

## Research Article

# Assessment of the Protective Effect of *Lepidium sativum* against Aluminum-Induced Liver and Kidney Effects in Albino Rat

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**Background and Objectives.** Environmental pollution with the different Aluminum (Al) containing compounds has been increased. Liver and kidney are two vital organs targeted by Al accumulation. The aim of this study was to assess the possible protective and curative effects of *Lepidium sativum* Linn (LS) against Al-induced impairment of liver and kidney in albino rat and to explore the mechanism behind this effect. **Materials and Methods.** This experimental animal-based study included fifty albino rats divided into five groups, the control, LS-treated (20 mg/kg), AlCl<sub>3</sub>-treated (10 mg/kg), AlCl<sub>3</sub> then LS, and AlCl<sub>3</sub> plus LS-treated, simultaneously for 8 weeks. At the end of the experiment, hepatic and renal functions as well as the biomarkers of antioxidants activities were assessed in the serum. Both liver and kidney were dissected out and histopathologically examined. **Results.** This study showed that administration of AlCl<sub>3</sub> caused a significant ( $p < 0.05$ ) reduction in rats body weight. It significantly increased serum AST, ALT, ALP, bilirubin, urea, and creatinine levels and decreased total protein and albumin. AlCl<sub>3</sub> significantly reduced enzymatic (catalase), nonenzymatic (reduced glutathione), and ferric reducing antioxidant power (FRAP) in the serum. Histopathologically, it induced necrosis and degeneration of hepatocytes, glomeruli, and renal tubules. Administration of LS after or along with AlCl<sub>3</sub> significantly restored the serum biomarkers of liver and kidney functions to their near-normal levels and had the ability to overcome Al-induced oxidative stress and preserved, to some extent, the normal hepatic and renal structure. The coadministration of LS had a superior effect in alleviating Al-induced changes. **Conclusion.** Exposure to AlCl<sub>3</sub> induced a set of functional and structural changes in the liver and kidney of rats evident through both biochemical and histopathological assessment. The antioxidant activity of LS seeds mediated a protective and curative effect of LS against such changes. Further study through a rigorous clinical trial to prove LS activity on human is recommended.

## 1. Introduction

Aluminum (Al) is among the most abundant elements on the earth. Absorption or accumulation of Al in humans occurs via diet as in some food products and additives medication like antacids vaccines and parenteral fluids, adding to cosmetics, inhaled fumes, and particles from occupational exposures [1]. It was believed that Al was nontoxic and was quickly excreted in the urine so it was widely used in daily life. Though, it was known later on that it negatively affects human health [2]. The Agency for Toxic Substances and Disease Registry (ATSDR) reported that Aluminum is mainly distributed in the bone, liver, testis, kidneys, and brain [3]. This metal disrupts the prooxidant/antioxidant balance in tissues

leading to biochemical and physiological dysfunctions due to an excessive reactive oxygen species (ROS) generation [4].

*Lepidium sativum* Linn (LS) is an edible annual herb which belongs to the family Brassicaceae, cultivated throughout India, Europe, and the United States as well as Arabian countries. It has many names like Asaliyo, pepper cress, and Elrshad [5]. The seeds and leaves of the plant have volatile oils and are a good source of amino acids, minerals, and fatty acids. They have the ability to act in vitro as antioxidants due to their high content of phenolic compounds, and thus they could have potential preventive effects towards chronic diseases [6]. LS seeds are used in Saudi folk medicine for multiple applications, but mainly in fracture healing and after maternity [7].

The methanolic extract of LS seeds is described to have hepatoprotective activity in rats as it significantly reduced the elevated liver enzymes and improved the severe fatty changes in the liver induced by carbon tetrachloride (CCl<sub>4</sub>) [8]. In another study ethanolic extracts of LS seeds were proved to have nephrocurative and nephroprotective activity as it reduced urea and creatinine level in serum of cisplatin-induced model of nephrotoxicity [9]. In previous toxicological studies, safety of LS seeds was reported [10]. So LS was selected in this study to investigate its ability to protect against Aluminum-induced kidney and hepatotoxicity. Therefore, this study was carried out to evaluate the protective and therapeutic potential of LS against the hepatic and renal functional and structural changes caused by AlCl<sub>3</sub> and to explore the mechanism behind these possible effects.

## 2. Materials and Methods

**2.1. Chemicals.** All chemicals, used in this study, were of analytical grade. Aluminum chloride (AlCl<sub>3</sub>) was purchased from Sigma Chemical Company, St. Louis, Missouri, USA. Seeds of *Lepidium sativum* (Family: Cruciferae) were obtained from the local herbalist shops in Jeddah. These seeds were previously characterized in a study conducted by Raouf et al. in the King Fahd Medical Research Center (KFMRC), King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia [11], and their aqueous extracts were prepared according to the method described by Eddouks et al. [12].

**2.2. Animals.** An ethical approval of this experimental study was obtained from the biomedical research ethics committee at the Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia.

Fifty albino rats with average body weight from 200 to 250 g were utilized in this study. They were obtained from the KFMRC and were left to acclimatize before the experiment for one week; then they were randomly divided into five groups (n=10 each).

The first group included the control rats which were intraperitoneally (i.p.) injected of 1 ml of normal saline and given 1 ml of normal saline by oral gavage for 8 weeks.

Rats of the second group (LS-treated group) were given water extract of LS daily at a dose 20 mg/kg in 1 ml of normal saline by oral gavage in addition to i.p. injection of normal saline.

Rats of the third group (AlCl<sub>3</sub>-treated group) were i.p. injected with AlCl<sub>3</sub> at a dose of 10 mg/kg of body weight dissolved in 1 ml of distilled water daily for 8 weeks [13].

Rats of the fourth group (AlCl<sub>3</sub> then LS group) were i.p. injected with AlCl<sub>3</sub> at the same dose for 8 weeks and then given water extract of LS by oral gavage at the same dose daily for another 4 weeks [14].

Rats of the fifth group (AlCl<sub>3</sub> plus LS group) were i.p. injected with AlCl<sub>3</sub> simultaneously with giving water extract of LS by oral gavage at the same dose for 8 weeks.

At the end of the experiment, rats were fasted overnight. The body weight of the rats was measured. Then, rats were sacrificed by cervical decapitation, under light anesthesia

with diethyl ether, and the blood samples were collected in plain tubes, centrifuged at 4000 rpm for 15 minutes to obtain serum, and stored at - 20°C till analysis. Livers and kidneys were rapidly dissected out and processed for histopathological examination.

**2.3. Biochemical Assessment.** Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were colorimetrically assessed according to the method of Reitman and Frankel [15] while serum alkaline phosphatase (ALP) was measured according to the method described by Belfield and Goldberg [16]. Total bilirubin, proteins, and albumin were measured according to the methods of Walter and Gerade [17] and Lowry et al. [18], respectively. Total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDLc) were determined as previously described by Richmond and Fossati and Principle [19, 20]. Reduced glutathione (GSH) level and enzymatic antioxidant catalase (CAT) activity were also assessed as previously described [21]. Ferric Reducing Antioxidant Power (FRAP), an antioxidant capacity indicator, was assessed using FRAP assay Kit (Cell Biolabs, USA, Cat. no. STA-859). Creatinine and urea in serum were measured using Chronolab kits (Spain).

**2.4. Histopathological Examination.** Parts of livers and kidneys of all rats were fixed in 10% buffered neutral formalin solution and further processed to obtain of paraffin blocks. Five-micron thick paraffin sections were prepared and routinely stained with Hematoxylin and Eosin (H&E) and examined for the histopathological changes using the light microscope [22].

**2.5. Statistical Analysis.** The data obtained were statistically analyzed by using the Statistical Package of Social Science (SPSS) version 20 (SPSS Inc., Chicago, IL). The results were expressed as mean ± standard deviation (SD). One Way ANOVA followed by (LSD) post hoc test was used to assess the statistical significance between the different groups. A  $p < 0.05$  was accepted as statistically significant.

## 3. Results

It was noticed that final body weights measured at the end of the experiment as well as the percentage of change in body weight were significantly lower in both groups receiving AlCl<sub>3</sub> alone or along with LS compared to the control. Both parameters were significantly higher in all groups receiving LS, compared to those receiving AlCl<sub>3</sub> alone. The final body weight and the percentage of change in body weight were significantly lower ( $P=0.001$ ;  $p=0.03$ ) in rats receiving AlCl<sub>3</sub> plus LS compared to those receiving AlCl<sub>3</sub> then LS, respectively (Table 1).

**3.1. Biochemical Results.** Serum cholesterol, triglyceride, and LDL-C levels were significantly lower in the groups receiving LS alone or with AlCl<sub>3</sub> compared with the group receiving AlCl<sub>3</sub> alone. There was no significant difference in these

TABLE 1: Comparison of body weights in different studied groups.

Parameters	Control	LS-treated	AlCl <sub>3</sub> -treated	AlCl <sub>3</sub> then LS	AlCl <sub>3</sub> plus LS
Initial body weight (g)	224.78±17.33	212.56±14.78	219.67±17.1	228.56±26.8	212.56±14.78
		P#=0.173	P#=0.565	P#=0.670 P##=0.319	P#=0.173 P##=0.425 P###=0.077
Final body weight (g)	316.78±13.45	326.11±29.15	227.56±17.5	309.44±40.1	251.56±10.7
Significance		P#=0.429	P#<0.001	P#=0.533 P##<0.001	P#=0.001 P##=0.046 P###<0.001
Weight gain (g)	92.00±18.61	110.22±33.41	7.67±2.87	69.78±29.6	39.00±14.07
Significance		P#=0.094	P#<0.001	P#=0.043 P##<0.001	P#<0.001 P##=0.005 P###=0.006
Percentage changes in body weight (%)	41.56±10.88	52.29±17.46	3.51±1.40	30.69±13.23	18.72±7.81
Significance		P#=0.055	P#<0.001	P#=0.052 P##<0.001	P#<0.001 P##=0.008 P###=0.033

Data are expressed as mean±standard deviation. Comparison was made using One Way ANOVA test (LSD). P#: p value of comparison versus control; P##: p value of comparison versus AlCl<sub>3</sub> group; P###: p value of comparison versus AlCl<sub>3</sub> then LS group.

TABLE 2: Comparison of lipid profiles in different studied groups.

Parameters	Control	LS-treated	AlCl <sub>3</sub> -treated	AlCl <sub>3</sub> then LS	AlCl <sub>3</sub> plus LS
Cholesterol (mg/100ml)	80.51±9.52	73.24±3.99	106.03±12.75	88.33±3.92	86.24±6.74
Significance		P#=0.104	P#<0.001	P#=0.082 P##<0.001	P#=0.056 P##=0.019 P###=0.184
Triglyceride (mg/100ml)	66.84±8.47	58.01±13.22	99.21±21.21	71.37±10.34	81.24±10.86
Significance		P#=0.233	P#<0.001	P#=0.537 P##=0.001	P#=0.197 P##<0.001 P###=0.634
LDL-C (mg/100ml)	17.17±3.02	14.91±1.46	21.04±2.90	19.03±1.46	18.19±1.28
Significance		P#=0.060	P#=0.002	P#=0.119 P##=0.092	P#=0.388 P##=0.020 P###=0.472

Data are expressed as mean +/- standard deviation. Comparison was made using One Way ANOVA test (LSD). P#: p value of comparison versus control; P##: p value of comparison versus AlCl<sub>3</sub> group; P###: p value of comparison versus AlCl<sub>3</sub> then LS group.

parameters in rats receiving AlCl<sub>3</sub> plus LS compared to those receiving AlCl<sub>3</sub> then LS (Table 2).

FRAP and reduced glutathione levels were significantly increased (p=0.001) in rats receiving LS compared to the control. On the other hand, these two parameters as well as catalase level were significantly reduced in AlCl<sub>3</sub>-treated group. FRAP and catalase levels were significantly increased in rats receiving AlCl<sub>3</sub> then LS and AlCl<sub>3</sub> plus LS compared to those receiving AlCl<sub>3</sub> alone. Receiving LS along with AlCl<sub>3</sub> has a more significant effect on increasing catalase and reduced glutathione levels (Table 3).

Serum AST, ALT, and ALP levels were significantly higher (p=0.001) in rats receiving AlCl<sub>3</sub> compared to the control. These levels were significantly reduced in groups receiving

AlCl<sub>3</sub> then LS as well as AlCl<sub>3</sub> plus LS compared with AlCl<sub>3</sub> group with no significant difference between the two groups (Table 4).

Total proteins and albumin levels were significantly reduced in rats receiving AlCl<sub>3</sub> compared to the control and they were significantly increased in groups receiving AlCl<sub>3</sub> then LS as well as AlCl<sub>3</sub> plus LS compared with AlCl<sub>3</sub> group with no significant difference between the two groups (Table 4).

Serum total bilirubin, creatinine, and urea levels were significantly higher (p=0.001) in rats receiving AlCl<sub>3</sub>, while they significantly decreased in groups receiving AlCl<sub>3</sub> then LS as well as AlCl<sub>3</sub> plus LS compared with AlCl<sub>3</sub> group (Tables 4 and 5).

TABLE 3: Comparison of oxidative stress markers in the serum of different studied groups.

Parameters	Control	LS-treated	AlCl <sub>3</sub> -treated	AlCl <sub>3</sub> then LS	AlCl <sub>3</sub> plus LS
FRAP ( $\mu$ U/L)	82.20 $\pm$ 13.33	150.80 $\pm$ 15.99	45.40 $\pm$ 5.68	65.20 $\pm$ 9.88	67.80 $\pm$ 7.79
Significance		P#<0.001	P#<0.001	P#=0.026 P##=0.01	P#=0.055 P###=0.005 P####=0.717
Catalase ( $\mu$ U/L)	97.60 $\pm$ 6.11	99.80 $\pm$ 3.11	28.60 $\pm$ 9.45	57.40 $\pm$ 10.74	83.00 $\pm$ 14.78
Significance		P#=0.724	P#<0.001	P#<0.001 P##<0.001	P#=0.027 P###<0.001 P####<0.001
Reduced glutathione (nmol/L)	2.81 $\pm$ 1.09	6.47 $\pm$ 1.51	0.55 $\pm$ 0.25	1.00 $\pm$ 0.27	2.29 $\pm$ 0.79
Significance		P#<0.001	P#<0.001	P#=0.005 P##=0.457	P#=0.379 P###=0.008 P####=0.039

Data are expressed as mean  $\pm$  standard deviation. Comparison was made using One Way ANOVA test (LSD). P#: p value of comparison versus control; P##: p value of comparison versus AlCl<sub>3</sub> group; P###: p value of comparison versus AlCl<sub>3</sub> then LS group.

TABLE 4: Comparison of liver functions in the serum of different studied groups.

Parameters	Control	LS-treated	AlCl <sub>3</sub> -treated	AlCl <sub>3</sub> then LS	AlCl <sub>3</sub> plus LS
AST (U/L)	105.82 $\pm$ 11.02	104.36 $\pm$ 25.41	154.43 $\pm$ 22.26	131.63 $\pm$ 26.15	133.25 $\pm$ 7.12
Significance		P#=0.871	P#=0.001	P#<0.006 P##=0.014	P#=0.004 P###=0.022 P####=0.857
ALT (U/L)	61.41 $\pm$ 5.50	55.17 $\pm$ 7.79	101.12 $\pm$ 6.64	78.93 $\pm$ 9.60	84.19 $\pm$ 5.91
Significance		P#=0.060	P#<0.001	P#<0.001 P##<0.001	P#<0.001 P###<0.001 P####=0.111
ALP (U/L)	193.00 $\pm$ 22.98	183.10 $\pm$ 11.97	92.50 $\pm$ 14.21	140.70 $\pm$ 15.84	138.00 $\pm$ 19.11
Significance		P#=0.206	P#<0.001	P#<0.001 P##<0.001	P#<0.001 P###<0.001 P####=0.728
Total proteins (g/L)	5.90 $\pm$ 0.31	5.80 $\pm$ 0.30	5.31 $\pm$ 0.18	5.62 $\pm$ 0.32	5.68 $\pm$ 0.19
Significance		P#=0.41	P#<0.001	P#=0.03 P##=0.013	P#=0.072 P###=0.004 P####=0.642
Albumin (g/L)	3.10 $\pm$ 0.26	3.12 $\pm$ 0.22	2.80 $\pm$ 0.12	3.02 $\pm$ 0.15	2.96 $\pm$ 0.13
Significance		P#=0.798	P#<0.001	P#=0.332 P##=0.008	P#=0.082 P###=0.055 P####=0.430
Total bilirubin (U/L)	0.057 $\pm$ 0.009	0.049 $\pm$ 0.007	0.090 $\pm$ 0.015	0.064 $\pm$ 0.022	0.073 $\pm$ 0.013
Significance		P#=0.25	P#<0.001	P#=0.29 P##<0.001	P#=0.015 P###=0.012 P####=0.156

Data are expressed as mean  $\pm$  standard deviation. Comparison was made using One Way ANOVA test (LSD). P#: p value of comparison versus control; P##: p value of comparison versus AlCl<sub>3</sub> group; P###: p value of comparison versus AlCl<sub>3</sub> then LS group.

**3.2. Histopathological Results.** It was observed that, in this study, kidney of control rats and those receiving LS had intact structure. On the other hand, renal cortex of rats receiving AlCl<sub>3</sub> showed shrunken renal corpuscles with marked hypocellularity and atrophied glomeruli. The renal tubules appeared dilated with hyaline casts in their lumina and some of them appear completely distorted. Rats receiving AlCl<sub>3</sub> then LS showed intact renal cortex, preserved cellularity of

renal corpuscles, and intact renal tubules apart from few with dilated lumina and hyaline casts. Renal cortex of rats receiving AlCl<sub>3</sub> plus LS had intact renal cortex (Figure 1).

When it came to the liver, it was observed that both control rats and those receiving LS showed intact liver. On the other hand, liver of rats receiving AlCl<sub>3</sub> showed massive focal hepatic necrosis with shrunken hepatocytes, damaged sinusoids with extravasation of blood cells, perivascular cell

TABLE 5: Comparison of kidney function tests in the serum of different studied groups.

Parameters	Control	LS-treated	AlCl <sub>3</sub> -treated	AlCl <sub>3</sub> then LS	AlCl <sub>3</sub> plus LS
Creatinine (mmol/L)	0.30±0.02	0.29±0.04	0.45±0.11	0.31±0.02	0.33±0.05
Significance		P#=0.869	P#<0.001	P#=0.681 P##<0.001	P#=0.206 P##<0.001 P###=0.389
Urea (mmol/L)	36.21±2.57	36.00±4.62	52.23±4.76	44.06±6.43	48.46±8.17
Significance		P#=0.944	P#<0.001	P#=0.014 P##=0.011	P#<0.001 P##=0.220 P###=0.154

Data are expressed as mean +/- standard deviation. Comparison was made using One Way ANOVA test (LSD). P#: p value of comparison versus control; P##: p value of comparison versus AlCl<sub>3</sub> group; P###: p value of comparison versus AlCl<sub>3</sub> then LS group.

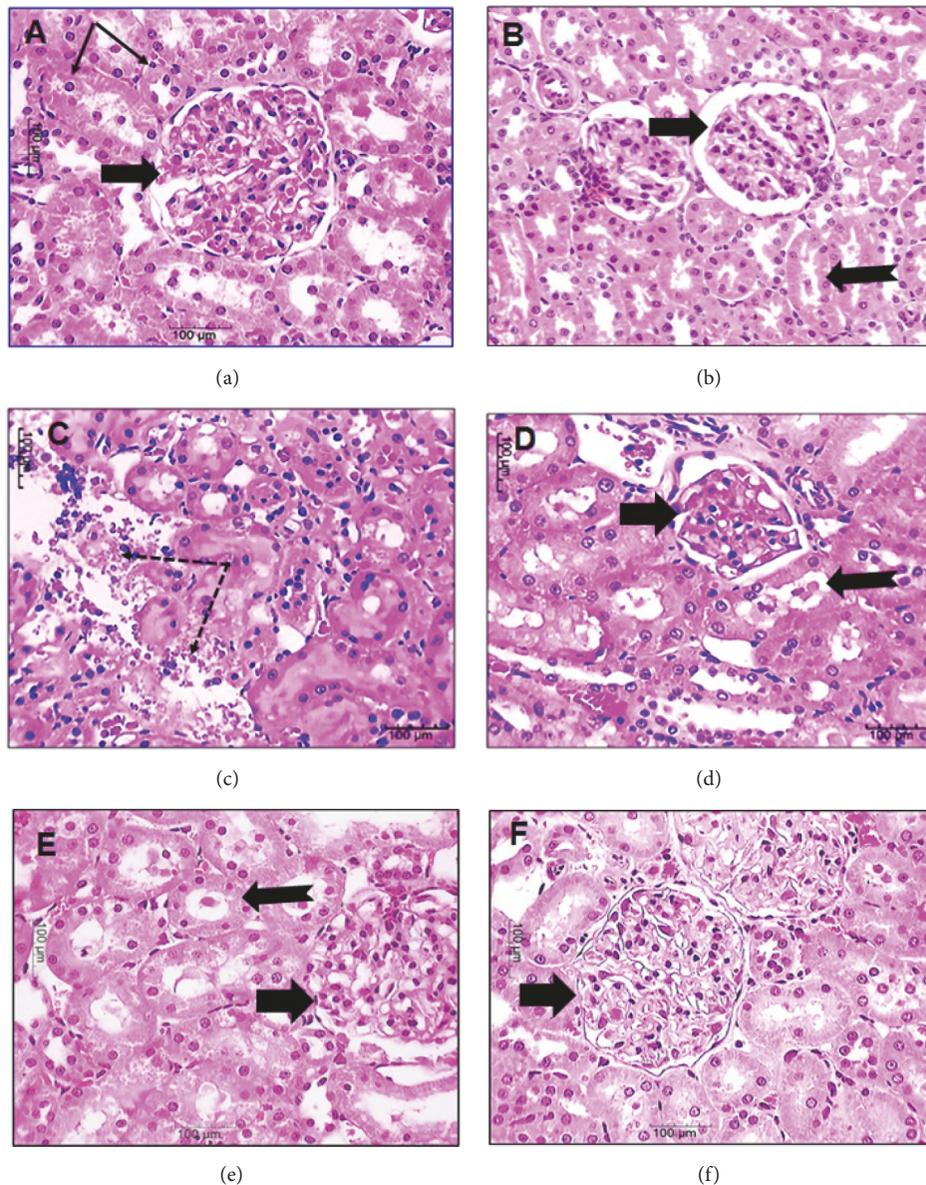


FIGURE 1: Sections of kidney of control rats (a) and rats receiving LS show intact renal cortex with intact renal corpuscle (arrows) and renal tubules. Renal cortex of rats receiving AlCl<sub>3</sub> (b-d) showing shrunken renal corpuscles (arrows) with marked hypocellularity and atrophied glomeruli. Renal tubules showed dilated lumina with hyaline casts (bifid arrows) and in some of them appear completely distorted (dotted arrows). Renal cortex of rats receiving AlCl<sub>3</sub> then LS (e) showing intact renal corpuscles with preserved cellularity (arrow) and intact renal tubules apart from few with dilated lumina and hyaline casts (thin arrows). Renal cortex of rats receiving AlCl<sub>3</sub> plus LS (f) showing intact structure of renal cortex (H&E X 400, Bar=100). LS: *Lepidium sativum*.

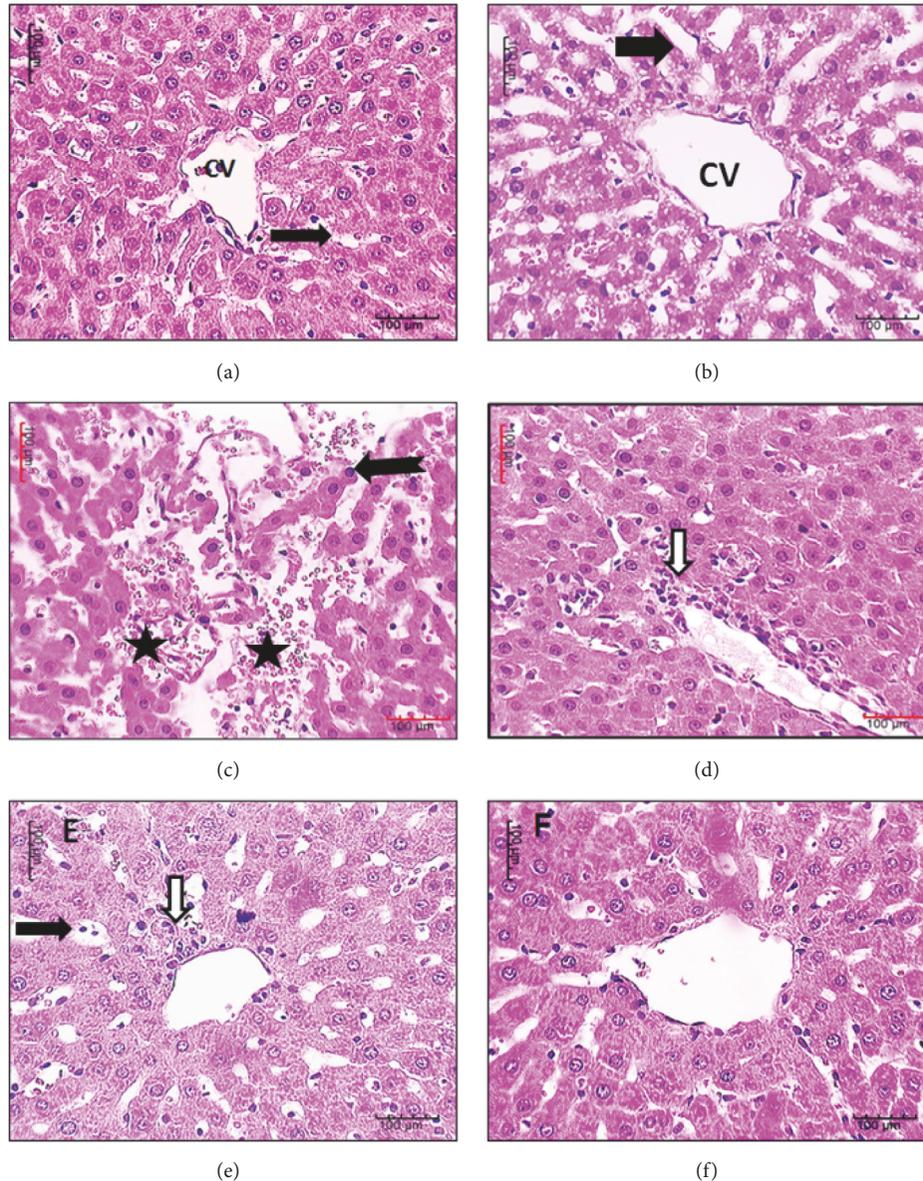


FIGURE 2: Sections in liver of control (a) and rats receiving LS (b) show intact liver apart from some dilated blood sinusoids (arrow). Liver of rats receiving  $\text{AlCl}_3$  (c, d) showing massive focal hepatic necrosis with shrunken hepatocytes (bifid arrows). Damaged sinusoids with extravasation of blood cells (stars) and perivascular cell necrosis and inflammatory cells (white arrow). Liver of rats receiving  $\text{AlCl}_3$  then LS (e) showing intact structure apart from some dilated sinusoids (arrows) associated with few inflammatory cells (white arrow) while livers of rat receiving  $\text{AlCl}_3$  plus LS (f) appear intact (H&E X 400, Bar=100). LS: *Lepidium sativum*.

necrosis, and inflammatory cells. Liver of rats receiving  $\text{AlCl}_3$  then LS showed intact structure apart from some dilated sinusoids associated with few inflammatory cells while liver of rats receiving  $\text{AlCl}_3$  plus LS appeared intact (Figure 2).

#### 4. Discussion

Aluminum chloride was considered a nontoxic metal for a long time, but more attention has been focused on its adverse effects on human and animal health [23]. Oxidative stress is considered to be a major contributor, a trigger for severe metal toxicities, and has been reported to be associated with long

retention of metals in some tissues [24]. It was well known that an imbalance between the overproduction of reactive oxygen species (ROS) and elimination of free radicals induces oxidative stress [4]. This study assessed the impact of  $\text{AlCl}_3$  on the function and structure of the liver and kidney, the possible protective and therapeutic effects of LS against this impact, and the mechanism behind these effects.

$\text{AlCl}_3$  was frequently reported to reduce body weight when administered in rats [25]. This is evident also in this study. LS administration during or after  $\text{AlCl}_3$  was found to protect against weight reduction and changes in weight percentage induced by  $\text{AlCl}_3$  in this study. In a previous

study, Sahane et al. observed that LS prevented weight loss in diabetic rats [26].

In the present study, the significant disturbing effect of  $AlCl_3$  administration on the lipid profile was evident as this was in agreement with previous studies of Ghorbel et al. who reported that  $AlCl_3$  induced abnormal activities of lipase enzymes that seem to be one of the chief factors responsible for the cholesterol rise in serum after  $AlCl_3$  administration [4]. In an earlier study, Al-Hashem reported that the increased cholesterol and triglycerides induced by  $AlCl_3$  indicated lost membrane integrity, disturbance of lipid metabolism, and/or liver dysfunction [27]. When it came to the effect of LS on the lipid profile, it was observed in this study that LS succeeded to reduce  $AlCl_3$ -induced elevation in the lipid profile. This was previously reported by Al-Khazraji on a diabetic animal model [28]. This hypolipidemic effect of LS might be attributed to its possible inhibitory effect on the endogenous synthesis of lipids. In a more recent study, both hypoglycemic and hypolipidemic effects of LS seeds extract administrated at a dose of 20 mg/kg were reported by Kamani et al. and they attributed these effects to the antioxidant activity of LS [29].

In the present study, assessment of antioxidants, mainly reduced glutathione (GSH), catalase, and FRAP, showed that  $AlCl_3$  treatment resulted in significant decrease in these parameters. This decrease was significantly alleviated by administration of LS seed aqueous extract. Significant differences in catalase and GSH levels in rats receiving LS along with  $AlCl_3$  compared to those receiving LS after  $AlCl_3$  indicated a more potent protective effect of LS. It was said that accumulation of Aluminum in organism can increase lipid peroxidation rates [30]. Lipid peroxidation is a chemical mechanism capable of disrupting the structure and the function of the biological membranes that occurs as a result of free radical attack on lipids [31]. In the present study, it was observed that LS repaired the oxidant/antioxidant balance as it significantly increased the antioxidants GSH, CAT, and FRAP in the serum. It was reported that LS and its metabolites are powerful antioxidants that can directly detoxify free radicals species by electron donation. It can also defend indirectly against oxidative damage by repair of the antioxidant system through enhancing the activities of a variety of antioxidants like GSH, CAT, and FRAP [32].

Exposure to  $AlCl_3$ , in the present study, resulted in alterations in the liver and kidney function and structure evident through both biochemical and histopathological assessment, respectively. Hepatic necrosis and degenerated and inflammatory changes were noted in livers of rats receiving  $AlCl_3$ . The exposure to  $AlCl_3$  significantly increased serum ALT, AST, ALP, and bilirubin and decreased total protein especially the albumin when compared to the control. This was in agreement with the findings of Imam et al. [23]. Liver manages a variety of metabolic substances and hepatocytes are easily affected by a variety of factors and harmful products like exposure to high doses of Aluminum, which proved to be accumulated in the liver and cause alterations of the hepatic function. Degeneration, inflammation, and necrosis caused by hepatocyte damage can lead to an increase in the permeability of cell membranes with subsequent increase of

AST and ALT into the blood, which are known to be effective indicators of liver damage [33].

Imam et al. reported that increased serum total bilirubin in the of  $AlCl_3$ -treated rats may be the result of decreased liver uptake (conjugation), increased production from hemolysis, and increased free radical production or due to the onset of periportal necrosis as proved histopathologically [23]. They added that decreased albumin may be due to changes in protein synthesis and/or metabolism in the liver. Furthermore, Al may promote proteinuria by causing a nephritic syndrome or chronic glomerulonephritis [27].

The role of antioxidant activity of LS seed aqueous extract against  $AlCl_3$ -induced alternations in both liver and kidney was also assessed. The presence of flavanoids, triterpens, alkaloid, tannin, and coumarins in LS explains its role in hepatoprotection by inhibiting the toxic radicals mediated damage. Our result agrees or corresponds with previous published results or studies [23].

Kidney is among the tissues in which Al accumulates. This accumulation promotes degeneration in the renal tubular cells and resulted in nephrotoxicity [34]. In this study, creatinine and urea were assessed as they are significant indicators of renal function.  $AlCl_3$  increased both parameters indicating impaired renal function as a result of glomeruli and tubules are damaged, which was evident histopathologically. This was in accordance with the findings of Joshi et al. and Imam et al. [23, 35]. Based on previous recommendations, LS was advised for treatment of hypertension, diabetes, and renal disease [5]. In this study, the protective and curative effect of ethanolic extract of LS on the renal function was observed as it significantly reduced the level of urea and creatinine, indicating increased glomerular filtration rate. Al Hamedan reported a diuretic activity of LS extract when administrated daily for 3 weeks [36].

In conclusion, exposure to  $AlCl_3$ , at a dose of 10 mg/kg of body weight daily for 8 weeks, induced a set of functional and structural changes in the liver and kidney of rats evident through both biochemical and histopathological assessment, respectively. The antioxidant activity of LS seed aqueous extract, at a dose of 20 mg/kg for 8 weeks, mediated a protective and curative effect of LS against  $AlCl_3$ -induced hepatic and renal changes. Further study, through a rigorous clinical trial to prove such effect of LS on human, is recommended.

## Data Availability

The data used to support the findings of this study are included within the article.

## Conflicts of Interest

The author declares that they have no conflicts of interest.

## Acknowledgments

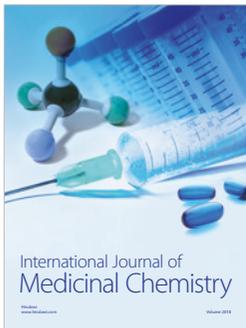
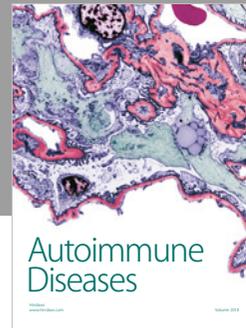
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