34[a] ±0.056 | 2.45[abc] ±0.062 | 3.22[abcd] ±0.060 |
| Hippo. CAT | Mean ±SE | 4.93 0.067 | 4.92 0.060 | 5.03 0.07 | 5.13 0.07 | 1.0[a] 0.026 | 1.01[a] 0.180 | 4.63[bc] 0.187 | 4.80[bc] 0.171 |
| CO. SOD | Mean ±SE | 141.3 ±1.7 | 142.6 ±1.36 | 144 ±1.44 | 144.6 ±1.15 | 77.7[a] ±1.09 | 91.5[ab] ±1.78 | 111.2[abc] ±2.99 | 126.2[abcd] ±1.47 |
| Hippo. SOD | Mean ±SE | 153.8 ±1.08 | 155.80 ±1.35 | 155.0 ±1.41 | 159.3 ±1.54 | 104.70[a] ±1.82 | 112.80[ab] ±1.45 | 150.17[bc] ±1.05 | 153.00[bc] ±1.41 |
| CO. GSH | Mean ±SE | 0.253 ±0.005 | 0.258 ±0.006 | 0.261 ±0.005 | 0.263 ±0.004 | 0.108[a] ±0.005 | 0.130[ab] ±0.004 | 0.163[abc] ±0.004 | 0.198[abcd] ±0.009 |
| Hippo. GSH | Mean ±SE | 0.250 ±0.007 | 0.260 ±0.003 | 0.256 ±0.008 | 0.271 ±0.007 | 0.108[a] ±0.005 | 0.145[ab] ±0.004 | 0.175[abc] ±0.008 | 0.216[abcd] ±0.004 |

Results are presented as means ± SE (n = 6)

S: Significant change at $P < 0.05$, a: Compared to control untreated, b: Compared to Al, c: Compared to Al + W, d: Compared to low dose, W: Wheat germ oil, Al: Aluminium, L: Omega-3 low dose, H: Omega-3 high dose

There was a highly dramatic significant increase in cortex and hippocampus protein carbonyl (PC) conc. of Al intoxicated group compared to normal control group. Wheat germ

oil and either of the two Omega-3 doses administration to rats intoxicated with Al caused a significant decrease in the cortex and hippocampus PC conc., compared to the Al intoxicated group. Also the two Omega-3 doses administration to rats intoxicated with Al caused a significant decrease in the cortex and hippocampus PC conc. compared to Al and wheat germ oil group. Comparing low dose and high dose on Al treated rats, the result showed that the high dose significantly decreased the cortex PC conc. The obtained results in table 1 explain a significant decrease in cortex and hippocampus CAT and SOD activities in Al intoxicated animal group compared to the normal control one. The two Omega-3 doses administration to rats intoxicated with Al caused a significant increase in the cortex and hippocampus CAT and SOD activity, compared to the Al intoxicated group and Al and wheat germ oil group. A significant reduction was observed in cortex and hippocampus in GSH contents of Al intoxicated group when compared to the normal control group. On the other hand, wheat germ oil and either of the two Omega-3 doses administration to rats intoxicated with Al caused a significant increase in the cortex and hippocampus GSH contents, compared to the Al intoxicated group. Comparing low dose and high dose on Al treated rats; the result showed that high dose of Omega-3 significantly increased the cortex and hippocampus GSH contents. Comparing low dose and high dose on Al treated rats; the result showed that high dose significantly increased the cortex CAT activity.

The obtained results in table 2 revealed a significant increase in the contents of serum total lipid, total cholesterol and triglycerides. However, phospholipids and HDL levels were significantly decreased in Al intoxicated animal group compared to the normal control one. On the other hand, Wheat germ oil and Omega-3 doses administration to rats intoxicated with Al caused a significant decrease in serum levels of total lipid, total cholesterol and triglycerides compared to the Al intoxicated group. Meanwhile, the serum levels of phospholipids and HDL were significantly increased in same previous groups. The result showed that treatment of animals with both Al and either low or high dose of Omega-3, significantly decreased serum levels of total lipid, total cholesterol and triglycerides compared to the Al and wheat germ oil group. Meanwhile, phospholipids and HDL contents were significantly increased in the same previous groups. Comparing low dose and high dose of Omega-3 on Al treated rats, the result showed that high dose of Omega- 3 significantly decreased triglycerides level while significantly increased the level of phospholipids.

Table 2. Serum, cortex, and hippocampus Total lipids(TL), Total cholesterol(TC), Triglycerides(TG), Phospholipids (PL) concentrations and serum high density lipoprotein cholesterol (HDL) concentration

| | | | Animal Groups | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Con. | W | L | H | Al | Al + W | Al + L | Al + H |
| Serum (mg/dl) | TL | Mean ±SE | 467.9 ±9.62 | 488.7 ±3.84 | 487.1 ±6.15 | 484.3 ±11.8 | 749.4$^{a}$ ±4.84 | 695.2$^{ab}$ ±3.97 | 497.2$^{bc}$ ±5.04 | 494.2$^{bc}$ ±3.75 |
| | TC | Mean ±SE | 132.1 ±2.03 | 132.3 ±1.43 | 131.1 ±2.50 | 130.3 ±2.03 | 180.36$^{a}$ ±0.954 | 165.7$^{ab}$ ±1.71 | 133.83$^{bc}$ ±0.872 | 133.33$^{bc}$ ±0.557 |
| | TG | Mean ±SE | 90.3 ±0.97 | 89.8 ±1.21 | 88.2 ±1.20 | 85.91 ±0.68 | 132.7$^{ab}$ ±1.18 | 113.40$^{ab}$ ±1.55 | 102.00$^{abc}$ ±0.905 | 90.67$^{bcd}$ ±0.71 |
| | PL | Mean ±SE | 106.3 ±2.09 | 106.7 ±1.38 | 112.3 ±1.4 | 110.7 ±2.36 | 76.3$^{a}$ ±2.41 | 75.5$^{ab}$ ±1.73 | 86.17$^{abc}$ ±2.49 | 96.5$^{abcd}$ ±2.67 |
| | HDL | Mean ±SE | 48.33 ±0.56 | 49.16 ±1.27 | 51.00 ±0.81 | 51.16 ±0.74 | 23.50$^{a}$ ±1.45 | 30.00$^{ab}$ ±0.77 | 44.17$^{bc}$ ±1.13 | 44.66$^{bc}$ ±1.45 |
| Cortex(mg/g) | TL | Mean ±SE | 114.5 ±6.35 | 118.23 ±7.03 | 117.5 ±4.7 | 113.9 ±7.7 | 228.4$^{a}$ ±5.17 | 194.9$^{ab}$ ±1.94 | 170.5$^{abc}$ ±1.81 | 145.6$^{abcd}$ ±2.67 |
| | TC | Mean ±SE | 55.8 ±2.17 | 57.55 ±1.7 | 56.7 ±1.9 | 55.3 ±2.0 | 106.6$^{a}$ ±2.9 | 90.89$^{ab}$ ±4.5 | 77.53$^{abc}$ ±1.5 | 69.25$^{abc}$ ±1.8 |
| | TG | Mean ±SE | 47.6 ±2.4 | 48.5 ±1.59 | 47.9 ±3.13 | 45.34 ±2.56 | 95$^{a}$ ±1.24 | 83.7$^{ab}$ ±2.92 | 67.3$^{abcd}$ ±0.94 | 59.5$^{abc}$ ±1.41 |
| | PL | Mean ±SE | 11.94 ±0.14 | 12.13 ±0.06 | 12.25 ±0.06 | 12.19 ±0.051 | 7.24$^{a}$ ±0.021 | 8.39$^{ab}$ ±0.048 | 9.49$^{abc}$ ±0.075 | 10.61$^{abcd}$ ±0.048 |
| Hippocampus (mg/g) | TL | Mean ±SE | 48.4 ±0.23 | 48.4 ±0.26 | 47.5 ±0.18 | 47.5 ±0.16 | 106.7$^{a}$ ±1.54 | 95.4$^{ab}$ ±1.69 | 79.9$^{abc}$ ±1.23 | 66.2$^{abcd}$ ±1.55 |
| | TC | Mean ±SE | 21.6 ±0.53 | 21.8 ±0.43 | 20.6 ±0.47 | 19.7 ±0.32 | 60.8$^{a}$ ±0.73 | 53.3$^{ab}$ ±1.08 | 42$^{abc}$ ±0.36 | 36.2$^{abcd}$ ±0.23 |
| | TG | Mean ±SE | 20.9 ±0.29 | 20.4 ±0.32 | 20 ±0.22 | 20 ±0.21 | 37.7$^{a}$ ±0.44 | 32.2$^{ab}$ ±0.56 | 28.6$^{abc}$ ±0.15 | 25.6$^{abcd}$ ±0.26 |
| | PL | Mean ±SE | 4.45 ±0.08 | 4.51 ±0.082 | 4.6 ±0.06 | 4.57 ±0.06 | 2.7$^{a}$ ±0.027 | 3.01$^{ab}$ ±0.076 | 3.95$^{abc}$ ±0.056 | 3.47$^{abcd}$ ±0.049 |

Results are presented as means+ SE (n=6)

S: Significant change at $P < 0.05$, a: Compared to control untreated, b: Compared to Al, c: Compared to Al + W, d: Compared to low dose, W: Wheat germ oil, Al: Aluminium, L: Omega-3 low dose, H: Omega-3 high dose

Also the obtained results in table 2 declared a significant increase in the cortex and hippocampus contents of total lipid, total cholesterol and triglycerides. However, phospholipids level was significantly decreased in Al intoxicated animal group compared to the normal control one. On the other hand, Wheat germ oil and Omega-3 doses administration to rats intoxicated with Al caused a significant decrease in cortex total lipid, total cholesterol and triglycerides levels compared to the Al intoxicated group. Meanwhile, the level of phospholipids was significantly increased in same previous groups. The result also showed that the treatment of animals with both Al and either low or high dose of Omega-3 significantly decreased the cortex levels of total lipid, total cholesterol and triglyceride compared to the Al and wheat germ oil group. Meanwhile, phospholipid levels were significantly increased in the same previous groups. Comparing low dose and high dose of Omega-3 on Al treated rats, the result showed that the high dose significantly decreased total lipid content and significantly increased the phospholipids level.

As seen in table 3 the serum, cortex and hippocampus total protein contents showed significant decreases in Al intoxicated animals compared to the normal control group. On the other hand, wheat germ oil and the two Omega-3 doses administration to rats intoxicated with Al caused a significant increase in the Serum, cortex and hippocampus SOD activity, compared to the Al intoxicated group. The result showed that the treatment of animals with both Al and either low or high dose of Omega-3, significantly increased serum, cortex and hippocampus TP contents compared to the Al and wheat germ oil group. Comparing low dose and high dose on Al treated rats, the result showed that the high dose of Omega-3 significantly increased the serum, cortex and hippocampus TP contents.

Table 3. Serum, Cortex (CO) and Hippocampus (Hippo) Total Protein (TP) concentrations

| | | Animal Groups | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Con. | W | L | H | Al | Al + W | Al + L | Al + H |
| Serum TP (mg/dl) | Mean ±SE | 7.66 ±0.07 | 7.76 ±0.111 | 7.98 ±0.06 | 8.06 ±0.13 | 3.71 [a] ±0.047 | 4.45 [ab] ±0.117 | 4.96 [abc] ±0.080 | 5.9 [abcd] ±0.147 |
| Co. TP (mg/g) | Mean ±SE | 2.72 ±0.06 | 2.71 ±0.048 | 2.81 ±0.07 | 2.86 ±0.08 | 1.08 [a] ±0.043 | 1.37 [ab] ±0.027 | 1.72 [abc] ±0.088 | 2.11 [abcd] ±0.050 |
| Hippo. TP (mg/g) | Mean ±SE | 3.26 ±0.07 | 3.15 ±0.08 | 3.25 ±0.04 | 3.36 ±0.07 | 1.17 [a] ±0.028 | 1.56 [ab] ±0.020 | 1.9 [abc] ±0.054 | 2.4 [abcd] ±0.071 |

Results are presented as means+ SE (n=6)

S: Significant change at $P < 0.05$, a: Compared to control untreated, b: Compared to Al, c: Compared to Al + W, d: Compared to low dose, W: Wheat germ oil, Al: Aluminium, L: Omega-3 low dose, H: Omega-3 high dose

The estimated data concerning serum, cortex and hippocampus alkaline phosphatase activities in control and different animal treated groups were given in table 4.

Table 4. Serum, Cortex and Hippocampus Alkaline phosphatase (ALP) and Acid Phosphatase (ACP) Activities:

| | | Animal Groups | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Con. | W | L | H | Al | Al + W | Al + L | Al + H |
| Serum ALP | Mean ±SE | 131.2 ±1.31 | 128.7 ±1.98 | 125.8 ±1.11 | 125 ±1.21 | 219.2 [a] ±1.25 | 183.4 [ab] ±1.66 | 163.3 [abc] ±1.12 | 152 [abcd] ±1.24 |
| CO. ALP | Mean ±SE | 3.62 ±0.02 | 3.59 ±0.038 | 3.61 ±0.07 | 3.51 ±0.03 | 5.66 [a] ±0.057 | 5.35 [ab] ±0.04 | 4.85 [abc] ±0.027 | 4.34 [abcd] ±0.13 |
| Hippo. ALP | Mean ±SE | 4.12 ±0.06 | 4.02 ±0.10 | 3.98 ±0.09 | 3.90 ±0.06 | 7.09 [a] ±0.067 | 6.57 [ab] ±0.059 | 5.74 [abc] ±0.049 | 5.0 [abcd] ±0.067 |
| Serum ACP | Mean ±SE | 36.17 ±0.6 | 36.5 ±0.76 | 34 ±0.58 | 33.5 ±0.76 | 74.83 [a] ±0.87 | 66.67 [ab] ±1.26 | 54.5 [abc] ±0.76 | 46.83 [abcd] ±0.79 |
| CO. ACP | Mean ±SE | 7.68 ±0.03 | 7.62 ±0.057 | 7.65 ±0.05 | 7.56 ±0.05 | 10.78 [a] ±0.057 | 10.17 [ab] ±0.03 | 8.86 [abc] ±0.062 | 8.1 [abcd] ±0.03 |
| Hippo. ACP | Mean ±SE | 8.3 ±0.02 | 8.28 ±0.024 | 8.23 ±0.02 | 8.23 ±0.03 | 11.3 [a] ±0.049 | 10.96 [ab] ±0.057 | 8.43 [bc] ±0.11 | 8.42 [bc] ±0.13 |

Results are presented as means ± SE (n = 6)

S: Significant change at $P < 0.05$, a: Compared to control untreated, b: Compared to Al, c: Compared to Al + W, d: Compared to low dose, W: Wheat germ oil, Al: Aluminium, L: Omega-3 low dose, H: Omega-3 high dose

Concerning serum, cortex and hippocampus ALP activity, Al intoxicated rat group showed a significant increase compared to normal control group. Wheat germ oil and Omega-3 doses administration in concomitant to Al decreased the elevation of serum, cortex and hippocampus ALP activity, compared to the Al intoxicated animals. The result showed that the treatment of animals with both Al and either low or high dose of Omega-3, significantly decreased the serum, cortex and hippocampus ALP activity, compared to the Al and wheat germ oil group. Comparing low dose and high dose of Omega-3 on Al treated rats, the result showed that high dose of significant decreased the cortex and hippocampus ALP activity. The estimated data concerning serum, cortex and hippocampus acid phosphatase activities in control and different animal treated groups were given in table (4).Concerning serum, cortex and hippocampus ACP activities, Al intoxicated rat group showed a significant increase compared to normal control group. Wheat germ oil and Omega-3 doses administration in concomitant to Al decreased the elevation of serum, cortex and hippocampus ACP activities, compared to the Al intoxicated animals. The result showed that the treatment of animals with both Al and either low or high dose of Omega-3, significantly decreased the serum, cortex and hippocampus ACP activities, compared to the Al and Wheat germ oil group. Comparing low dose and high dose of Omega-3 on Al treated rats, the result showed that the high dose significantly decreased serum and cortex ACP activities.

## DISCUSSION:

The present study revealed that the administration of aluminium chloride to rats increased the levels of thiobarbituric acid reactive substances and protein carbonyl contents of the brain cortex and hippocampus. These results are similar to the data reported by Julka and Gill (1996a) and Yousef (2004) who indicated that Al intake by rabbits produces oxidative stress. Although aluminium is not a transition metal and therefore cannot initiate peroxidation, many investigations have searched for a correlation between Al accumulation and oxidative damage in the body tissues (Wilhelm *et al.*, 1996; Nehru and Anand, 2005). In fact, Al, a non-redox-active metal, is a pro-oxidant both *in vivo* and *in vitro* (Exley, 2004).) Similarly, significant increases in brain thiobarbituric acid reactive substances after stimulation by Al salts were reported by Nehru and Anand (2005). Aluminium is known to be bound by the $Fe^{3+}$ carrying protein transferrin thus reducing the binding of $Fe^{2+}$. The increase in free intracellular $Fe^{2+}$ causes the peroxidation of membrane lipids and thus causes membrane damage (Nehru and Anand, 2005). Moreover, mice chronically fed with this metal showed high levels of brain tissue lipid peroxidation (Fraga *et al.*, 1990). On the basis of the production of thiobarbituric acid reactive substances in animal brains (Fraga *et al.*, 1990) or brain subcellular fractions (Oteiza *et al.*, 1993) after treatment with Al salts. Aluminium administration also causes a significant increase in protein carbonyl content, a marker of protein oxidation and an index of oxidative stress (Butterfield and Lauderback, 2002).

Another possible mechanism involved in the peroxidative process relates to glutamate. Glutamic acid concentration was significantly increased by Al treatment. Cerebral accumulation of glutamic acid resulted from a blood-brain-barrier (BBB) modification by the Al (Deloncle *et al.*, 1999). Aluminium, as an L-glutamate complex, was able to cross the BBB produces alterations in it and increases its permeability (Deloncle *et al.,* 1990). Then, it was selectively deposited in different brain areas especially the striatum, hippocampus and occipito-parietal cortex (Deloncle *et al.*, 1999) distribute their functions. Glutamic acid accumulated after Al L-Glu treatment stimulated the N-methyl-D- aspartate (NMDA) receptors, which are particularly dense in the hippocampus (Monaghan and Cotman, 1985), leading to lipid peroxidation. It has been demonstrated that NMDA-receptor activation induces a neuronal increase in calcium (Villalba *et al.*, 1992) which activates phospholipase $A^2$ and facilites the release of arachidonic acid (Sanfeliu *et al.*, 1990). The metabolisation of this acid could lead to the production of oxygen free radicals (Lafon-Cazal *et al.*, 1993) and thus induce lipid peroxidation. Oxidative reactions inducing neuronal membrane alteration may have been implicated in the increase of dopamine uptake in hippocampal slices observed in rats after *in vitro* application or *in vivo* treatment with Al L-Glu (Huguet *et al.*, 1993).

In the present study, aluminium chloride treatment inhibited the enzymes involved in antioxidant defence, that is SOD and CAT and caused a significant decline GSH content of the hippocampus and cortex I brain of Al treated rats, which function as blockers of free radical processes. The results are in accordance with the findings of Dua and Gill (2001) and Nehru and Anand (2005), who observed a significant decrease in the activities of SOD and CAT in rat brain after Al treatment. Similarly, intragastrical exposure to Al resulted in 50% decrease in MnSOD activity in hippocampus and 30% in cerebral cortex of rat (Kumar *et al.*, 2009 a&b). The decrease in both enzyme activities could be the result of a reduced synthesis of the enzyme proteins as a result of higher intracellular concentrations of Al (Nehru and Anand, 2005).

The parallel reduction in SOD activity could be due to clearing the free radicals inside the cells and thus indicates a high degree of free radical production and LPO occurrence. The findings of the present study, also, showed that the rise in LPO in Al treated rats was accompanied by concomitant decrease in the activity of some antioxidant enzymes involved in the detoxification of ROS, namely SOD, CAT, as well as the level of GSH in the cortex and hippocampus tissues comparing with the control declaring the prooxidant effect of Al. These findings agreed with the antecedent studies of Savory *et al*. (2003), Johnson *et al*. (2005), and Orihula *et al*. (2005) who showed that Al exposure enhanced the neuronal lipid peroxidative damage with concomitant alterations in the enzymatic antioxidant defense status, thus having serious bearing on the functional and structural development of the central nervous system (Dua and Gill, 2001). Similar data recorded a decrease in the antioxidants such as GSH level (Wu and Cederbaum, 2003) and SOD activity in the brain of Al exposed, rabbits (Yousef, 2004) rats (Chainy *et al*., 1996) and human (Dua and Gill, 2001).

Moreover, such results are consistent with earlier studies that have indicated that Al intake produced an oxidative stress-related change, contributed to its neurotoxicity (Flora *et al*., 2003). However, in rats, a significant relationship between Al exposure and the presence of oxidative stress was established also by Esparza *et al*. (2005) and Gómez *et al*. (2005). This could be caused by inflicting damage to membrane lipids, and proteins and anti-oxidative enzyme defense system (Jyoti *et al*., 2007).

The elevation of LPO in the cortex and hippocampus in the present study and other ones (Dua and Gill, 2001) suggested participation of free-radical-induced oxidative cell injury in mediating neurotoxicity of Al. Lipid peroxidation of biological membranes results in the loss of membrane fluidity, changes in membrane potential, an increase in membrane permeability and alterations in receptor functions (Albendea *et al*., 2007).

However, the increased Al concentration could deleteriously affect the neurons, leading to depletion of antioxidants and metal ions (Kumar *et al*., 2008) through the induction of free radicals, that exhausting SOD and CAT which function as blockers of free radical processes. These results are in accordance with (Nehru and Anand, 2005) who recorded a significant decrease in the activities of SOD and CAT in brain of rats after Al treatment. Alternatively, the decreased enzyme activities could be related to a reduced synthesis of the enzyme proteins as a result of higher intracellular concentrations of Al (Albendea *et al*., 2007).

The data obtained by the present study illustrated, further, that the administration of Omega-3fatty acids to Al treated rats caused a significant decrease in the level of TBARS and protein carbonyl in the cerebral cortex and hippocampus but elevated the SOD and CAT enzymes activities and GSH contents when compared with Al intoxicated rats.

Similarly ,The dietary supplementation with PUFAs or its chronic administration shortly prior to a severe ischemic insult may ameliorate some of the symptoms associated with cerebral injury probably by increasing antioxidative capacity, lowering lipid peroxidation, inducing chaperon molecules or stabilizing membrane integrity (Choi-Kwon *et al*., 2004; Cao *et al*., 2007). Such results were confirmed by the studies of Kondo *et al*. (1997) and Kim *et al*. (2002) that showed that SOD deficiency exacerbated cerebral infarction and that chronic daily administration of DHA for 6 weeks increased SOD activity and elevated reduced GSH, leading to effective reduction of the brain lipid peroxidation product (MDA).

Regarding oxidative stress, it is possible that chronic administration of PUFAs may make the brain more vulnerable to lipid peroxidation, thus inducing antioxidative defense capacity and leading to elevated tolerance and protection against free-radical-induced injury (Innis, 2007; Cao *et al.,* 2008). This assumption was partly supported by the results of the present study.

Omega-3 fatty acids lowered TBARS production, superoxide anion secretion, and LDL peroxidation . One explanation is that the Omega-3 series, because of the position of their double bonds, is less susceptible to oxidative damage. Also, *in vivo* study Supari *et al*. (1995) showed that myocardia from fish oil-fed monkeys exhibited lower superoxide generation. Interestingly, DHA was shown to increase glutathione synthesis in the same cell type (Arab *et al*., 2006).

The present data indicated that serum, cortex and hippocampus total lipids, total cholesterol, and triglycerides, were significantly increased by Al ingestion, while phospholipids and serum HDL-C levels were decreased significantly. These results are in accordance with the results reported by Yousef (2004). Similarly, Wilhelm *et al*. (1996) reported that Al exposure can result in Al accumulation in the liver and this may lead to a disturbance of lipid metabolism and an elevation of serum cholesterol in rats. They suggested that long-term exposure to Al specifically altered the brain lipid/phospholipids metabolism and/or their transfer to various membrane systems and resulted in significant changes in phospholipid classes and in cholesterol contents of the rat brain. Also in monkeys Sarin *et al*. (1997) revealed an alteration of the lipid composition

and the activities of various membrane-bound enzymes. The authors added that Al was found to decrease significantly the phospholipids concentration in the primate brain. In addition, cholesterol and cholesterol/phospholipids ratios were shown to be remarkably increased, indicating a relevant loss of membrane integrity, and consequently a strong effect of Al on the activity/functionality of various membrane-bound enzymes, including AChE (Atack *et al*., 1983). Similarly, the long-term exposure to $AlCl_3$ was shown by Pandya *et al.* (2004) to result in a 60% decrease in the total phospholipids content while total cholesterol content increased by 55%. It is possible that this altered lipid /phospholipids content and composition could affect the insulation properties of the myelin. These finding may have some bearing on loss of short-term memory in Alzheimer's disease.

The increase in serum cholesterol and total lipids due to Al administration indicated a loss of membrane integrity (Sarin *et al.*, 1997). This was further confirmed when Al was found to have a significant effect on the various membrane-bound enzymes (Newairy *et al*., 2009). From the foregoing results it is clear that Al resulted in a significant reduction in the phospholipids content accompanied by major compositional changes, which is consistent with membrane hypothesis of AD (Wurtman, 1985). According to this hypothesis, in order to make up for the choline deficiency, the neurons try to extract choline from choline-containing phospholipids. These results lead to the disruption of cell membranes and ultimately to neuronal cell death (Roth *et al*., 1995).

The elevations in TL,TC together with the reduction of HDL-C following Al intoxication shown herein, represent risk factors for atherosclerosis and decreased blood flow to the brain (ischemia) which may be added to the mechanisms involved in Al-induced neurotoxicity.

On the other hand, the present study showed that treatment of rats with $AlCl_3$ plus Omega-3 decreased serum and brain total lipids, total cholesterol and triglycerides and enhanced phospholipids and serum HDL-C levels compared to $AlCl_3$ intoxicated group. These results are in agreement with Raghu and venkatesan (2008) who found that oral administration of Omega-3 or fish oil significantly lowered total cholesterol, triglycerides in serum of rats; and increased serum levels of HDL-C. Also, Lesan and Taziki (2005) showed that consumtion of Omega 3 for 3 months lowered the serum triglyceride. However, the efficacy of Omega-3 fatty acids has been demonstrated in the improvement of the lipidic pattern in myocardiaium (La Guardia *et al*., 2005) considered as anti lipidemic agent (studer *et al*., 2005) .The ameliorating effects of Omega-3 on the lipid profile may be attributed to the fact that Omega-3 fatty acids; EPA and DHA are the ones incorporated into neuronal phospholipids (Yuen *et al*., 2005) and DHA is an essential and sometimes rate-limiting precursor of the phosphatides in cellular membranes (yehuda *et al.,*1998). On other hand, DHA stimulates the expression of peroxisomal enzymes, that essential for plasmalogen synthesis, which in turn is essential for myelin formation, thus, DHA stimulates remyelination. Furthermore DHA is concentrated in membrane phospholipids at synapses (Roberts *et al*., 1998) and is decreased in the brain with AD (Guan *et al*., 1994; Lukiw *et al*., 2005) indicating its role in neurotransmission. However , the hypolipidimic action of Omega-3 may be attributed to its antioxidative effect (Supari *et al*., 1995) and lowering the generation of ROS with improving the scavenching ( Massaro *et al*., 2006), as well as enhancing the antioxidant status (Choi-Kwon *et al*., 2004), leading to stabilizing the membrane integrity (Cao *et al*., 2007) . Besides, n-3 potential the fluidity and neuroplasticity of the nerve membrane (Mazza *et al*., 2007) and consequently improve neurons functions. Additionally, it's noteworthy that the elevation of HDL-C and reduction of LDL-C shown by n-3 has a significant importance in the protection from atherosclerosis and heart disease, so improves the blood supply to organs including brain.

The present results revealed that aluminium chloride decreased serum, cerebral cortex and hippocampus total protein. The inhibitory effect of AlCl3 on protein profile is in agreement with the finding of Yousef (2004) who recorded a significant decrease in the concentrations of total proteins in rats treated with AlCl3 particularly the albumin which could be attributed on one hand to an under nutrition and on the other hand to a reduction of the protein synthesis in the liver (Cherroret *et al*., 1995)

Also, the decline in the levels of protein in Al-treated rats is in agreement with Chinoy and Memon (2001) and might be due to changes in protein synthesis and/or metabolism, as well as to reduce enzymes of protein synthesis as a result of higher intracellular concentration of Al (Tripathi *et al*., 2009).

These observed alterations could be attributed to direct or indirect effects of aluminium on protein synthesis and breakdown and interaction with neurotransmitter synthesis and degradation, through a series of reactions that depends on many enzymatic pathways and regulatory mechanisms (Goncalves and Silva, 2007). Furthermore, the decreased protein content may be associated with the increase rate of

protein oxidation as illustrated in the present work and other studies.

Alternatively, since GSH has been reported to be involved in protein and DNA biosynthesis so, the reduction in its content and in the antioxidant enzymes (SOD and CAT) resulted from Al intoxication may partly explain the decline in the total protein content (Kumar *et al*., 2009b).

Additionally, Al induced reactive oxygen species formation (Oteiza *et al*., 1993a) and promoted oxidative stress (Exley, 2004; Kumar *et al*., 2009a&b) enhancing peroxidative damage to lipids and proteins of the cellular membranes (Julka and Jill, 1996b; Jyoti *et al*., 2007) is another suggestion for protein decline. Actually exposure of proteins to free radicals leads to gross structural and functional modifications including protein fragmentation, formation of cross-links and aggregates, protein peroxides generation, and enzymatic oxidation and degradation or clearance (Albendea *et al*., 2007).

On the other side, the present results indicated that Omega-3 with two doses (400 or 800 mg/kg BW/day) enhanced the protein contents in serum and cerebral cortex and hippocampus of Al intoxicated rats reached them within or near the normal levels comparing to the control group.

In fact, proteins in the membrane bilayer have crucial cellular functions as they operate as receptors and transporters. Omega-3 fatty acids modify membrane fluidity by shifting cholesterol from the membrane (Yehuda *et al*., 1998), as it is required for neurotransmitter binding and signaling within the cell (Heron *et al*., 1980). The enhanced protein contents by Omega-3 administration may be attributed to reducing the oxidative stress (Coa *et al*., 2008) and improving the antioxidant enzymes and GSH (Arab *et al*., 2006), as well as enhancing the enzymes responsible for neurotransmitters synthesis or degradation. Calon *et al.* (2004) outlined that n-3 fatty acids are essential for selective protection of post synaptic proteins.

Also, the administration of EPA induces the expression of genes, and protects against memory deficit in AD model rats after its transformation into DHA. This is accompanied by the accumulation of DHA and/or an increase in the DHA/AA ratio in the corticohippocampal tissues, with a corresponding decrease in oxidative stress and an increase in the expression of synaptic plasticity- related proteins (Hashimoto *et al*., 2006).

An alternative mechanism of EPA induced amelioration of memory, as PUFAs, may be due to the increase in the expression of the FOS protein, the immediate early gene c-fos (which acts as a transcription factor and as a functional marker of neuronal activity) of the rat CA1 hippocampus (Kitajka *et al*., 2002; Tanabe *et al*., 2004).

The present study illustrated that Al ingestion led to a significant elevation in alkaline phosphatase (ALP) and acid phosphatase (ACP) activities in sera, cerebral cortex and hippocampus.

Alkaline phosphatase is a membrane-associated enzyme, which predominantly concentrated in the vascular endothelium in the brain. There is a more or less continuous sheath of ALP covering all internal and external surfaces of the central nervous system including the spinal cord and thus it may functionally be part in the blood-brain barrier mechanism (Nayak *et al*., 2006). Aluminium-induced damage in neurons increases the permeability of membranes thus increasing the ALP activity in the soluble portions of the nerve cells (Dasgupta and Ghosh, 1993).

Acid phosphatase activity was found to be increased compared to their respective control in response to aluminium exposure. Intracellular ACP is largely confined to lysosomes, which primarily respond to cellular injury (Dasgupta and Ghosh, 1993). Within the brain, ACP is found to be concentrated in the gray matter, although it shows the activity in the white matter also to some extent. However, significant contribution by Al was observed to induce changes in ACP activity.

The increased activity of ALP and ACP in serum and brain of animals treated with $AlCl_3$ is in accordance with the findings of Szilagyi *et al*. (1994); El-Sebae *et al*. (1997) and Ochmański and Barabasz (2000). Also El–Demerdash (2004) found that the activities of these enzymes were increased in plasma of mice fed on wheat containing Al residue of 0.2g /kg BW Further, Szilagyi *et al*. (1994) found that exposure to Al caused an increase in the activity of serum ALP and attributed it to increased osteoblastic activity, provoked by the disturbance of bone formation. In addition, Ochmański and Barabasz (2000) suggested that such increase in the activity of ALP or ACP in blood might be due to the necrosis of liver, kidney and lung (Sallam *et al*., 2005).

However, earlier observation recorded an alteration in the activities of specific lysosomal hydrolytic enzymes in non-neuronal (Laske *et al*., 1989) and neuronal tissues (Suzuki *et al*., 1988) in rats due to Al administration. From this observation it can be suggested that Al induced an increase in ACP activity of brain may be an indication of lysosomal proliferation. The elevated activity of lysosomal enzymes in various conditions was suggested to be due to increased synthesis of the enzymes that may be true for ACP also (Cohen, 1970; Hussain *et al*., 1990).

In the present work, administration of Omega-3, high dose and low dose caused a marked reduction in the elevated activities of

ALP and ACP in Al treated rats. Such decrease could be attributed to the antioxidant properties of Omega-3 constituents as through scavenging of free radicals (Massaro *et al.*, 2006), as well as its anti-inflammatory action and by protecting cellular membranes integrity from Al-induced oxidative damage and considered as an indication to the improved brain structure and function and its protection against Al toxicity.

## CONCLUOSION:

The results of the present study indicated that aluminium chloride was capable of causing pronounced alterations in some biochemical markers of oxidative stress and inhibited the antioxidant system, which may be concomitant to disturbances in the cerebral neurotransmitters balance and some histopathological changes associated with dementia of AD type especially in the cortex and hippocampus regions. In addition, Omega-3fatty acids proved to be beneficial in decreasing the levels of free radicals improving the antioxidant system, lipid profile, protein and neurotransmitter contents, as well as reducing the pathological alteration in the brains of Al intoxicated rats

Consequently, the study recommended that attention should be paid to reduce the sources of exposures to aluminium. The usage of diet rich in Omega-3 fatty acids could be beneficial in alleviating aluminium neurotoxicity and employed as additional to conventional medicine for treatment of neurodegenerative and psychotic disorders.

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# الإجهاد ألتأكسدي بالمخ المحدث بالألمنيوم في ذكور الجرذان وإمكانية الدور المحسن لأوميجا-3

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يهدف هذا البحث لدراسة مخاطر الضغط ألتأكسدي الذي يحدثه الألمنيوم بمخ ذكور الجرذان وكذلك لمعرفة مدي التأثير المحسن لأوميجا-3 علي تلك المخاطر. استخدم في هذه الدراسة ذكور الجرذان البالغة التي تزن في المتوسط 130±10جم حيث قسمت الي ثمانية مجموعات تضم كل منها 6 جرذان كما يلي : المجموعة الضابطة ؛ مجموعة معامله بزيت جنين القمح, مجموعتان معامله بزيت أوميجا-3 بجرعتين ا( 0.4 جم/ كجم و 0.8 جم/ كجم من وزن الجسم علي التوالي)ثم مجموعة معامله بالألمنيوم مخلوطا بالطعام بجرعة قدرها 100 مجم/كجم من وزن الجسم وهناك ثلاثة مجموعات أخرى معامله بالألمنيوم بالإضافة إلى زيت جنين القمح أو زيت أوميجا-3 بالجرعتين المذكورتين سابقا. أظهرت نتائج هذا البحث زيادة في مستوي نواتج التأكسد الفوقي للدهون وكذلك مستوى البروتينات المؤكسدة في كل من قشرة المخ وكذلك الحصيين في الوقت الذي نقص فيه نشاط الإنزيمات المضادة للأكسدة (SOD,CAT) وكذلك محتوي (GSH) وصحب ذلك ارتفاع ملحوظ في مستوي الدهون الكلية و الكوليسترول الكلي والجليسريدات الثلاثية في مصل الدم وقشرة المخ وكذلك الحصيين كما سجل انخفاض في الدهون الفوسفوريه و مستوي الدهون البروتينية ذات الكثافة العالية (HDL-C) في مصل الدم ومحتوي البروتين في مصل الدم وقشرة المخ وكذلك الحصيين. علي العكس من ذلك ارتفاع ملحوظ في كل من إنزيمي الفوسفاتيز القاعدي (ALP) و ألحامضي (ACP) في مصل الدم وقشرة المخ وكذلك الحصيين وكان ذلك في المجموعة التي تعرضت للألمنيوم لمدة 90 يوما. وعلى الجانب الآخر أظهرت الدراسة أن استخدام أوميجا- 3خاصة الجرعة المرتفعة قد أحدثت تحسناً واضحاً في مستوى المعايير التي سبق الإشارة إليها وذلك بإحداث انخفاض في مستوي نواتج التأكسد الفوقي للدهون ومستوى البروتينات المؤكسدة وتحسن في مستوي الإنزيمات المضادة للأكسدة (SOD, CAT) ومحتوي الجلوتاثيون (GSH)وتحسن في صورة الدهون ومحتوي البروتينات الكلية وذلك مع ظهور تثبيط ملحوظ لنشاط إنزيمي الفوسفاتيز القاعدي (ALP) و الحامضى (ACP) . وخلاصة ما انتهت إليه النتائج هو إلقاء الضوء علي الدور الفعال لأوميجا-3 كمضاد فعال للأكسدة، ومقدرته علي القيام بالحماية من الشقائق الحرة، والحد من بعض التغيرات السلبية التي تنتج عن التعرض للألمنيوم لفترات طويلة.