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Hepatoprotective effect of sesame oil against lead induced liver damage in albino mice: Histological and biochemical studies

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Abstract: The liver performs many vital functions to eliminate toxins and harmful substances from the body. Hepatotoxic agents can react with the basic cellular components and consequently induce almost all types of liver lesions. The aim of this study was to investigate the possible hepatoprotective role of sesame oil against lead acetate induced hepatotoxicity in albino mice from the histological and biochemical aspects. In this study, thirty two adult male albino mice were used for this study and divided into four groups. The first group was control group, the 2nd was the sesame oil group orally received sesame oil (5 ml/kg body wt.), the 3rd group was the experimental and received lead acetate (500 mg /kg diet), the 4th one co-administered lead acetate (500 mg/kg diet) with sesame oil (5 ml/kg body wt.) daily for 30 days. The livers were dissected out, weighted and specimens were taken and processed for light microscopic examinations. Blood samples were obtained for assessment of serum alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and γ- glutamyltransferase activities, serum total proteins and albumin. Results indicate that, in lead treated animals, there were severe structural damage in the liver. The hepatocytes appeared irregularly arranged with disorganization of hepatic architecture. The hepatocytes appeared large with light and foamy cytoplasm filled with numerous vacuole-like spaces. The nuclei appeared with pyknotic nuclei. The central vein appeared dilated and congested with massive hemorrhage extending to the nearby cells. Also, there were focal degenerative and necrotic changes along with inflammatory cell infiltration. Decrease in body weight and increase in liver weight were observed. Biochemically, the serum alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and γ- glutamyltransferase activities were increased and serum total proteins and albumin were decreased. Co-administration of sesame oil significantly improved the structural changes in the liver and also the serum alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and γ- glutamyltransferase activities were significantly declined and serum total proteins and albumin were elevated. Conclusion: It can be concluded that, the lead had adverse effects on the liver. Sesame oil showed effective hepatoprotective action against lead acetate induced hepatotoxicity in albino mice. So, the populations of high risk to lead should be advised to take sesame oil.

Keywords: Lead Acetate, Hepatotoxicity, Hepatoprotective, Serum Enzymes Activities (ALT, AST, ALP, γ-GT), Histology, Serum Total Proteins, Serum Albumin, Sesame Oil

1. Introduction

Liver plays a vital role in detoxification and excretion of many endogenous and exogenous substances [1]. Continuous exposure and intoxication of liver to different types of exogenous compounds on a daily basis may lead to hepatic dysfunction [2]. Hepatic dysfunction due to exposure to environmental toxic agents is increasing worldwide. Toxins and drugs are among the basic etiopathogenetic agents of acute liver failure in Western countries [3].

Lead is a poisonous metal, which exist in both organic and inorganic forms in the environment [4]. Lead poisoning is one of the oldest and the most widely studied occupational and environmental hazards [5]. The exposure to lead can occur from a multitude of sources such as soil, air, water and industrial pollutants. It has been used in medicines, paintings, pipes, ammunition and in more recent times in alloys for welding storage materials for chemical reagents [6]. There are worldwide, six categories of products considered as source of

lead exposure, that is, gasoline additives, food cane soldering, lead based paints, ceramic glazes, drinking water systems, and folk remedies [7]. Autopsy studies of lead exposed humans indicate that liver tissue is the largest repository (33%) of lead among the soft tissues followed by kidney cortex and medulla [8]. Several reports have indicated that lead can cause neurological, hematological, gastrointestinal, reproductive, circulatory and immunological pathologies, all of them related to the dose and the duration of time of lead exposure [9 &10]. Toxicities due to lead exposure have been attributed to the ability of lead to induce oxidative stress through the generation of reactive oxygen species [11].

Nowadays, there is an increasing interest in discovering the protective biological function of natural compounds contained in dietary plants due to safe use, their antioxidative properties and their possible roles in intra and extracellular defense against oxygen radicals and lipid peroxides in response to oxidative stress [12]. The ability of lead to induce reactive oxygen species could be supported by the fact that lead induced toxicities were found to be mitigated by some chelating agents [13] and certain antioxidants such as vitamin C, E, green tea, pectin, flaxseed oil [14 & 15], methionine, N-acetylcysteine, homocysteine and α-lipoic acid [16]. Plant extracts and materials of animal origin were also observed to protect against lead induced toxicity in experimental animals. The abilities of these extracts to mitigate these toxicities were attributed to the antioxidant properties of principles contained in these extracts [11].

Sesame oil is derived from the plant species *Sesamum indicum* L, a herbaceous annual in the Pedaliaceae family [17]. It contains several antioxidants and chemo-preventive agents such as tocopherol [18], sesamolin, sesaminol [19] and sesamin [20]. They also contain a good type of mono-unsaturated and polyunsaturated fatty acids [21], highly nutritious, rich in vitamin A, B and E as well as the minerals iron, calcium, magnesium and copper [22]. Sesame oil is incredibly popular for its nutritional antioxidant and medicinal properties [23]. It is well known for its multiple health benefits, including hypocholesterolemic, anti-hypertensive, anti-carcinogenic, anti-aging, immuno- regulatory, hypoglycemic, antithrombotic, hepatoprotective [24, 25], anti-bacterial, anti-viral, anti-fungal and anti-inflammatory [26].

Antioxidant potential of the sesame oil in the amelioration of metal induced oxidative stress need thorough investigation because these natural antioxidants are components of many edible substances and has the potential for safe future use by humans. The evidence reporting the protective effect of sesame oil against chronic lead toxicity in liver are hardly found. So, the present work aimed to evaluate effectiveness of sesame oil against the histological and also biochemical alterations of lead induced hepatotoxicity in albino mice.

2. Materials and Methods

2.1. Chemicals

Lead acetate and sesame oil were purchased from Sigma Chemical Co., USA.

Sesame oil was given orally by gavages at a volume of 5 ml/kg body weight according to the previous study of Hussien *et al.* [27]

Lead acetate was given in diet as 500 mg/kg diet daily [4] for 30 days. The choice of the dose of sesame oil was based on the results of the previous studies, where the antioxidant effect of this agent was confirmed.

2.2. Animals

Thirty two adult male albino mice (*Mus musculus*) weighting 25-30 g were used for this study. The animals were obtained from animal house unit in the Faculty of Pharmacy, Tripoli University, Libya. The animals were housed in plastic cages measuring about (29×15×12) cm, with about four mice per cage. Floors of cages were covered with soft crushed wood shaving; all cages were washed two times per week with 70% alcohol throughout the period of the study. The animals were provided with tape water *ad libitum* and fed with the standard commercial chow. The animals were kept in the animal house of Faculty of Science, Alejelat, Zawia University in an air conditioned room with an optimum temperature of 25±2 °C, humidity (60-70%) and light/dark condition (12/12). The animal procedures were performed in accordance with Guide Lines for Ethical Conduct in the Care and Use of Animals.

2.3. Experimental Design

After one week of acclimation, the animals were randomized and divided into four groups (8 albino mice for each) as follow:

Group I (control group): provided with tape water and fed with normal diet.

Group II (sesame oil group): The animals received sesame oil (5 ml/kg body wt/day) orally by gavage daily for 30 days.

Group III (lead acetate treated group): The animals received 500 mg lead acetate/kg diet daily for 30 days.

Group IV (lead acetate/sesame oil co-administered): The animals received 500 mg lead acetate/kg diet concurrently with sesame oil (5 ml/kg body wt/day) orally by gavage daily for 30 days.

At the end of the experimentation and 24 hours after the last dose, all animals were weighted and then sacrificed under light ether anesthesia, then rapidly dissected and subjected to the following examinations:

2.4. Histological Examination

The liver was exposed by mid line incision and then rapidly dissected from the surrounding structures and weighted. Liver specimens were obtained and fixed in buffered 10 % formaldehyde solution for 24 hours and processed for paraffin sections of 5 micron thickness. The sections were stained with Hematoxylin and Eosin and examined under light microscopy [28].

2.5. Biochemical Analysis

Blood samples were drown by cardiac puncture and centrifuged at 3000 rpm for 15 minutes to harvest the serum

with which the liver functions assessment were analyzed. The activities of Alanine aminotransferase(ALT), aspartate aminotransferase (AST) were determined in serum according to the methods described by Reitman and Frankel [29]. Serum alkaline phosphatase (ALP) activity was determined according to Kind *et al*. [30]. Serum γ-GT activity was determined according to the method of Szas [31]. Serum total proteins concentration was determined according to Biuret method explained by Tietz [32]. Serum albumin concentration was determined according the method of Doumas *et al.* [33].

2.6. Statistical Analysis

The values were presented as means ± SD of different groups. Differences between the mean values were estimated using one way ANOVA. The results were considered statistically significant when $p < 0.05$.

3. Results

Histologically, by light microscopic examination, the liver appeared with normal structure in all control groups (negative and positive control animals). The hepatocytes arranged in cell strands radiating from the central vein with intervening blood sinusoids which appeared to be lined by Kupffer cells. The hepatocytes appeared pentagonal and contained large nuclei. No detectable pathological changes showed in the liver of mice treated with sesame oil alone as well as the controls (Fig. 1).

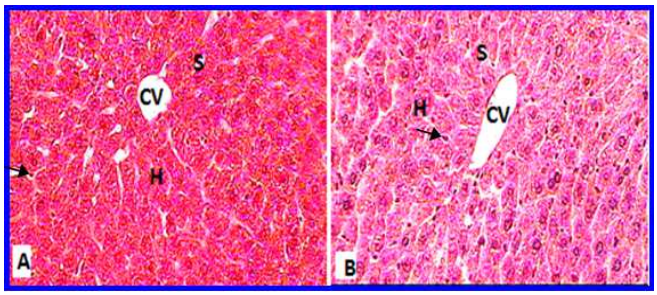

Fig. (1). *Light micrograph of sections in the liver of control albino mice ; A: Negative control, B: Positive control (administered sesame oil only); Central vein (CV); Kupffer cells (( ); Hepatocytes (H); Sinusoids (S). (Haematoxylin & Eosin×400).*

Lead acetate treated mice showed distortion of the arrangement of parenchyma of the liver, loss of radial arrangement of sinusoids from the central vein of the liver. Marked necrosis of hepatocytes, that appeared deeply esinophilic, and some with pyknotic nuclei (Fig. 2A, B & C) when compared with the control (Fig. 1A). The hepatocytes appeared large with light and foamy cytoplasm filled with numerous vacuole-like spaces. Many hepatic cells were damaged and lost their characteristic appearance. Others showed severe cytoplasmic vacuolation (Fig. 3B) which is so extensive in some cells to the extent that only slight remnants of the cytoplasmic mass were left. Hyper activation of Kupffer cells were observed (Fig. 2A). There were severe diltations and congestions of centeral veins, sinus and portal blood vessels (Fig. 2). Some areas showed multifocal to diffuse type of coagulative necrosis. Most of the portal veins appeared congested with inflammatory cells infiltrations (Fig. 3A). Marked vacuolar degeneration mainly hydropic degeneration (Fig. 3B). The bile ducts were seen enlarged and hyperplasic (Fig. 2D).

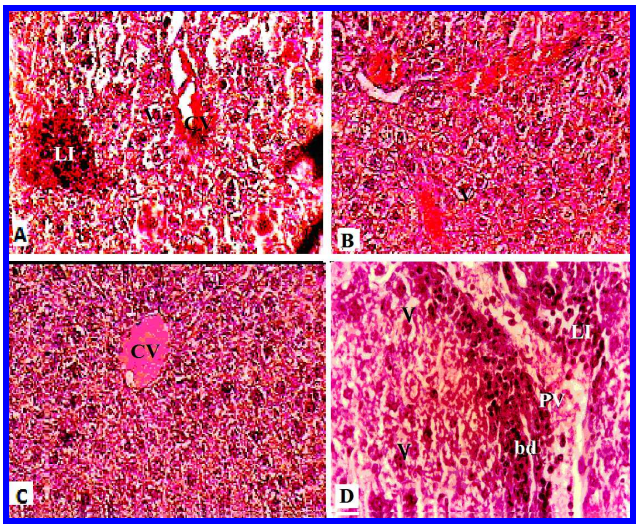

Fig. (2). *Light micrograph of sections in the liver of lead treated group presenting; A: wide spread necrobiotic changes in the hepatocytes, dilatation of blood sinusoid lumen, and marked vacuolar degeneration (V) mainly hydropic degeneration. B & C: Distortion of the arrangement of parenchyma of the liver, loss of radial arrangement of sinusoids from the central vein of the liver and loss of hexagonal shape of the hepatocytes. Dilatation and congestion of central veins (CV), sinus and portal veins. Marked necrosis of hepatocytes, that appeared deeply esinophilic, and some with pyknotic nuclei. D: Marked vacuolar degeneration of hepatocytes mainly hydropic degeneration (V), congested and dilated portal vein (PV), inflammatory cells infiltration (LI), hyperplasic bile duct (bd), (Haematoxylin & Eosin×400).*

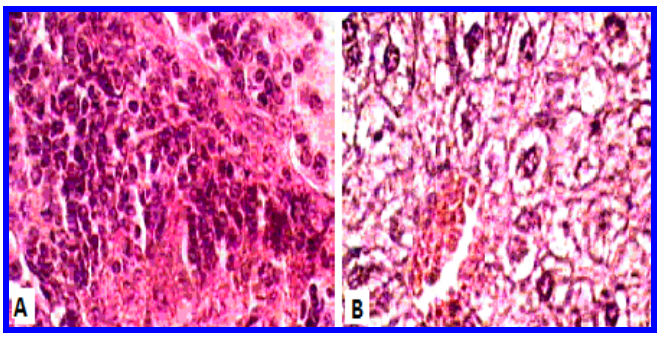

Fig. (3). *Light micrograph of sections of a higher magnification in the liver of lead acetate treated albino mice. A: Marked inflammatory cells infiltration B: Marked vacuolar degeneration mainly hydropic degeneration, the central vein appeared congested with massive hemorrhage extending to the nearby cells. These necrotic cells appeared homogenous structurless with degenerated nuclei. (Haematoxylin & Eosin× 1000).*

The liver of lead acetate treated albino mice co-administered sesame oil showed marked improvement in its histological structure in comparison to the group treated with lead acetate alone. the central vein appear more or less normal. The liver sections showed the hepatocytes regained their normal organization and architecture (Fig. 4).

Tables 1, 2 showed the means and standard deviations for

serum ALT, AST, ALP, and γ- GT activities in control groups, lead acetate treated group and albino mice group co-administrated of lead acetate with sesame oil. The levels of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and γ-glutamyltransferase (γ-GT) activities were elevated in lead acetate treated animals compared with the control groups with statistically significant differences ($p<0.05$). The enzyme activities in the co-administration of lead acetate with sesame oil were decreased with statistically significant differences ($p<0.05$) (Figs. 5, 6, 7 & 8), when compared with lead acetate group.

Table (1). *Effect of sesame oil on the serum alanine aminotransferase, and aspartate aminotransferase activities of lead acetate treated male albino mice in different groups.*

Groups	ALT (U/L)	AST (U/L)
	Mean ± SD	Mean ± SD
Control	29.6 ± 1.67	51.23± 3.12
Sesame oil	27.4 ± 1.01	48.61± 1.31
Lead acetate	47.2± 3.50a	76.45± 4.18a
Lead acetate + Sesame oil	31.22 ± 1.35b	55.51 ± 2.46b

[a] : Significant differences as compared with control group (P < 0.05) .
[b] : Significant differences as compared with lead acetate treated group (P < 0.05). All data are mean of 8 individuals.

Table (2). *Effect of sesame oil on the serum alkaline phosphatase, and Ɣ-glutamyltransferase activities of lead acetate treated male albino mice in different groups.*

Groups	ALP (U/L)	Ɣ-GT (U/L)
	Mean ± SD	Mean ± SD
Control	44.19±2.05	8.54±0.41
Sesame oil	46.01±1.06	9.16±0.33
Lead acetate	72.12±3.98[a]	13.31± 0.82[a]
Lead acetate + Sesame oil	49.13 ±3.27[b]	9.62± 0.39[b]

[a] : Significant differences as compared with control group (P < 0.05) .
[b] : Significant differences as compared with lead acetate treated group (P < 0.05). All data are mean of 8 individuals.

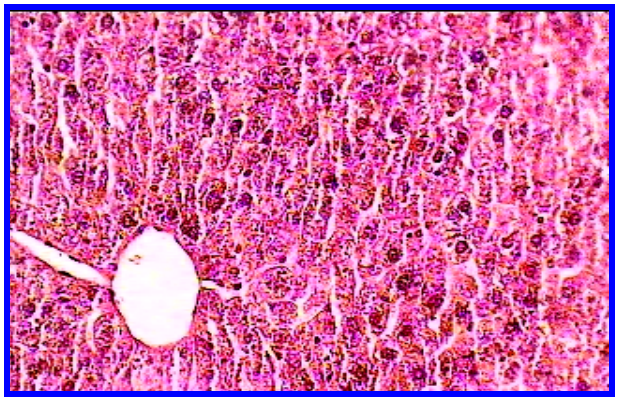

Fig. (4). *Light micrograph of a sections in the liver of lead acetate treated albino mice co-administered sesame oil. The central vein appear normal. The hepatocytes regained their normal organization and architecture. (Haematoxylin & Eosin×400).*

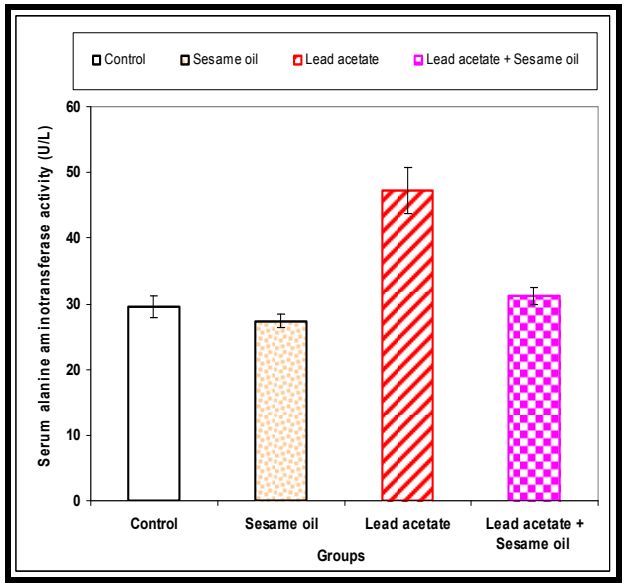

Fig. (5). *The serum alanine aminotransferase (ALT) activity in different animals groups. The serum ALT activity is the highest in lead acetate treated group in comparison with control groups (normal control and sesame oil treated).The serum ALT activity shows declining in co-administered lead acetate and sesame oil treated.*

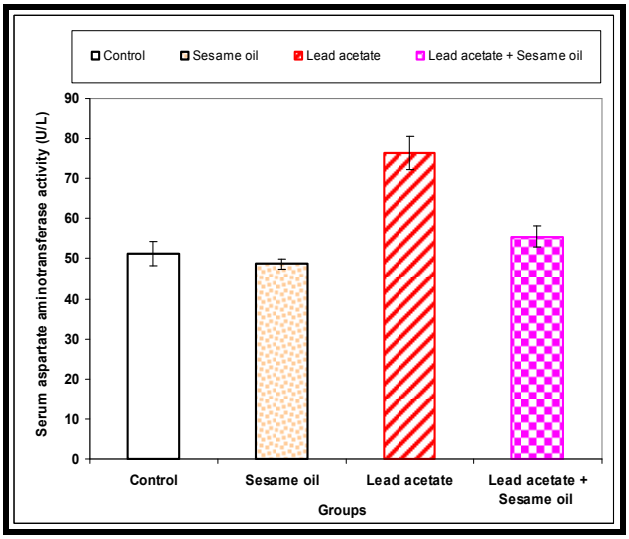

Fig. (6). *The serum aspartate aminotransferase(AST) activity in different animals groups. The serum AST activity is the highest in lead acetate treated group in comparison with control groups (normal control and sesame oil treated).The serum AST activity shows declining in co-administered lead acetate and sesame oil treated.*

Table (3) displays the serum total proteins and albumin concentration of control groups and experimental animals groups. The levels of serum total proteins and albumin concentrations were declined in lead acetate treated animals compared with the control groups with statistically significant differences ($p<0.05$). The levels of serum total proteins and albumin concentrations in the co-administration of lead acetate with sesame oil were increased with statistically significant differences ($p<0.05$) (Figs. 9 & 10), when compared with lead acetate group.

Regarding the changes in body and relative liver weight of

the animals in the present study, the body weight at the end of the experiment decreased in the lead acetate treated animals compared with the control groups with statistically significant differences ($p<0.05$). The weight increased in co-administered lead acetate and sesame oil with significant differences ($p<0.05$) from the lead acetate treated group. The relative liver weight increased in lead acetate treated group as compared with the control group with statistically significant differences ($p<0.05$). The relative liver weight decreased in co-administered lead acetate and sesame oil with significant differences (Table 4 and Figs 11 & 12) , when compared with lead acetate group.

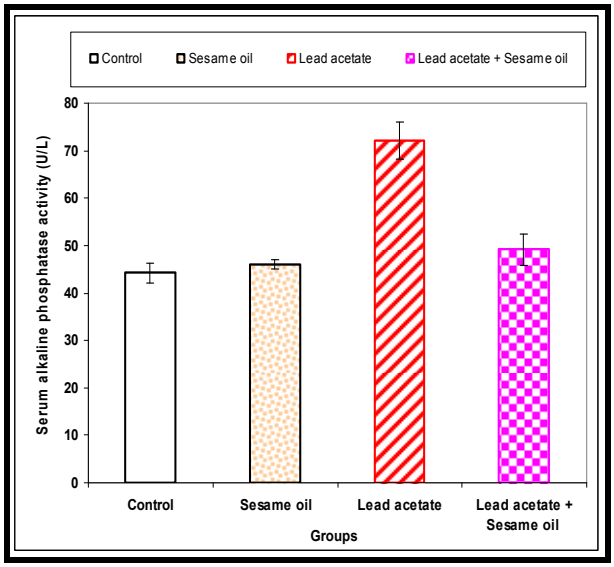

Fig. (7). *The serum alkaline phosphatase activity (ALP) in different animals groups. The serum ALP activity is the highest in lead acetate treated group in comparison with control groups (normal control and sesame oil treated). The serum ALP activity shows declining in co-administered lead acetate and sesame oil treated.*

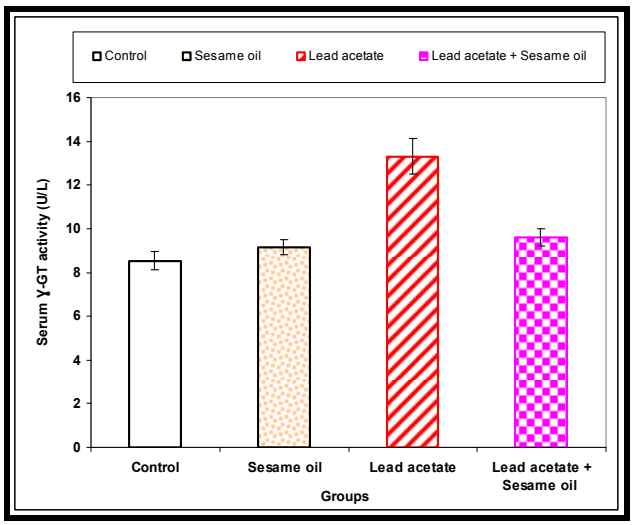

Fig. (8). *The serum γ- glutamyltransferase (γ-GT) activity in different animals groups. The serum γ- glutamyltransferase activity is the highest in lead acetate treated group in comparison with control groups (normal control and sesame oil treated).The serum γ- glutamyltransferase activity shows declining in co-administered lead acetate and sesame oil treated.*

Table (3). *Effect of sesame oil on total proteins and albumin in the serum of lead acetate treated male albino mice in different groups.*

Groups	Total proteins (g / dl)	Albumin (g / dl)
	Mean ± SD	Mean ± SD
Control	6.67±0.29	4.19±0.22
Sesame oil	6.86±0.25	4.30±0.0.13
Lead acetate	4.55± 0.32[a]	2.99± 0.17[a]
Lead acetate + Sesame oil	6.63± 0.24[b]	4.01± 0.19[b]

[a] : Significant differences as compared with control group ($P < 0.05$) .
[b] : Significant differences as compared with lead acetate treated group ($P < 0.05$). All data are mean of 8 individuals.

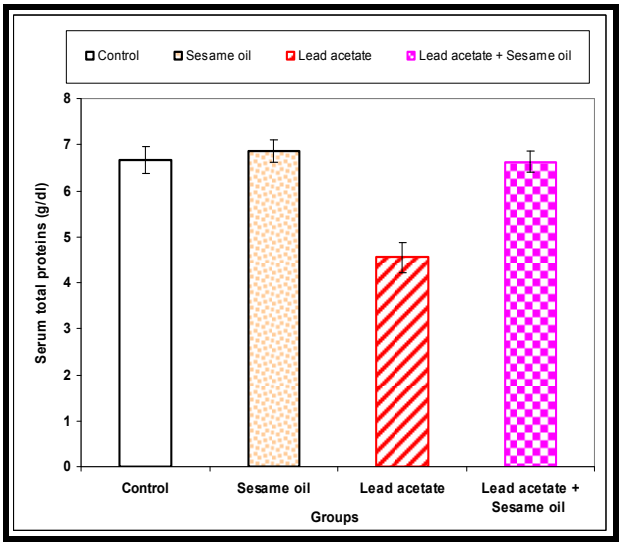

Fig. (9). *The serum total proteins concentration in different animals groups. The serum total proteins concentration is markedly declined in lead acetate treated group in comparison with control groups (normal control and sesame oil treated). The serum total proteins concentration shows declining in co-administered lead acetate and sesame oil.*

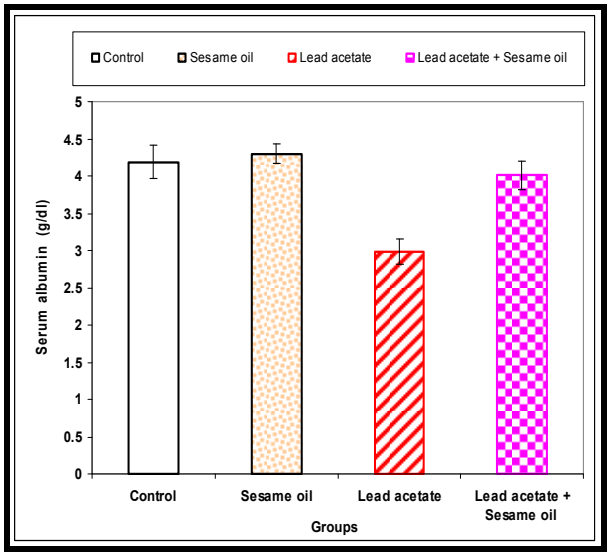

Fig. (10). *The serum albumin concentration in different animals groups. The serum albumin concentration is markedly declined in lead acetate treated group in comparison with control groups (normal control and sesame oil treated). The serum albumin concentration shows declining in co-administered lead acetate and sesame oil.*

Table (4). *Effect of sesame oil on body weight and relative liver weight of lead acetate treated male albino mice in different groups.*

Groups	Body weight (g)	Relative liver weight (gm/100 gm of body weight)
	Mean ± SD	Mean ± SD
Control	32.5 ± 1.21	4.25 ± 0.33
Sesame oil	31.3 ± 1.03	4.11 ± 0.15
Lead acetate	26.00 ± 1.5[a]	5.77 ± 0.30[a]
Lead acetate + Sesame oil	30.2 ± 1.35[b]	4.31 ± 0.21[b]

[a] : Significant differences as compared with control group (P < 0.05) .
[b] : Significant differences as compared with lead acetate treated group (P < 0.05). All data are mean of 8 individuals.

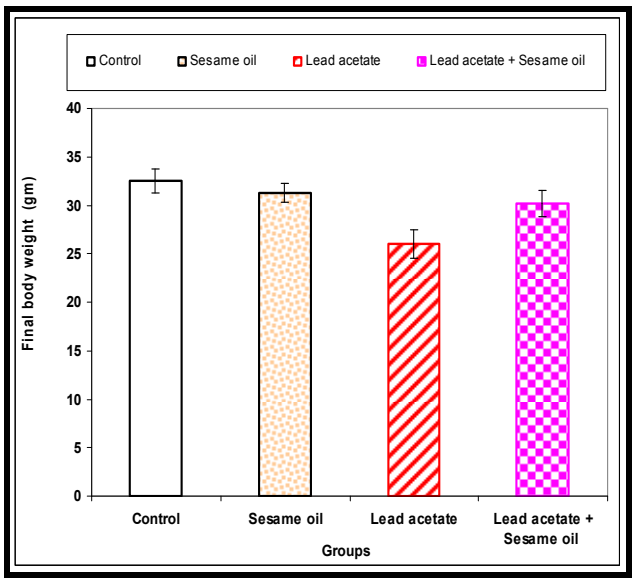

Fig. (11). *The body weight in different animals groups. The body weight decreased in lead acetate treated group in comparison with control groups (normal control and sesame oil treated). The body weight increases in co-administered lead acetate and sesame oil.*

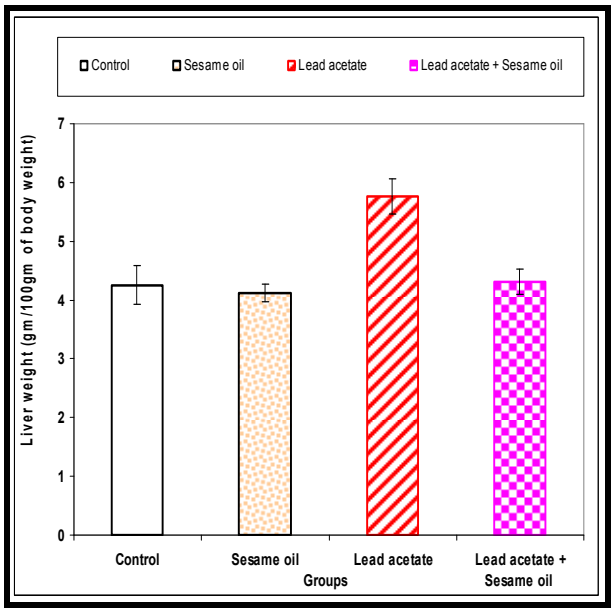

Fig. (12). *The liver weight in different animals groups. The liver weight increases in lead acetate treated group in comparison with control groups (normal control and sesame oil treated). The weight declines in co-administered lead acetate and sesame oil.*

4. Discussion

In this study, the lead acetate had adverse effects on the liver. Histologically, the hepatocytes appeared irregularly arranged with disorganization of hepatic architecture. The hepatocytes appeared large with light and foamy cytoplasm filled with numerous vacuole-like spaces. The nuclei appeared pyknotic nuclei. The central vein appeared dilated and congested with massive hemorrhage extending to the nearby cells. Also, there were focal degenerative and necrotic changes along with inflammatory cell infiltration. This is in agreement with many authors who reported the toxicity of lead on the liver [4, 8, 34-36]. Similar observations were reported by Suradkar *et al.* [37] who found that lead acetate can cause lesion characterized by engorgement of blood vessels along with sinusoidal hemorrhages, perivascular mononuclear cell infiltration, dilatation of central veins, vacuolar degeneration of hepatocytes and increased cytoplasmic eosinophilic granularity, swelling of hepatocytes with the variable degree of nuclear changes, distortion of hepatic chords and areas of diffused vacuolar and granular degeneration. Lead exposure produced pronounced hepatic histopathology evidenced by histological alternations in liver including focal necrosis with inflammatory cells, congestion at places, sinusoids not patent, centre lobular swelling, hepatocyte vacuolization and swelling, parenchyma disorganization, dilation of the inter hepatocyte space, and hemorrhagic clots [35]. Abd El Kader *et al*. [34] found that the lead can cause severe hepatocytes damage, dilation of blood sinusoids and loss of architecture were seen after acute treatment for 7 days. The appearance of inflammatory cells in the hepatic tissue, due to lead chronic exposure, may suggest that lead could interact with proteins and enzymes of the hepatic interstitial tissue interfering with the antioxidant defense mechanism and leading to reactive oxygen species generation which in turn may imitate an inflammatory response [38].

Cell necrosis and vacuolization induced by lead toxicity as shown in the present work were described previously by other studies [39 & 40]. Robbins and Angell [41] regarded such vacuolation to represent primary morphologic response to many forms of cell injury. They also attributed it to the noxious effects of treatment on the cell membranes, both structurally and functionally, causing marked disturbances in its permeability system. This presumably leads to enhanced imbibition of water into the cells. When it sufficiently accumulates in the cells, such intracellular water produced clear cytoplasmic vacuoles indication the occurrence of the pathologic symptoms commonly referred to as hydropic degeneration or fatty degeneration caused by lipid abundance in such instance.

The patho-morphological lesions in liver may be due to the action of lead on hepatic glycogen, DNA content and the ability to incorporate amino acid into protein [42]. Mechanisms of lead-induced liver injury include increased production of reactive oxygen species, and induced oxidative stress which results in DNA damage [43]. These reactive species interfere with cellular macromolecules and deactivates

cellular antioxidant pool [44]. Many heavy metals, including lead, are known to induce over production of Reactive Oxygen Species and consequently enhance lipid peroxidation [45], decrease the saturated fatty acids and increase the unsaturated fatty acid contents of membranes [46], which become a hindrance in membrane transport [47].

In this work, treatment of albino mice with lead acetate caused a significant increase of the activities of serum AST, ALT, ALP and γ-GT. Similar observations were reported in many experimental investigations on animals exposed to lead [46 & 48]. In addition, Shalan *et al.* [4] has reported that serum ALT, AST, ALP and GGT activities were elevated in rats treated with lead acetate as early as the end of the second week of treatment and ALT was elevated significantly more than AST on lead exposure. The increase in such enzymes might be due to increased cell membrane permeability [49], or damage of hepatocytes caused by lead acetate [50]. Treatments with lead acetate were found to cause a significant increases in serum ALT, AST and ALP activities [51 &52]. Attia *et al.* [53] reported increased activities of ALT and AST in rats during lead poisoning. Increasing levels of AST and ALT in the plasma of treated rats is mainly due to the leakage of these enzymes from the liver cytosol into the blood stream [54]. Releasing of AST and ALT from the cell cytosol can occur as secondary changes to cellular necrosis [55]. Furthermore, Ibrahim *et al*. [55] reported that the high plasma AST and ALT activities are accompanied by high liver microsomal membrane fluidity, free radical generation and alteration in the liver tissue.

The present study, revealed that treatment of albino mice with lead acetate induced a significant decrease in the values of serum levels of total proteins, and albumin. Similar findings coincided by Ibrahim *et al*. [46]. The level of total proteins was decreased in rats treated with lead [4, 46 & 48]. The decrease in serum total proteins may be due to both hepatic and renal damage induced by lead [56], or may be due to binding of lead to some metal binding proteins and their removal through detoxification processes [57], where it causes alteration in a high number of enzymes and can also disturb protein synthesis in hepatocytes [58]. Moreover, the decreasing of serum total proteins values may be attributed to a decrease in hepatic DNA and RNA induced by lead intoxication or due to decreased utilization of free amino acids for protein synthesis [4]. The DNA damage by lead may be due to depletion of antioxidant enzymes [59]. Moreover, El-Zayat *et al*. [60] found that a decrease in hepatic total proteins content in response to lead intoxication. They attributed that to a decreased utilization of free amino acids for protein synthesis. Also, the observed decrease in the total proteins and albumin in the liver could be attributed to the damaging effect of lead acetate on liver cells as confirmed by increasing in the activities of serum AST and ALT after treatment of rats with lead acetate [61& 62]. Hypoproteinemia is reflecting liver injury [63], which may be due to significant fall in protein synthesis [64].

From the obtained results, the weight of the animals exposed to lead acetate were significantly decreased. The present results are in accordance with other studies which found that exposure of rats to lead acetate causes a decrease in body weight gain [36, 46 & 65]. Decreased body weight was previously observed by Allouche *et al.* [65] who administered 0.1% lead acetate to male rats during 11 months. Moreover, The decrease in body weight is not only a consequence of decreased food consumption [17, 24, 54], but also from direct toxicity of the lead acetate, perhaps by the interruption in absorption, and metabolism of feed nutrients essential for health [66], from toxic effects on the gastrointestinal tract or by inhibition of protein synthesis [67]. The decreased body weight explained by Kaltreider *et al*. [68] who found that exposure to low level of heavy metals impairs the glucocorticoid system. The glucocorticoid hormones play a vital role in glucose regulation as well as carbohydrate, lipid and protein metabolism. Dysfunction in the glucocorticoid system has been linked to weight gain loss.

This study shows that, the relative liver weight increased at the end of the experiment in lead acetate treated group. This is in agreement with many authors who reported the toxicity of lead on the liver weight [36]. Prabu *et al*. [69] who found that oral administration of cadmium chloride as a heavy metal resulted in increase of the relative liver weight. Also, the liver weight increased in cadmium treated male rats, and mice [70].

Co-administration of sesame oil with lead acetate significantly regained their normal organization and architecture of the hepatocytes, and the central vein appeared normal. Similarly, pretreatment of rats with two different doses (400mg/kg and 700mg/kg) of *Sesamum indicum* for 21 days before administration paracetamol produced a significant reduction of paracetamol-induced elevation of serum enzymes markers and reduced histopathological scores of fatty degeneration, centre lobular necrosis with significant evidence of regeneration. The results of the study indicate that the extract of *Sesamum indicum* possesses significant protection against Paracetamol-induced hepatocellular injury [71].

Also, Prasanthi *et al*. [22] found that the liver of rats fed dietary sesame oil and Fenvalerate showed normal histology suggesting marked protection afforded by sesame oil. The mechanism by which dietary sesame oil attenuates the oxidative damage is not clear, it is speculated that the antioxidant components (sesamol and sesamolinol and sesaminol) present may be largely responsible for this protective response.

This study revealed that administration of sesame oil along with lead acetate, showed a good protective effect by restoration of biochemical profiles in the hepatic functional indicators in serum. This was also well correlated with normal histological architecture in the liver. This is in agreement with Uthandi and Ramasamy [72] who found that the elevation in ALT, AST, ALP activities and reduction total proteins level significantly restored towards normalization by sesame meal treatment in high fat fed Wistar rats. Also, the activities of hepatic ALT, AST and ALP in rats fed dietary sesame oil and Fenvalerate were significantly modulated suggesting varying degree of protection [22]. Sesame normalized the elevated levels of Serum glutamate oxaloacetate transaminase, serum

glutamate pyruvate transaminase, alkaline phosphatase, total proteins, and albumin [73]. Levels of ALT and AST increased with co-exposure to lead and lipopolysaccharide induced liver injury but were lower with sesamin treatment, suggesting that sesamin may protect rats from lead and lipopolysaccharide liver injury [74 & 75]. Sesamin could protect from liver injury by attenuating the increased serum IL-1, IL-6, TNF-a and nitrite in the lead induced rats [76].

Sesame oil ameliorated the reduction in plasma total proteins and albumin induced by cypermethrin. The protective effect of sesame oil against the toxicity of cypermethrin may be related to its antioxidant effect and its ability to inhibit the lipid peroxidation [27].

Co-administration of sesame oil with lead acetate to albino mice significantly improves the body and liver weights. This in agreement with Hussien *et al*. [27] who demonstrated that treatment with sesame oil ameliorated the alteration in body weight induced by cypermethrin, which may be attributed to the vital role of sesame oil as antioxidant. The antioxidant activity of sesame oil could be attributed to its phenolic lignans type compounds namely sesamol, sesamin and sesaminol [76]. The liver weights were significantly reduced in rats fed dietary sesame oil and Fenvalerate when compared to rats fed dietary Fenvalerate [22].

Sesame oil have been shown to possess free radical scavenging properties and protect oxidative stress induced toxic injuries. Many researchers investigated the role of sesame oil in the attenuation of hepatic injury. Chiang *et al*. [75] have shown that sesamin effectively ameliorated lead and lipopolysaccharide-induced acute liver injury in rats by the inhibition of proinflammatory cytokines and nitric oxide. They further pointed out that the inhibition of liver injury is through the suppression of several signaling pathways, such as c-Jun N-terminal kinase, p38 mitogen-activated protein kinase, cyclooxygenase-2, inducible nitric oxide synthase, and growth arrest DNA damage 45b. It seems that sesamin can mitigate the hepatic injury through these gateways. The authors found that the effect of sesamin was through the suppression of several signaling pathways. The interaction and real role of these pathways in relation to the effect of sesamin are unknown. Hsu *et al.* [77] reported that sesame oil attenuates cisplatin induced hepatic and renal injuries by inhibiting nitric oxide associated lipid peroxidation in mice. Erol *et al.* [78] found that, sesame oil treatment has a potent protective effect against apoptosis induced by cyclosporine-A in rats, as revealed by remarkable decrease in apoptotic cells in the liver. The mechanisms underlying hepatoprotection of sesame oil may be related to both their radical scavenging properties and indirect effects as a regulator of antioxidative systems. Sesamin has been reported to protect against alcohol and chemical-induced liver injury. It is speculated that the mechanism underlying hepatoprotection of sesamin is via suppression of the free radical- mediated process triggered by hepatotoxins [24]. Furthermore, Chaudrasekaran *et al*. [79] stated that sesame oil enhanced the antioxidant status and inhibited lipid peroxidation in rats with acetaminophen induced acute liver injury. These findings indicate that sesame oil is a potent antioxidant rich oil as it possesses some preventive substances such as sesamin, sesaminol and sesamolin besides its wealth with fat soluble vitamins like tocopherol [18]. Sesame oil was found to protect against oxidative stress and hepatic injury after cecal ligation and puncture in rats, which may be attributable to the antioxidant components in sesame oil [20 & 80].

5. Conclusion

From the previous discussion, it can be concluded that, the lead had adverse effects on the liver. Sesame oil showed effective hepatoprotective action against lead acetate induced hepatotoxicity in albino mice. So, the populations of high risk to lead should be advised to take sesame oil. Further studies are necessary to elucidate exact mechanism of protection of hepatotoxicity and potential usefulness of sesame oil as a protective agent against heavy metals toxicity in clinical trials.

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