Research Article

Antioxidant Effect of Alpha Lipoic Acid on Hepatotoxicity Induced by Aluminium Chloride in Rats

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ABSTRACT

The present study was planned to investigate the ameliorative effects of α-lipoic acid (α-LA) supplementation against aluminium chloride ($AlCl_3$) induced hepatotoxicity in rats. The results showed that rats consuming diets with $AlCl_3$ added had poor growth performance, and most serum hematological indexes were significantly altered compared to the control. Biochemical results showed that lipid peroxidation increased significantly in Al-treated rats, as evidenced by high liver malondialdehyde (MDA) levels. Alteration of the antioxidant system in treated group was confirmed by the significant decline of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) activities and reduced glutathione (GSH) content in liver. Moreover, $AlCl_3$ exposure induced an increase in the activities of the aspartate transaminase (AST), alanine transaminase (ALT), lactate deshydrogenase (LDH) and bilirubin levels, while albumin and total protein were significantly decreased. These results strongly suggest that aluminium affected antioxidant defence system and both haematological and biochemical parameters, co-administration of α-lipoic acid exerted a protective effect against aluminium induced oxidative stress.

Keywords: Aluminium chloride, Alpha-lipoic acid, Biochemical studies, Liver, Oxidative stress, Rat.

INTRODUCTION

Aluminium is very abundant metal in the earth's crust which constitutes 8.13%. It is a constituent of cooking utensils, medicines such as antacids, cosmetics such as deodorants, and food additives. Also it can be found in food especially corn, yellow cheese, salt, herbs, spices and tea. In addition, aluminium salts are widely used as flocculants in the treatment of drinking water for purification purposes.[1,2] Considering the large utilisation of aluminium in different fields, many available data reported that aluminium exposure increased recently, which have allowed its easy access into the body via gastrointestinal tract and lung tissue.[3] A several authors indicate that an excessive and prolonged aluminium exposure affects directly haematological and biochemical parameters, disturbs lipid peroxidation and attenuate the activities of the antioxidant enzymes in plasma and tissues of animals models especially rats and rabbits.[2,4,5] This impairment of the physiological prooxidant/antioxidant balance causes oxidative stress.

Lipoic acid (1, 2-dithiolane-3-pentanoic acid, LA) has been known for a long time as a cofactor of α-ketoacid dehydrogenases.[6,7] This compound is found naturally in our diets but it is synthesized in human cells. In vivo lipoic acid is rapidly converted into its reduced form, dihydrolipoic acid (DHLA).[8,10] Recent studies demonstrated that LA and dihydrolipoic acid can act as potent antioxidants. They can scavenge a number of free radicals both in hydrophilic and lipophilic phases of cell.[11,12] In addition, they were found to be capable of regenerating endogenous antioxidants in the body including Vitamin C, Vitamin E and intracellular reduced glutathione, therefore it has been proposed that both LA and dihydrolipoic acid are a therapeutic agents in the prevention or treatment of pathological conditions mediated via oxidative stress.[13,14] Because of the health problems induced by many environmental pollutants, much effort has been expended in evaluating the relative antioxidant potency of α-LA. Consequently, this study aimed to evaluate (i) the influence whether $AlCl_3$ induced hematological and biochemical perturbations in rats and (ii) the protective role of α-LA in alleviating the detrimental effect of $AlCl_3$ induced toxicity.

MATERIALS AND METHODS

Chemicals

All chemicals used in this study were purchased from Sigma chemical co. (USA).

Animals and experimental procedure

12 rats weighing around 235 ± 10 g were obtained from Pasteur institute (Algiers, Algeria). Animals were acclimated for 2 weeks under the same laboratory conditions of photoperiod (12-h light: 12-h dark cycle), a minimum relative humidity of 40% and room temperature 23±2°C. Food (standard diet, supplied by the "ONAB, El-Harrouch", Algeria) and water were available *ad libitum*. The animals were randomized into three groups of 6 animals each.

- Group **(A, Control group):** served as control rats which received standard diet.

- Group **(B, $AlCl_3$-treated group):** received only $AlCl_3$ (34 mg/kg bw administered in the diet).

- Group **(C, $AlCl_3$+α-LA group):** received both $AlCl_3$ and α-LA (35mg/kg bw) by oral gavage once per day.

During all period of treatment (three weeks), food consumption was measured daily, while the body weights were recorded weekly. The amount of ingested diet was calculated as the difference between the weight of feed that remained in the food bin (D1) and the amount placed 1 day before (D2). These data were then used to calculate the daily average feed intake, according to the formula:

Average feed intake: D_2-D_1

Quantities of $AlCl_3$ ingested by each rat were calculated from daily food consumption. The doses of $AlCl_3$ and α- LA were selected on the basis of previous works[1,15-17] respectively.

Samples preparation

Blood collection

At the end of the experimental period, animals were weighed, overnight fasted and they sacrificed by cervical decapitation. The blood samples were immediately collected into tow ice –cold polypropylene tubes. The first one containing EDTA as anticoagulant and used for determination of haematological parameters. The second tube containing heparin as anticoagulant, which the plasma samples obtained from, by centrifugation (2200g for 15 min) after that the result supernatants were aliquoted and stored at -20°C prior to use for biochemical assay of aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatise (ALP), lactate dehydrogenase (LDH), total bilirubin, albumin and total protein.

Preparation of liver homogenate

The liver were quickly removed washed in 0.9% NaCl solution and weighed after the removal of the surrounding-connective tissues carefully, and then, one gram of liver was homogenised in 2 ml of phosphate buffer solution (PBS: 50mm Tris, 150 mm NaCl, pH 7.4) in ice cold condition. Homogenates were centrifuged at 10.000g for 15 min at 4°C, the supernatants were divided into aliquots to use each one for one time and stored at -20°C before being used.

Haematological variables

Haematological parameters were evaluated by electronic haematological counter (selectra coulter, Germany).

Plasma biochemical markers

Transaminases activities, total bilirubin, albumin and total protein levels were determined spectrophotometrically according to appropriate standardised procedures, using commercially available kits from Spinreact (Spain, refs: AST-1001 160-1001161, ALT-1001170-1001171, ALP-1001130-1001131, LDH-1001260, total bilirubin -1001044, albumin -1001020-1001023, total protein -1001291).

Estimation of lipid peroxidation level

The lipid peroxidation (LPO) level in the liver homogenates was measured as malondialdehyde (MDA), which is the end product of lipid peroxidation, and react with TBA as a TBA reactive substance (TBARS) to produce a red colored complex which has peak absorbance at 530nm according to Buege and Aust.[18] 375µl of supernatant were homogenized by sonication with 150µl of PBS, 375µl of TCA-BHT (trichloroacetic acid-butylhydroxytoluene) in order to precipitate proteins and then centrifuged (1000g, 10min, 4°C). 400µl of obtained supernatant were mixed with 80µl of HCl (0.6M) and 320µl of TBA dissolved in Tris solution and the mixture was incubated at 80°C for 10 min. The absorbance of the resultant supernatant was red at 530nm.The amount of MDA was calculated by using an extinction coefficient of 1.56×10^5 $mM^{-1}cm^{-1}$.

Reduced Glutathione level

Reduced glutathione **(**GSH) contents in liver and erythrocyte homogenates was estimated using a colorimetric technique, as mentioned by Ellman[19], modified by Jollow et al.[20], based on the development of a yellow colour when DTNB [(5, 5 dithiobis-(2-nitrobenzoic acid)] was added to compounds containing sulfhydryl groups. In brief, 0.8 ml of liver supernatant was added to 0.2ml of 0.25% sulphosalycylic acid and tubes were centrifuged at 2500xg for 15min. The resulting supernatant (0.5 ml) was mixed with 0.025 ml of 0.01M DTNB and 1ml phosphate buffer (0.1M, pH 7.4). The absorbance at 412 nm was recorded. The amount of GSH was expressed as nmoles of GSH/mg protein.

Antioxidant enzymes activities

Glutathione peroxidase activity

Gutathione peroxidase (GPx) (E.C.1.11.1.9) activity was measured according to the procedure of Flohe and Gunzler.[21] Supernatant obtained after centrifuging 5% liver homogenate at 1500 x g for 10 min followed by 10000 x g for 30 min at 4°C was used for GP_x assay. One ml of reaction mixture was prepared which contained 0.3ml of phosphate buffer (0.1M, pH7.4), 0.2ml of GSH (2mM), 0.1ml of sodium azide (10mM), 0.1ml of H_2O_2 (1mM) and 0.3ml of liver supernatants. After incubation at 37°c for 15min, reaction was determined by addition of 0.5ml 5% TCA. Tubes were centrifuged at 1500 x g for 5 min and the supernatant was collected. 0.2ml of phosphate buffer (0.1M pH7.4) and 0.7ml of DTNB (0.4mg/ml) were added to 0.1ml of reaction supernatant. After mixing, absorbance was recorded at 420 nm.

Catalase activity

The activity of catalase (CAT) (E.C.1.11.1.6) was measured according to the method of Aebi.[22] The reaction mixture 1ml contained a 100mM phosphate buffer (pH 7), 500mM H_2O_2 and liver supernatants. The reaction started by adding H_2O_2 and its decomposition was monitored by following the decreased in absorbance at 240nm for 1

min. The enzyme activity was calculated by using an extinction coefficient of 0.043mM^{-1}cm^{-1}.

Superoxide dismutase activity

The superoxide dismutase (SOD) (E.C.1.15.1.1) activity was determined using a method of Asada et al.,[23] SOD activity was evaluated by measuring of its ability to inhibit the photo reduction of nitro-blue tetrazolium (NBT). One millilitre of homogenate's supernatant was combined 50mM phosphate buffer (pH 7.8), 39 mM methionine, 2.6 mM NBT and 2.7 mM EDTA-Riboflavin, as to obtain a final concentration of 0.26 mM, was added as the last and switching on the light started the reaction, changes in absorbance at 560nm were recorded after 20min. In this assay, one unit of SOD is defined as the amount that inhibits the NBT reaction by 50%. Specific activity was defined as units/mg of protein.

Protein content

Protein supernatants concentration in liver was measured spectrophotometrically at 595 nm according to the method of Bradford[24], using bovine serum albumin as standard.

Statistical analysis

All data are expressed as mean ± SD for six rats in each group. Significant differences between the group's means were determined by paired student's test. The statistical signification of difference was taken as p≤0.05.

RESULTS

Effects of treatments on body and relative liver weights

Changes in total body weight and liver relative's weights are shown in Table1. The total body weight showed a pronounced reduction by 20.09% and 16.068% in rats of $AlCl_3$ treated group compared to the $AlCl_3$+α-LA treated group and to the controls respectively. Besides, a highly significant increase in liver relative weights of $AlCl_3$ treated rats (a hypertrophy of the liver) was noted compared to the $AlCl_3$+ α-LA treated rats and to the controls ones.

Table 1: Changes in body weight (g) and liver relative weights (g/100g bw) of control and treated rats

Parameters studied	Control	$AlCl_3$	$AlCl_3$+ α-LA
Initial body weight (g)	236.33 ± 51.34	242.67 ± 41.63	243.17±29.74
Final body weight (g)	311.17 ± 54.61	261.17 ± 38.20*	326.5±46.85$^{\#}$
Relative liver weight (g/100g bw)	2.63 ± 0.16	3.423 ± 0.48**	2.68±0.22$^{\#}$

Values are given as mean ± SD for groups of 6 animals each. Significant difference; All treated groups compared to the controls one (*p≤0.05, **p≤0.01); $AlCl_3$ + α-LA group compared to the $AlCl_3$ treated one ($^{\#}$p≤0.05).

Effects of treatments on food intake

The decrease in body weight was associated with a reduction in food intake by 10.867% and 12.010% in $AlCl_3$ treated group compared to $AlCl_3$+ α-LA group and to the control respectively (Table 2).

Table 2: Daily food intake and $AlCl_3$ ingested of control and treated rats

Parameters and treatments	Control	$AlCl_3$	$AlCl_3$+ α-LA
Food intake (g/day/rat)	21.14±2.26	18.601±4***	20.87±2.31$^{\#\#\#}$
Quantities of $AlCl_3$ ingested (mg/day/rat)	-	6.324±1.35	7.1±1.35

Values are given as mean ± SD for groups of 6 animals each. Significant difference; All treated groups compared to the controls one (***p≤0.001); $AlCl_3$ + α-LA group compared to the $AlCl_3$ treated one ($^{\#\#\#}$p≤0.001).

Effects of treatments on haematological parameters

As shown in Table 3, hematological parameters in control and treated groups. Red blood cell (RBC), haemoglobin (Hb) content and mean corpuscular haemoglobin concentration (MCHC) in $AlCl_3$ treated group were significantly decreased compared to those in the controls. While, white blood cell number (WBC) were significantly increased than those of the controls. There was no significant effect of adding 34 mg/kg AlCl3 on all haematological indexes in rats treated with $AlCl_3$+ α-LA compared control rats.

Table 3: Changes on haematological parameters of control and treated rats

Parameters and treatments	Control	$AlCl_3$	$AlCl_3$+ α-LA
RBC (10^6/µl)	8.96±0.31	7.26±0.32*	8.80±0.50$^{\#}$
WBC (10^3/µl)	10.31±1.81	13.01±0.72*	11.58±1.12$^{\#}$
Hb (g/dl)	14.81±0.58	12.18±0.53**	14.28±0.57$^{\#\#}$
HT (%)	44.55±1.33	43.6±1.50	43.85±1.78
MCV (mm^3/RBC)	49.66±1.75	49.33±2.16	49.16±1.47
TCMH (pg/RBC)	16.55±0.69	16.30±0.62	16.58±0.39
MCHC (g/dl)	33.26±0.46	31.56±0.60**	33.21±0.62$^{\#}$
PLT (10^3/µl)	721.66±7.99	688.00±7.11	701.83±2.19
VMP	9.50±0.43	9.40±0.42	9.73±0.46

Values are given as mean ± SD for groups of 6 animals each. Significant difference; All treated groups compared to the controls one (*p≤0.05, **p≤0.01); $AlCl_3$ + α-LA group compared to the $AlCl_3$ treated one ($^{\#}$p≤0.05, $^{\#\#}$p≤0.05).

Effects of treatments on plasma biochemical markers

Table 4 showed some biochemical indexes which indicated liver injury in rats. $AlCl_3$ treated rats data

showed a significant increase in plasma AST, ALT, ALP, LDH and total bilirubin by 94%, 29%, 56%, 37%, and 28% respectively compared with control group and then by 50%, 45%, 50% and 22% compared to those of $AlCl_3$+α-LA treated group, while albumin and total protein were decreased in $AlCl_3$ treated group by 27% and 11% compared to the control one and by 28.734% and 3.28% compared to the $AlCl_3$+α-LA group.

Table 4: Effects of treatments on some biochemical parameters in plasma of control and treated rats

Parameters and treatments	Control	$AlCl_3$	$AlCl_3$+ α-LA
AST (U/L)	152.71±4.72	296.571±1.88**	197.32±7.32$^{###}$
ALT (U/L)	162.368±3.94	209.506±5.67*	144.49±10.24$^{###}$
ALP (U/L)	113.253±2.14	177.478±8.09***	117.68±1.17$^{###}$
LDH (U/L)	704.833±5.44	964.5±5.97***	882.66±4.62**
Total bilirubin (mg/l)	1.6±0.01	2.05±0.28*	1.683±0.01$^{##}$
Albumin (g/dl)	43.09±3.20	31.195±7.14**	43.77±2.02$^{##}$
Total protein (g/dl)	92.69±4.12	82.266±5.93**	85.06±5.55

Values are given as mean ± SD for groups of 6 animals each. Significant difference; All treated groups compared to the controls one (*p≤0.05, **p≤0.01, ***p≤0.001); $AlCl_3$ + α-LA group compared to the $AlCl_3$ treated one ($^{##}$p≤0.05, $^{###}$p≤0.001).

Effects of treatments on lipid peroxidation

MDA levels in liver tissue (Figure 1) were increased in $AlCl_3$-treated group compared to those of $AlCl_3$+α-LA-treated group (12%) and the control (21%) ones. $AlCl_3$+α-LA-treated rats did not show any significant changes in liver MDA level compared to the control.

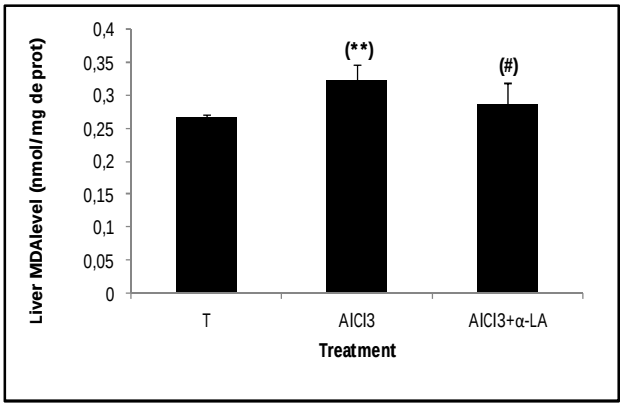


Figure 1: Liver homogenate malondialdehyde (nmol/mg protein) levels of control and treated rats. Values are given as mean ± SD for groups of 6 animals each. Significant difference: All treated groups compared to the controls one (**p≤0 .01). $AlCl_3$+α-LA group compared to the $AlCl_3$ treated one ($^{#}$p≤0.05).

Effects of treatments on GSH content

Results in Figure 2 Showed changes of GSH levels in liver tissue which indicated liver oxidative injury. Exposure rats to $AlCl_3$ produced a significant decline in GSH levels compared to those of $AlCl_3$+α-LA-treated group (14%) and the control (22%) ones.

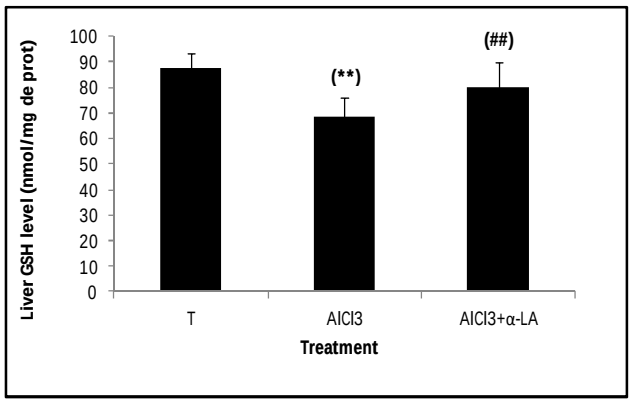
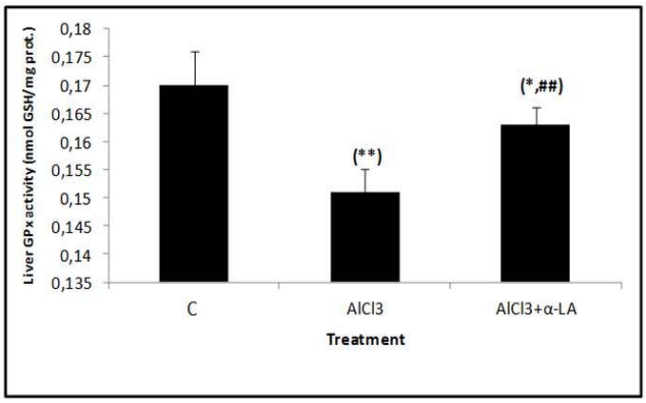
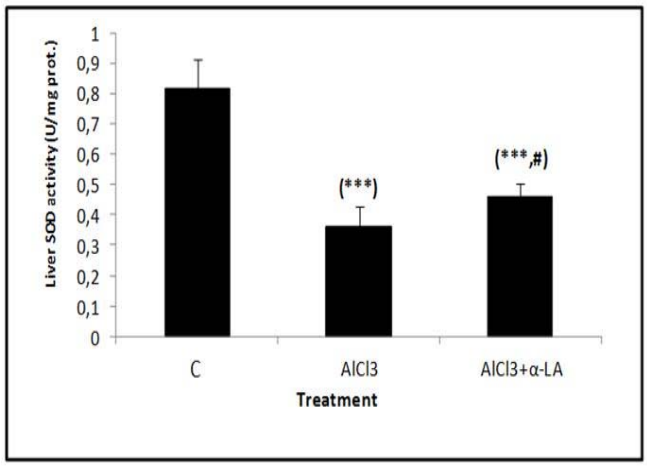


Figure 2: Liver homogenate reduced glutathione (nmol/mg protein) levels of control and treated rats. Values are given as mean±SD for groups of 6 animals each. Significant difference: All treated groups compared to the controls one (**p≤0 .01). $AlCl_3$+ α-LA group compared to the $AlCl_3$ treated one ($^{##}$p≤0.01).

Effects of treatments on antioxidant enzyme activities

Results in Figure 3 showed Changes of GPx, SOD and CAT activities in liver tissue which indicated liver oxidative damage. Exposure rats to $AlCl_3$ produced a significant decline in GPx, SOD and CAT enzyme activities compared to those of control group. In contrast, treatment with 35 mg/kg of α-lipoic acid resulted in a significant amelioration of 4-43% in the enzyme activities (GPx, SOD and CAT).





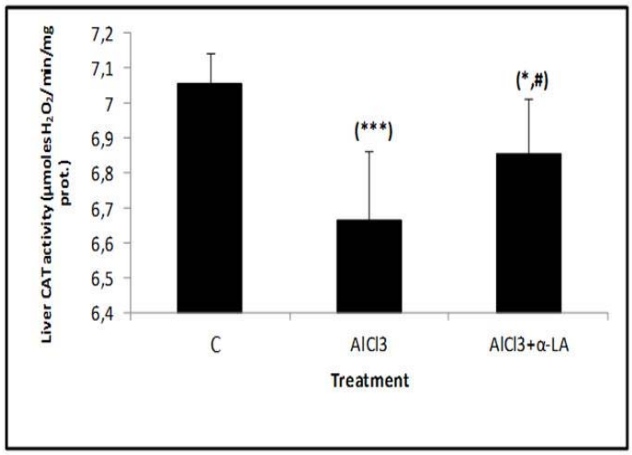


Figure 3: Liver homogenate glutathione peroxidase (nmoles of GSH/min/mg protein), superoxide dismutase (U/mg de protein) and catalase (µmoles H_2O_2/min/mg protein) activities of control and treated rats. Values are given as mean ± SD for groups of 6 animals each. Significant difference: All treated groups compared to the controls one (*p≤0.05), (**p≤0 .01), (***p≤0.001). $AlCl_3$+ α-LA group compared to the $AlCl_3$ treated one ($^{\#}$p≤0.05), ($^{\#\#}$p≤0.01).

DISCUSSION

In our experimental study, reduction in body weight is used as an indicator for the deterioration of rat general health status. It has been reported that $AlCl_3$ could induce toxicological effects and biochemical dysfunctions representing serious health hazards.[2,25,26] The findings from the present work indicate that excessive $AlCl_3$ exposure has changed body weight, absolute and relative liver weights, leading however to significant decrease in animal growth and production performances. This could be probably attributed to the reduction of feed consumption and/or malabsorption of nutrients induced by $AlCl_3$ effects on the gastro-intestinal tract and/or inhibition of protein synthesis.[2,25,26] $AlCl_3$ exposure may account to reduced food intake seen in the $AlCl_3$-treated group. Hence, these findings were similar to the results published by El-Demerdash, and Zhu et al.[1,26] who reported that high Al exposure have significantly induced disturbances of the total body weight, absolute and relative liver weights of rats. Accordingly, among the main approaches used to ameliorate Al-induced hepatotoxicity is the use of agents with powerful antioxidant properties. However, recent studies have reported that lipoic acid showed significant protective effects against tissue damage induced by some xenobiotics like arsenic[8,27], Bisphenol A[28] and adriamycin.[17]

The co-administration of lipoic acid attenuated the in vivo effects of $AlCl_3$ by scavenging or neutralizing ROS. These results indicated that α-LA might have a beneficial role in lowering $AlCl_3$ toxicity probably due to its radical scavenging property. Thus, α-LA treatment corrects the body weight slow-down and the relative liver weight increases. This may be attributed to an increases food intake and /or lipoic acid capability to interfere with the absorption of $AlCl_3$ in the intestine. It can also be suggested that both α-LA and DHLA chelate heavy metals, restricts the molecular damage and reduce hepatic injury.

Exposure rats to $AlCl_3$ decreased hematological parameters (RBCs and Hb) and developed anemia in rats. Our experimental were in line with previous reports which demonstrated that heavy metals exposure altered hematological parameters in rats[29,30] In fact, according to the earlier reports[29,31,32] this anaemia could be explained by the inhibition of erythropoiesis and/or haemoglobin synthesis reduction, the same reports indicate that $AlCl_3$ could be interfering with Fe incorporation to the heme group witch induce Fe deficiency and reduce heme synthesis. Also the observed microcytic anaemia it might be due to an increase in the rate of erythrocytes destruction in haematopoietic organs. So, $AlCl_3$ might be crossing the erythrocyte membrane which is a result of its ability to initiate a lipid peroxidation.[2,5,30] In our study, $AlCl_3$-treated rats also exhibited significantly higher WBC compared with controls rats. This increase might be indicative of the activation of defence and immune system showed that there were oedema and inflammation in the tissues.[5]

The results of the present study showed that α-LA supplementation has potentially beneficial effects on haematological system. Our results are similar to a previous studies reported by Caylak et al.[33] In fact, this beneficial effect are probably due to the direct chelating activity of α-LA which have possibility to decrease the $AlCl_3$ concentration in blood cells and inhibit its entry into erythrocytes, resulting an increase of Fe and facilitate its incorporation to the hem group. It could be also related to the anti-inflammatory effects of α-LA reported in several prior studies.[11,34]

The disturbance in the transport function of the hepatocytes as a result of hepatic injury causes the leakage of enzymes from the liver cytosol into the blood due to altered permeability of membrane. In this work, $AlCl_3$-treated rats showed a significant increase in plasma levels AST, ALT, ALP and LDH, which confirmed the liver injury or dysfunction these results are in line with that reported by El-Demerdash[1] and Gaskill et al.[15] Also, increases enzymes plasma levels may be due to the disturbance in the balance between biosynthesis and degradation of these enzymes.[35,36] Additional effects of $AlCl_3$ treatment revealed decreased plasma total protein, albumin and increased total bilirubin as compared to control. This data are in agreement with previous studies.[15,36] So, the significant decrease in the concentration of the albumin could be attributed on the one hand to an under nutrition and on the other hand to a reduction of the protein synthesis in the liver results a decreasing plasma total protein which confirmed the direct damaging effect of $AlCl_3$ on liver cells.[2,36] The increase in plasma total bilirubin may result from decreased liver uptake, conjugation or increased bilirubin production from haemolyse. El-Sharaky et al.[37] found that

the induction rat in bilirubin was associated with free radical production.

On the other hand, lipoic acid prevent the increase in the activities of these enzymes is the primary evidence of their hepatoprotective activity.[7] In the present finding, lipoic acid co-administration produced an effective action against the hepatocytes damaging effects, as shown by a decrease of the elevated plasma hepatic key enzymes (AST, ALT, ALP and LDH) and by a normalisation of albumin, total protein and total bilirubin. The mechanism proposed to explain these results could be attributed to α-LA preventive effects against $AlCl_3$ induced damages in rats hypatocytes.[7,14] So, the α-LA prevents cellular necrosis as well as the membrane failure, this hepatoprotective effects might be related to both its radical scavenging proprieties and indirect effect as a regulator of antioxidative systems.[16, 17, 25]

The increased level of MDA in $AlCl_3$ treated rats could be linked to the peroxidation damages of biological membranes, caused by an increased reactive Fe^{+2}.[38,39] According to Newairy et al.,[15] and Wu et al.[39] study's, aluminium is able to be bound by the Fe^{+3}carying transferrin protein because of most closely Al^{+3} ionic radical resemble those of Fe^{+3}, results an accumulation of Fe^{+2} in cells. Besides[1,38] reported that an increased MDA concentration could be caused by inactivation of enzymes involved in antioxidant system such as GPx, SOD and CAT activities. In fact, $AlCl_3$ accumulation induced alteration of zinc and copper homeostasis and decreasing its binding ability to the antioxidant enzymes which caused antioxidant enzymes dysfunction. The decreasing GSH activity might be related to the inhibitor $AlCl_3$ effect on Glutamyl-cysteine-synthetase activity, the enzyme that controls the biosynthesis of glutathione in liver, thus resulting a reduction in GSH synthesis. This might be coupled to the aluminium inhibiting ability of NADPH-generating enzymes such as glucose 6-phosphate dehydrogenase and NADP-isocitrate dehydrogenase, resulting a slowing down in the GSH regeneration.[15] Oxidative stress occurred as a consequence of imbalance between the production of reactive oxygen species and the antioxidative process in favor of radical production. In the current study, the significant decrease in the antioxidant enzyme activities (GPx, SOD and CAT) in liver proved the failure of antioxidant defense system to overcome the influx of reactive oxygen species generated by Al exposure. α-LA supplementation produced protective effect against antioxidant defense system failure our result is in agreement with data reported from similar studies on rats.[8,28] This study suggested that α-LA antioxidants capacity may be due to its ability to chelate both heavy and transition metals, to scavenge reactive oxygen species by the sulphydryl group to regenerate endogenous antioxidants (such as vitamin C, vitamin E, and GSH) and to repair oxidative damage of cellular macromolecules which prevent the increase in lipid peroxidation level and increasing the antioxidants enzymes activities. Several reports[8,9,14] evidenced that a combination of α-LA could prevent GSH depletion by scavenging reactive oxygen species and /or increasing cysteine uptake, which is a rate limiting step for GSH biosynthesis.

CONCLUSION

This study clearly indicates that $AlCl_3$ affects both haematological and biochemical parameters as well as antioxidative system inducing oxidative stress. Co-administration of α-LA ameliorates this disturbance. In fact, the ameliorative effect of α-LA against oxidative stress in $AlCl_3$ treated rats due to its antioxidant propriety by scavenging free radical and chelating metals as well as regeneration of endogenous antioxidant. Nevertheless, further studies are needed to investigate the precise mechanism(s) of action of α-LA on oxidative stress biomarkers in rat under $AlCl_3$ intoxication.

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