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Lead Acetate Induced Hepatotoxicity and Attenuation by *Trigonella foenum-graecum* and *Curcuma longa* in Male Albino Rats

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Abstract: Background: Lead is widely used in many applications and so the potential to expose to its toxicity (animals and human) and environmental contamination is easier than other heavy metals. The exposure to lead possesses the potentials to induce hazardous biological effects in both animals and human beings. The antioxidants are important species that possess the ability to protect the body from damage caused by free radicals induced oxidative stress. Natural antioxidants strengthen the endogenous antioxidants defenses and restore the optimal balance by neutralizing reactive species. **Objectives:** The current study aimed to evaluate the alterations of liver function and histological structure of the liver induced by lead acetate in male albino rats and assess the protective role of natural materials (*Trigonella foenum-graecum* and *Curcuma longa*) against these alterations. **Materials and Methods:** Forty male albino rats *(Rattus rattus*) weighing between 150 and 210 grams were used in this study. Following a week of acclimatization, the animals were randomly assigned to five groups, each consisting of ten male albino rats: Group I (control group) was fed a regular diet and given tape water. Group II (group treated with lead acetate): For 30 days, the animals were fed 500 mg of lead acetate per kilogram of body weight. Group III (lead acetate/*Trigonella foenumgraecum L* seeds co-administered): For 30 days, the animals were given 500 mg of lead acetate per kilogram of feed along with 7.5 g of *Trigonella foenumgraecum L* seeds per kilogram of diet. Group IV (lead acetate/*Curcuma longa*): For 30 days, the animals were given 500 mg of lead acetate per kilogram of feed along with 20 g of *Curcuma longa* per kilogram of diet. Group V (lead acetate/*Trigonella foenumgraecum L* seeds + Curcuma longa co-administered): For 30 days, the animals were given 500 mg of lead acetate per kilogram of chow along with 7.5 g/kg of Trigonella foenumgraecum L seeds and 20 g/kg of *Curcuma longa*.. At the end of the experiment and 24 hours following the final dosage all animals were given ether anesthesia, and cardiac punctures were used to obtain blood samples for estimating the activities of serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Animals were then promptly dissected, and small pieces of liver were removed and preserved in Bouin's solution for histological examination. **Results:** Serum ALT and AST activity were considerably ($P<0.01$) higher in male rats that were fed 500 mg of lead acetate per kilogram of body weight for 30 days compared to the control group. When compared to the lead acetate group, the co-administration of lead acetate and\or *Trigonella foenumgraecum L* seeds and\or *Curcuma longa* in the diet every day for 30 days caused a significant ($P<0.01$) reduction in serum ALT and AST activity. Histologically, rats treated with lead acetate exhibited loss of the radial distribution of sinusoids from the liver's central vein as well as distortion of the liver's parenchyma. There was a noticeable necrosis of hepatocytes that looked highly esinophilic and some had pyknotic nuclei. The bright, foamy cytoplasm of the hepatocytes, which had many vacuole-like gaps, gave them a huge appearance. Numerous liver cells suffered damage and lost their distinctive appearance. Others had extreme cytoplasmic vacuolation, which is so widespread in certain cells that only very little pieces of the cytoplasmic mass remain. Kupffer cell hyperactivation was noted. The portal blood sinusoids, and central veins all had significant dilatation and congestion. Multifocal to widespread coagulative necrosis was seen in certain places. Infiltrations of inflammatory cells were seen in the portal veins. The ingestion of *Trigonella foenumgraecum L* seeds and\or *Curcuma longa* prevent the hepatoxicity induced by lead acetate. **Conclusion:** It can be concluded that lead acetate significantly affected both the histological structure and function of the liver. Lead acetate hepatotoxicity can be avoided by consuming *Trigonella foenumgraecum L* seeds and/or *Curcuma longa.* According to the current study, *Trigonella foenumgraecum L* seeds and *Curcuma longa* may prevent the hepatotoxicity caused by lead acetate. These findings imply that *Trigonella foenumgraecum L* seeds and/or *Curcuma longa* may find use in clinical settings to treat liver diseases.

Keywords: Lead Acetate, Hepatotoxicity, liver function, histological structure of the liver, Attenuation, Fenugreek Seeds, *Trigonella foenum-graecum*, *Curcuma longa*, Male Albino Rats

1. Introduction

One of the environmental contaminants that poses a serious risk to public health is lead (Saad and El Sayed, 2014). Due to its extensive use in several applications, it is more likely than other heavy metals to be hazardous to humans and animals and to contaminate the environment (Diab *et al.,* 2024). Fuel additives, food cane soldering, lead-based paints, ceramic glazes, drinking water systems, and traditional treatments are the six product categories that are thought to be the global source of lead exposure (Markowitz, 2000). Lead exposure has the capacity to cause harmful biological effects in both humans and animals (Sharma *et al.*, 2013). Because people are constantly exposed to lead in the environment, especially industrial workers, lead toxicity is a global health concern (Mannem, 2014).

Lead is a protoplasmic toxin that can harm a variety of living things (Hwang & Wang, 2001). Lead is harmful to the body's systems, including the gastrointestinal and hematological systems, and disrupts a number of bodily functions (Meyer *et al.,* 2008). Numerous organ systems may be impacted, and it is linked to hypertension, neurological diseases, cognitive impairment, and several types of cancer (Pitot and Dragan, 1996, Ahamed *et al.,* 2007). By producing reactive oxygen species, lead, a hazardous heavy metal of worldwide concern, causes oxidative stress that is harmful to a number of organs (Adikwu *et al.,* 2013, Abdelhamid *et al.,* 2020).

Oxidative stress has received more attention in recent years. An imbalance that favors oxidants over antioxidants is known as oxidative stress. causing components like proteins, carbohydrates, lipids, and nucleic acids to sustain oxidative damage (Prior, R and Cao,1999, Azab *et al.,* 2017).

Antioxidants are crucial organisms that can shield the body from harm brought on by oxidative stress brought on by free radicals (Robinson *et al.,* 1997). In affluent nations, the use of herbs for medical purposes has been steadily growing as they are usually regarded as safe and efficient against a variety of human disorders (Garaza *et al.,* 2006). By neutralizing reactive species, natural antioxidants bolster the body's defenses against endogenous antioxidants and help to restore equilibrium (Ho *et al.,* 1994).

Since ancient times, curcumin, a naturally occurring dietary ingredient, has been utilized to improve human health (Joe *et al.*, 2004). One of the main yellow pigments found in the rhizomes of *Curcuma longa* linn is curcumin, which is frequently used as a coloring ingredient and spice in a variety of meals (Tirkey *et al.,* 2005). It belongs to a class of antioxidants and anti-inflammatory drugs that have been shown to be highly effective at preventing the production of reactive oxygen species (ROS) (Venkatesan *et al.*, 2000).

The annual herb fenugreek (*Trigonella foenumgraecum L.*), which is a member of the Legume family, is produced extensively in Egypt, India, and the Middle East (Flammang *et al.,* 2004). Due to the inclusion of various active ingredients, including flavonoids, alkaloids, vitamins, and amino acids, it is used as a spice in food and medicine and has been shown to have antioxidant effects in diabetes mellitus (Basch *et al.,* 2003). Compounds with intriguing properties found in yellowish seeds account for their usage in a variety of contexts, including as medicine, nutrition, drinks, cosmetics, scents, smoking, and other industrial applications (Djeridane*et al.,* 2006). Actually, powdered and toasted fenugreek seed is frequently used with breadstuffs and is a necessary component of curry powders (Blank *et al.,* 1997).

In traditional medicine, plant seeds and herbs are utilized to treat illnesses. Because they are safe and have fewer negative effects than chemical medications, their use has expanded in many disciplines (Alhawari, 1986). Animal-derived products and plant extracts have been shown to shield experimental animals from lead-induced poisoning. The antioxidant qualities of the components included in these extracts were thought to be responsible for their capacity to lessen these toxicities (Adikwu *et al.*, 2013). *Curcuma longa* and *Trigonella foenumgraecum L.* seeds' antioxidant potential in reducing metal-induced oxidative stress requires careful research because these naturally occurring antioxidants are found in many edible foods and may one day be used safely by people. There is very little data indicating that *Trigonella foenumgraecum L*. and *Curcuma longa* protect against lead-induced hepatotoxicity.

2. Objectives

The current study aimed to evaluate the alterations of liver function and histological structure of the liver induced by lead acetate in male albino rats and assess the protective role of natural materials (*Curcuma longa* and *Trigonella foenumgraecum L.*) against these alterations.

3. Materials and Methods

3.1. Experimental animal

Forty male albino rats *(Rattus rattus*) weighing between 150 and 210 grams were used in this investigation. For the duration of the experiments, the animals were housed in normal settings and under conventional veterinary hygienic conditions for sanitation and medical treatment. Rats were kept apart in cages made of plastic. The rats were fed conventional rodent pellets, which are a blend of protein, fat, fiber, and ash. Water and food were provided on an as-needed basis.

3.2. Chemicals

Lead acetate was purchased from Sigma Chemical Co., USA. It was given in a diet as 500 mg/kg diet daily (Shalan *et al.,* 2005) for 30 days.

3.3. *Trigonella foenumgraecum L* seeds and *Curcuma longa*

For 30 days, 7.5 g/kg of finely powdered *Trigonella foenumgraecum L*. seeds were introduced to the experimental meals every day (Bagees and Mangara, 2012). For 30 days, 20 g/kg of *Curcuma longa* was added to the diet every day (Sharma *et al.*, 2001).

3.4. Experimental Design

Following a week of acclimatization, the animals were randomly assigned to five groups, each consisting of ten male albino rats:

Group I (control group) was fed a regular diet and given tape water.

Group II (group treated with lead acetate): For 30 days, the animals were fed 500 mg of lead acetate per kilogram of body weight.

Group III (lead acetate/*Trigonella foenumgraecum L* seeds co-administered): For 30 days, the animals were given 500 mg of lead acetate per kilogram of feed along with 7.5 g of *Trigonella foenumgraecum L* seeds per kilogram of diet.

Group IV (lead acetate/*Curcuma longa*): For 30 days, the animals were given 500 mg of lead acetate per kilogram of feed along with 20 g of *Curcuma longa* per kilogram of diet.

Group V (lead acetate/*Trigonella foenumgraecum L* seeds + Curcuma longa co-administered): For 30 days, the animals were given 500 mg of lead acetate per kilogram of chow along with 7.5 g/kg of Trigonella foenumgraecum L seeds and 20 g/kg of *Curcuma longa*.

3.5. Blood Sampling

All animals were given ether anesthesia at the end of the experiment and 24 hours following the final dosage, and cardiac punctures were used to obtain blood samples. After collecting the blood sample in a clean, dry tube and centrifuging it for 15 minutes at 3000 rpm, the serum was separated and stored at -20°C in a deep freezer until biochemical analyses were completed.

3.6. Determination of Serum Aspartate Aminotransferase (s-AST) and Alanine Aminotransferase (s-ALT) Activities

Bergmeyer and Horder's 1980 UV technique was used to estimate the activities of serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

3.6. Histological Preparation :

All animals were given ether anesthesia at the end of the experiment and 24 hours following the last dose. They were then promptly dissected, and tiny fragments of liver were swiftly removed and preserved in Bouin's solution. To guarantee thorough dehydration and clearing, specimens were dehydrated in a succession of increasing alcohols after fixation and then stored in terpineol for three days. Following three xylol rinses, the cleared specimens were embedded in paraffin wax (m.p. 56–58°C). Each liver sample was divided into three pieces, each 5 microns thick, and placed on clean slides devoid of any adhesive media. Each section was separated from the next by at least 500 microns. Sections were stretched using Ehrlich's haematoxyline and eosin for histological analysis.

Statistical Analysis:-

The data was analyzed using a one-way ANOVA, and the results were presented as mean ± SD. The Duncan's multiple range test was used to examine the difference between means ± SD at $P < 0.05$. A significance level of $P < 0.05$ was applied to all statistical tests.

4. Results

4.1. Effect of administration of lead acetate, and\or co-administration with *Trigonella foenumgraecum L* seeds and\or *Curcuma longa* on the serum ALT and AST activities in male rats.

Table.1 and Figures 1 and 2 display the serum ALT and AST levels of the various groups. Serum ALT and AST activity were considerably ($P<0.01$) higher in male rats that were fed 500 mg of lead acetate per kilogram of body weight for 30 days compared to the control group.

When compared to the lead acetate group, the co-administration of lead acetate and *Trigonella foenumgraecum L* seeds in the diet every day for 30 days caused a significant ($P<0.01$) reduction in serum ALT and AST activity (Table.1& Figures 1&2).

Also, when compared to the lead acetate-treated group, the co-administration of lead acetate and *Curcuma longa* in the diet every day for 30 days resulted in a significant ($P<0.01$) decrease in serum ALT and AST activity (Table.1&Figures 1&2).

Serum ALT and AST activity were significantly (*$P<0.01$*) lower in the animals treated simultaneously with *Trigonella foenumgraecum L* seeds and *Curcuma longa* in food daily for 30 days as compared with the lead acetate group (Table.1 & Figures 1&2).

Table.2: Effect of administration of lead acetate, and\or co-administration with *Trigonella foenumgraecum L* seeds and\or *Curcuma longa* on the serum ALT and AST activities in male rats.

Groups	Control	Lead Acetate	Lead Acetate + *Trigonella foenumgraecum L* seeds	Lead Acetate + *Curcuma longa*	Lead Acetate + *Trigonella foenumgraecum L* seeds + *Curcuma longa*
Parameters	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
ALT (U/L)	28.25 ± 2.75	48.26 ± 6.21**	34.67 ± 3.05$$	35.18 ± 3.17**$$	32.18 ± 2.19$$
AST (U/L)	30± 2.4	70± 4.32**	39.12 ± 4.16$$	45.18 ± 3.62**$$	34.20 ± 3.63$$

**: Significant at ($P<0.01$) when compared with control group, $$: Significant at ($P<0.01$) when compared with lead acetate group.

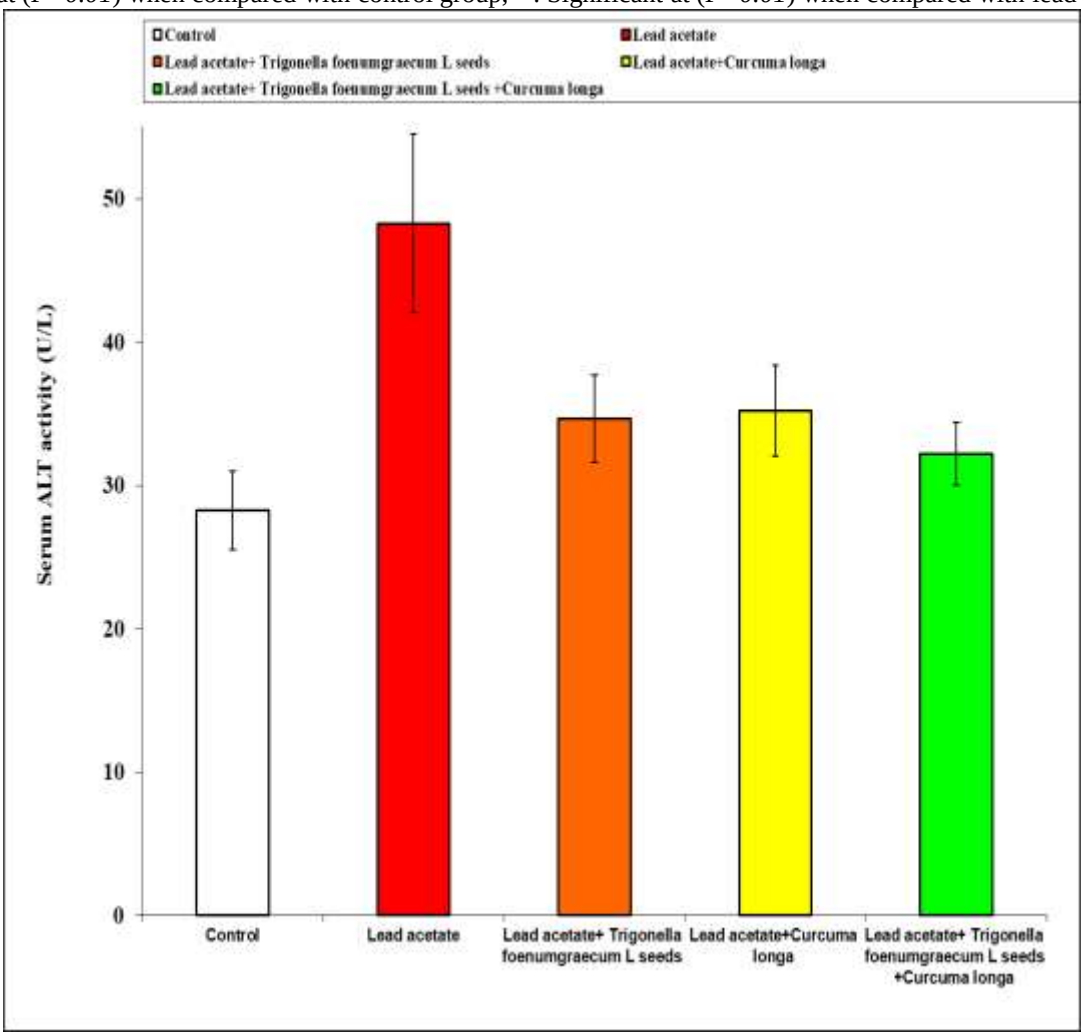

Figure.1: Effect of administration of lead acetate, and\or co-administration with *Trigonella foenumgraecum L* seeds and\or *Curcuma longa* on the serum ALT activity in male rats.

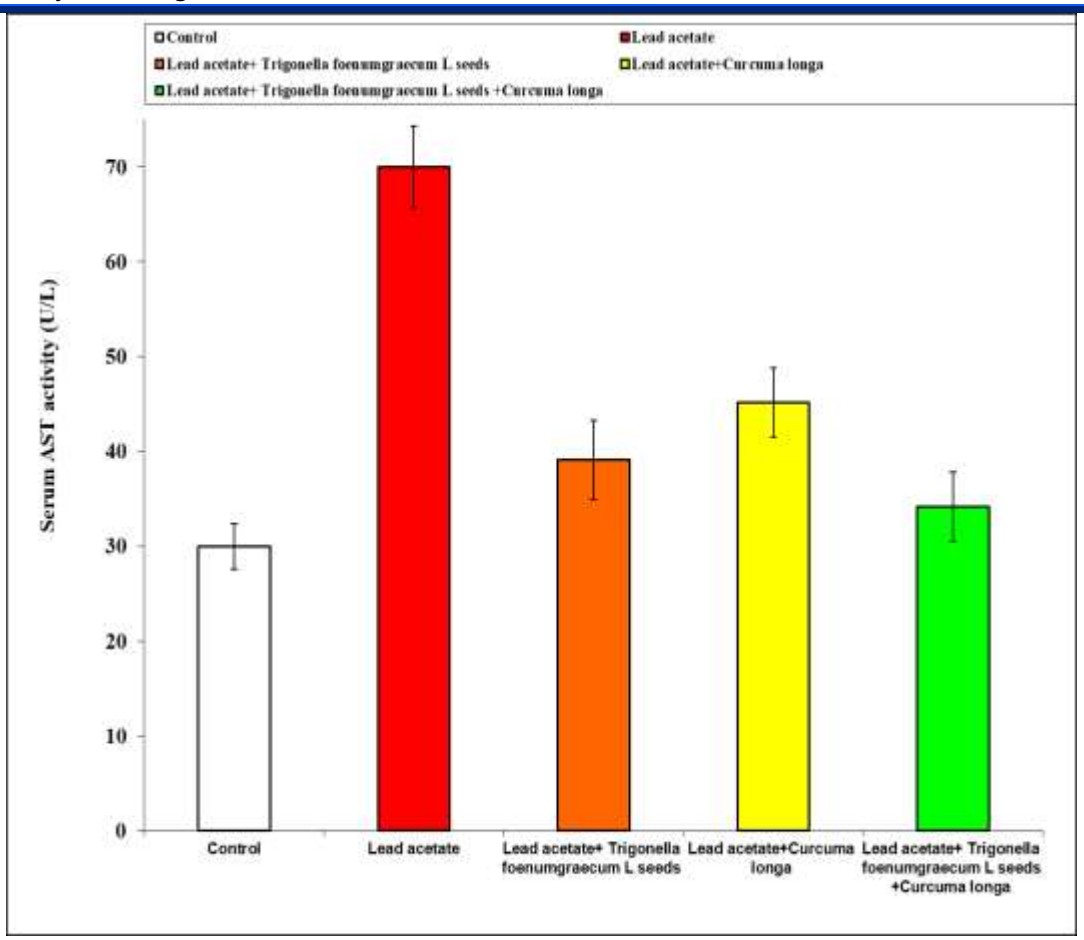

Figure.2: Effect of administration of lead acetate, and\or co-administration with *Trigonella foenumgraecum L* seeds and\or *Curcuma longa* on the serum AST activity in male rats.

4.2. Histological Examinations

4.2.1. Effect of administration of lead acetate, and\or co-administration with *Trigonella foenumgraecum L* seeds and\or *Curcuma longa* on the Structure of the Liver of male albino rats.

4.2. 1. 1. Liver sections of control rats

The hepatic lobule, which is composed of radiating plates of cells that create a network around a central vein, is the structural unit of the rat liver, as demonstrated by the liver histology of control animals and other mammals. The polyhedral liver cells have granular cytoplasm and big, centrally placed nuclei. The sinusoids are irregularly shaped, narrow blood passages made up of giant Kupffer cells, which are known to be actively phagocyte cells, and endothelial cells. A layer of cuboidal cells surrounded by a thin coating of connective tissue (Figures.3).

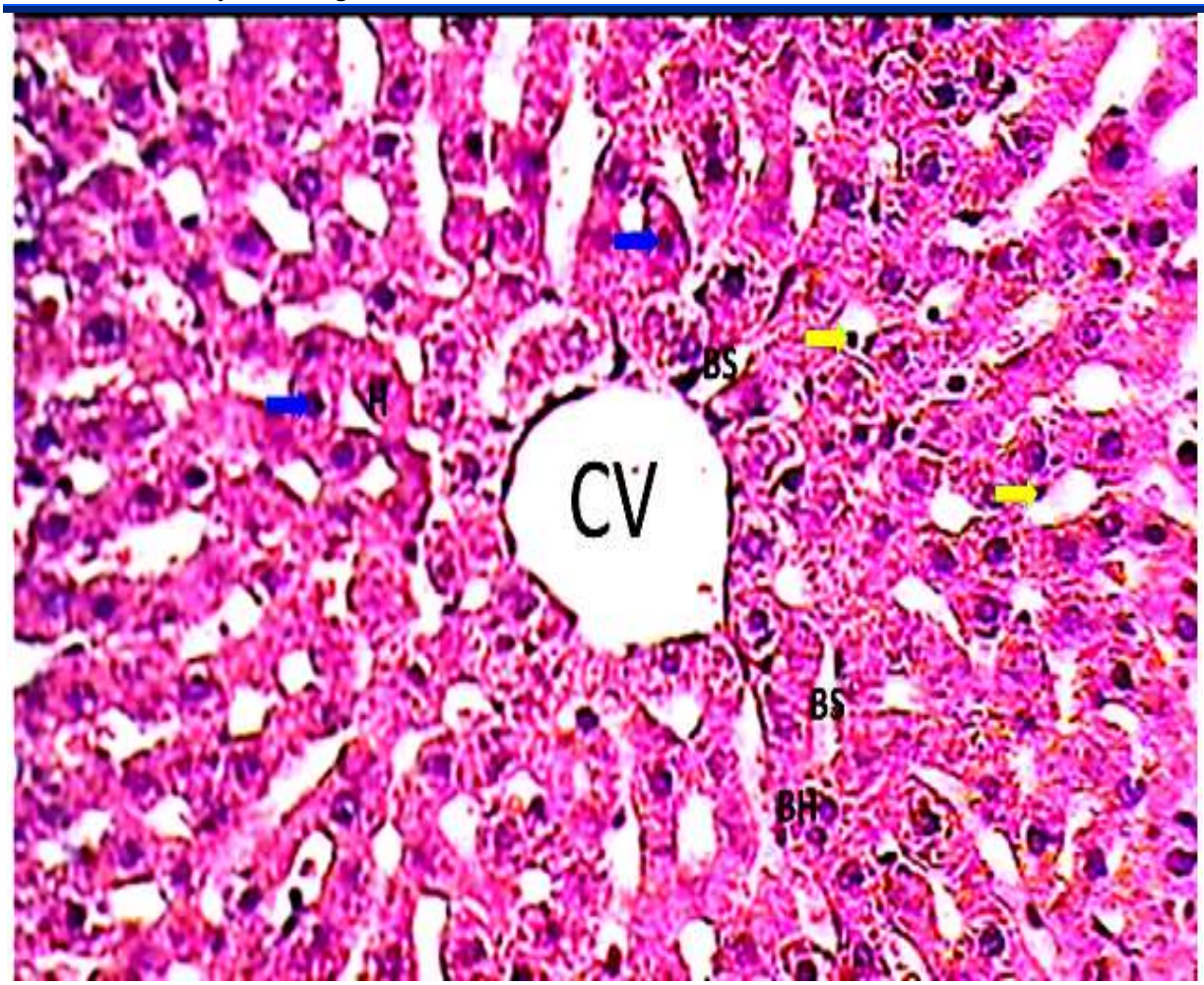

Figure 3. Light micrograph of section in the liver of the control rat; Central vein (CV); Hepatocyte (H); Binucleated hepatocyte (BH); Blood sinusoid (BS); Kupffer cells (Yellow arrow); Nucleus (Blue arrow) (Hematoxylin &Eosin ×400).

4.2.1.2. Liver sections of lead acetate treated rats

Rats treated with lead acetate exhibited loss of the radial distribution of sinusoids from the liver's central vein as well as distortion of the liver's parenchyma. Compared to the control, there was a noticeable necrosis of hepatocytes that looked highly esinophilic and some had pyknotic nuclei. The bright, foamy cytoplasm of the hepatocytes, which had many vacuole-like gaps, gave them a huge appearance. Numerous liver cells suffered damage and lost their distinctive appearance. Others had extreme cytoplasmic vacuolation, which is so widespread in certain cells that only very little pieces of the cytoplasmic mass remain. Kupffer cell hyperactivation was noted. The portal blood sinusoids, and central veins all had significant dilatation and congestion. Multifocal to widespread coagulative necrosis was seen in certain places. Infiltrations of inflammatory cells were seen in the portal veins (Fig. 4 A, B, C, & D).

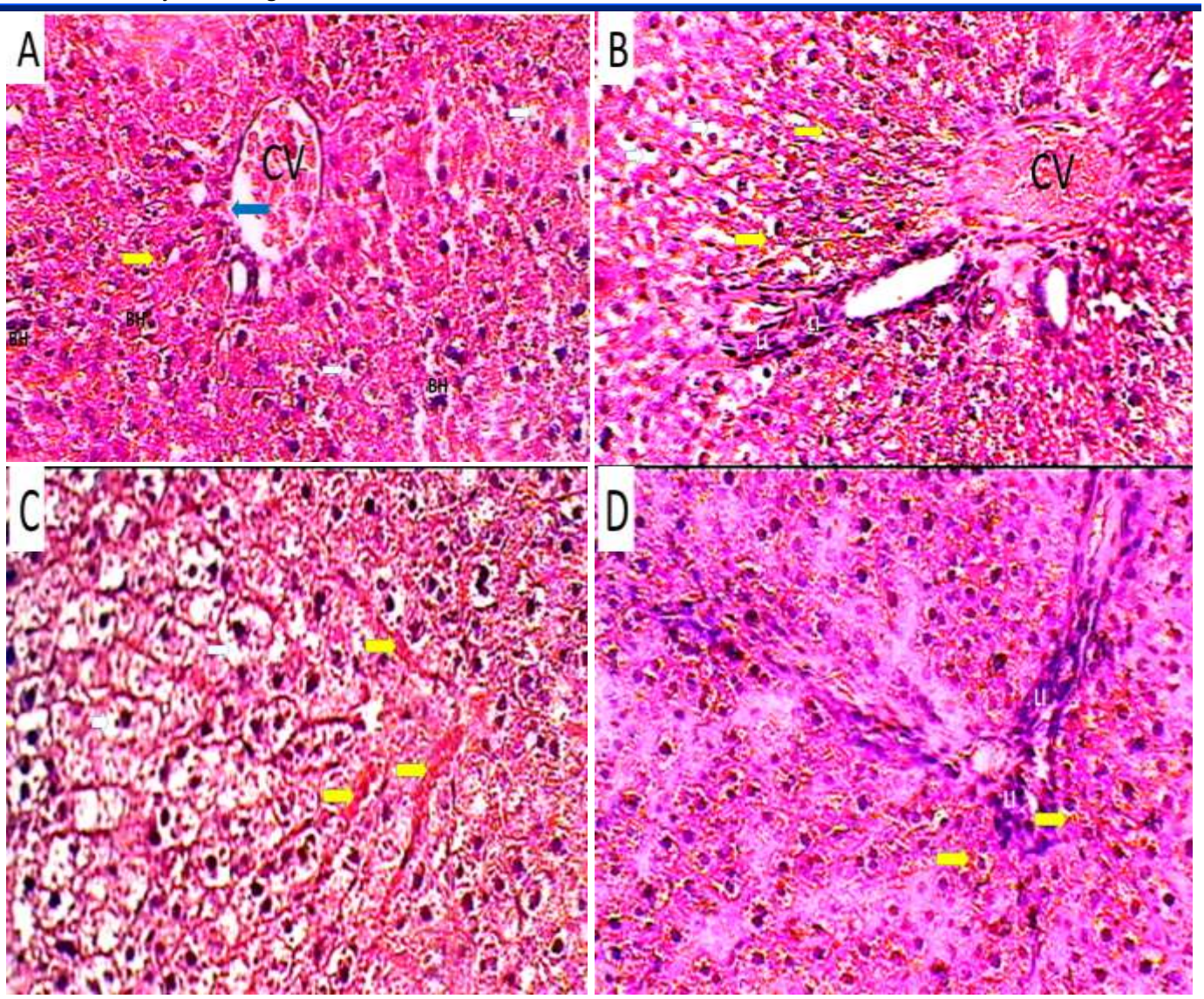

Figure 4. Light micrographs of sections in the liver of the rat treated with lead acetate; A: Blood sinusoid (BS), Leukocytic filtration (LI), Marked vacuolar degeneration mainly hydropic degeneration (White arrow), Binucleated hepatocyte (BH), RBCs (yellow arrow); Damage in lining endothelium of central vein (Blue arrow) B: Dilated congested central vein (CV); Leukocytic infiltration (LI); Hemorrhage in blood sinusoid (Yellow arrow). C: Hemorrhage in blood sinusoid (Yellow arrow) and Marked vacuolar degeneration mainly hydropic degeneration, necrosis. D: Hemorrhage in blood sinusoid (Yellow arrow); Leukocytic infiltration (LI). (Hematoxylin &Eosin, ×400).

4.2.1.3. Liver sections of the rats co-administered of lead acetate and *Trigonella foenumgraecum L* seeds:

Giving the animal *Trigonella foenumgraecum L* seeds with lead acetate for the same period caused improvement in the histological structure of the liver tissues. The structure of the hepatic lobule appears normal. Some liver sections show damage in lining endothelium of central vein, activated kupffer cells, dilated blood sinusoids with RBCs (Figure. 5).

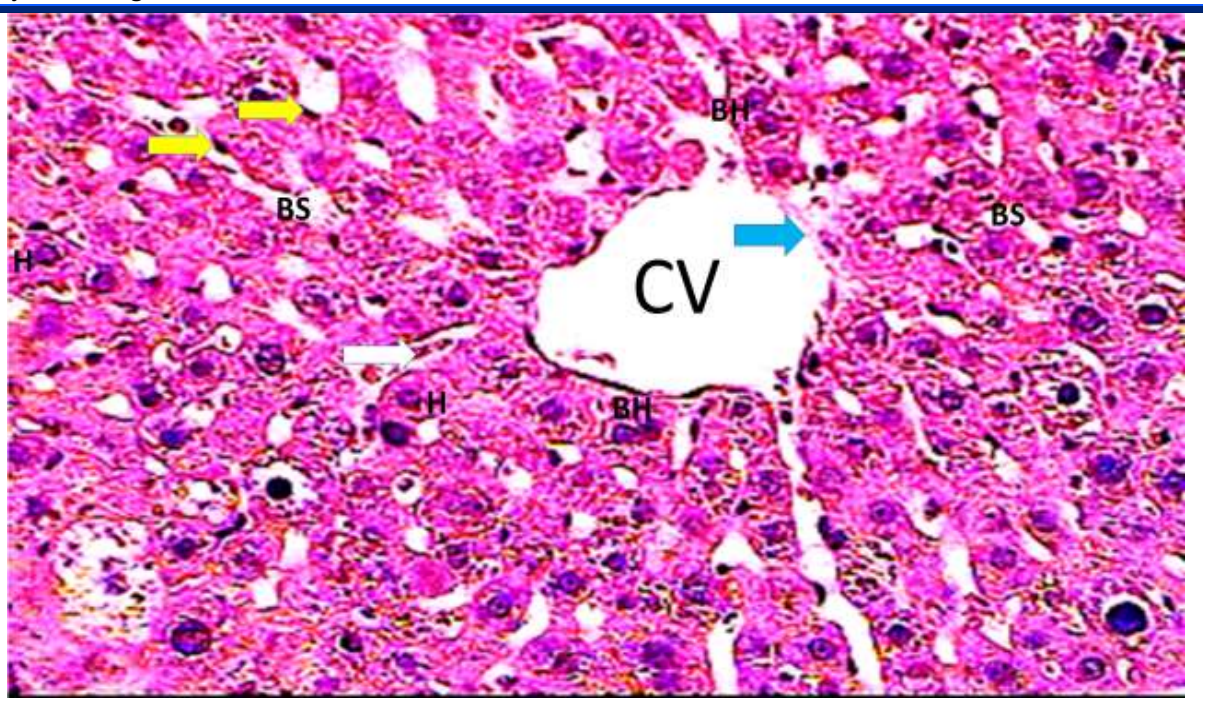

Figure 5. Light micrograph of section in the liver of rat's co-administration of lead acetate and *Trigonella foenumgraecum L* seeds. The structure of the hepatic lobule appears normal; Central vein (CV); Hepatocyte (H); Binucleated hepatocyte (BH); Blood sinusoid (BS); Some liver sections show damage in lining endothelium of central vein (Blue arrow), activated kupffer cells (Yellow arrow), and some dilated blood sinusoids with RBCs (Hematoxylin &Eosin ×400).

4.2.1.4. Liver sections of the rats co-administered lead acetate and *Curcuma longa*:

Treatment of rats with lead acetate and *Curcuma longa* for 4 weeks caused improvement in the histological structure of the liver tissues. The structure of the hepatic lobule appears normal. Some liver sections show activated kupffer cells, and some dilated blood sinusoids with RBCs (Figure. 6).

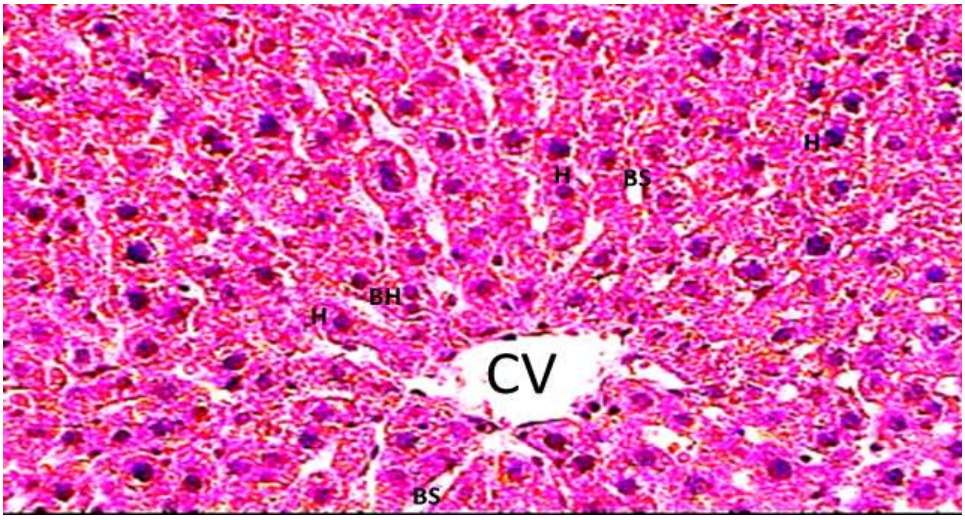

Figure 6. Light micrograph of section in the liver of the rats co-administered lead acetate and *Curcuma long*. The structure of the hepatic lobule appears normal; Central vein (CV); Hepatocyte (H); Binucleated hepatocyte (BH); Blood sinusoid (BS), and some dilated blood sinusoids with RBCs. Some liver sections show activated kupffer cells, and some dilated blood sinusoids with RBCs (Hematoxylin &Eosin ×400).

4.2.1.5. Liver sections of the rats treated simultaneously with *Trigonella foenumgraecum L* seeds and *Curcuma longa*:

Co-administration of rats with *Trigonella foenumgraecum L* seeds and *Curcuma longa* for 4 weeks caused improvement in the histological structure of the liver tissues. The structure of the hepatic lobules appeared normal (Figure. 7).

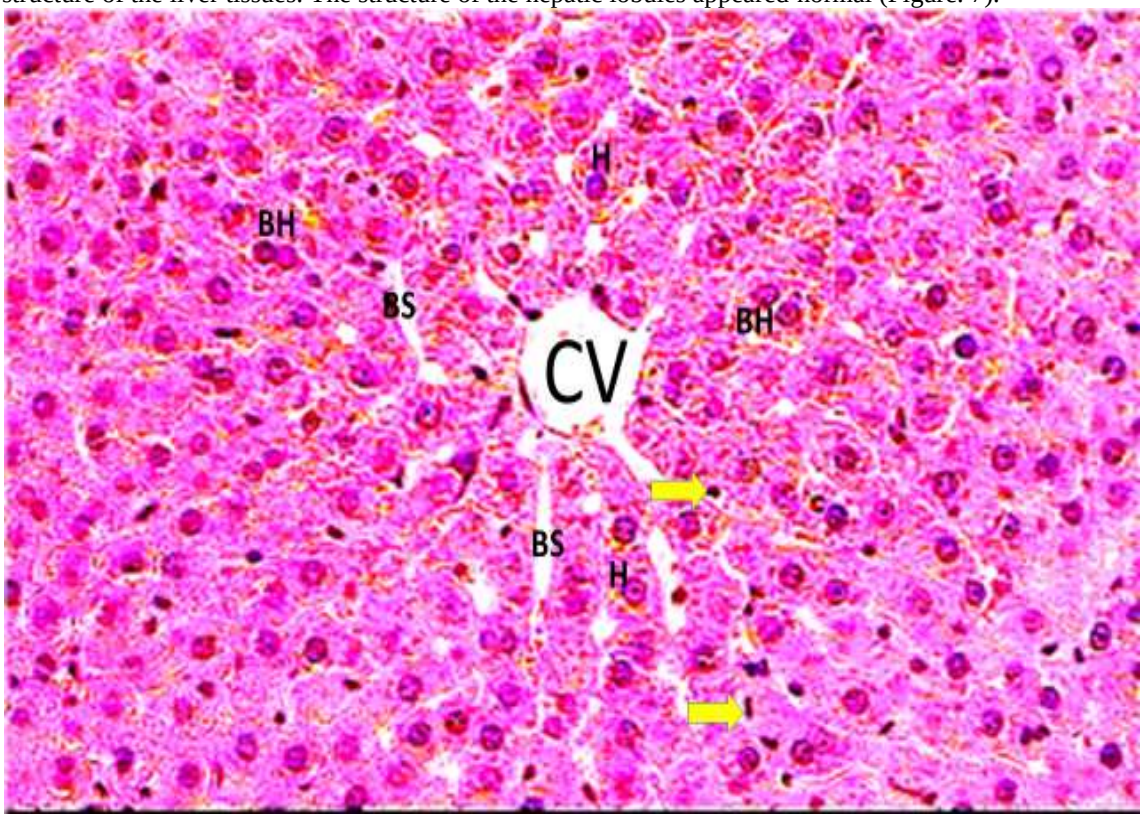

Figure 7. Light micrograph of section in the liver of the rats treated simultaneously with *Trigonella foenumgraecum L* seeds and *Curcuma longa*, Central vein (CV); Hepatocyte (H); Binucleated hepatocyte (BH); Blood sinusoid (BS); Kupffer cells (Yellow arrow)(Hematoxylin &Eosin ×400).

5. Discussion

Forty male albino rats *(Rattus rattus*) were used to evaluate the alterations of liver function and histological structure of the liver induced by lead acetate in male albino rats and assess the protective role of natural materials (*Trigonella foenum-graecum* and *Curcuma longa*) against these alterations.

Lead is one of the most toxic heavy metals that induce numerous biochemical, and pathological effects to both humans and animals (El-Tantawy 2016, El-Boshy *et al.* 2019, Abdelhamid *et al.*, 2020).

The present study showed that serum ALT and AST activity were considerably ($P<0.01$) higher in male rats that were fed 500 mg of lead acetate per kilogram of body weight for 30 days compared to the control group. A similar finding has been reported by Suleman, *et al.*, 2011 and Diab *et al.*, 2024 exhibited that administration of lead acetate led to hepatotoxicity which was marked by a significant elevation in serum levels of liver damage indicators (AST and ALT) that may beattributed to disruption and destruction of hepatocytes cell membranes, leading to escape of liver enzymes to the circulation (Abdelhadya *et al.*, 2017, Abdelhady *et al.*, 2017, Mohamed *et al.*, 2019, El-Magd *et al.*, 2022, Diab *et al.*, 2024). Abdelhamid *et al.*, 2020 mentioned that lead acetate intoxicated rats showed a marked elevation in the liver enzyme activities compared to the control rats.

The antioxidant system impaired by lead acetate, leading to accumulation of ROS oxidative stress damage to proteins, DNA and lipids (El-Magd *et al.*, 2016). The latter are abundantly located in cell membranes and mitochondrial membranes and so can be easily targeted by free radicals, resulting in lipid peroxidation and loss of cell membrane integrity and subsequently release of liver enzymes (AST, ALT) to circulation. Thus, it is likely that the loss of liver function and significant increase of AST and ALT activities induced by lead acetate may be due to lipid peroxidation of hepatocytes plasma membranes (Farida *et al.* 2012, Laamech *et al.* 2017, Diab *et al.*, 2024).

The current study mentioned that the co-administration of lead acetate and\or *Trigonella foenumgraecum L* seeds and\or *Curcuma longa* in the diet every day for 30 days caused a significant ($P<0.01$) reduction in serum ALT and AST activity When compared to the lead acetate group. These results similar to the results obtained many of previous studies (Kaviarasan *et al.*, 2006, Kumar and Bhandari, 2013, Das, 2014). A water extract of Fenugreek seeds concurrently during 60 days of alcohol ingestion was associated with a reduction in the rise of the liver enzymes noted in the serum of rats given ethanol alone, suggesting protective effects (Kaviarasan *et al.*, 2006). Kumar and Bhandari, 2013 demonstrated that the activities of serum ALT and AST were increased in rats treated with monosodium glutamate. Administration of aqueous *Trigonella foenum-graecum* seeds significantly reduced the elevated ALT and AST levels, which could be attributed to the protective effect on hepatic tissues. Das, 2014 reported that administration of extract of fenugreek seeds in CCl4 treated rats caused reduction in Serum ALT, and AST levels. The co-treatment of CUR with LA seems to reduced hepatic damage that was confirmed histopathologically and associated with partial alleviation in the liver function parameters, and reduced lipid peroxidation reflected by reduced hepatic MDA level and restored SOD and CAT activities. This indicated the CUR ability to stabilize the cell membrane and protect the tissue from free radical-mediated damage or promote the regeneration of damaged cells and thus reduce releases of transaminases from the cell cytosol (Abdel-Daim and Abdou 2015, El-Maddawy and El-Sayed 2018, Cheraghi and Roshanaei 2019). The same results were detected in potassium dichromate, cisplatin, cinnabar, and diazinon-induced hepatic damage in rats and treated with curcumin (García-Niño *et al.* 2013, Waseem *et al*. 2014, Wang et al. 2015, Abdel-Diam et al. 2019).

The results of the present study revealed that the liver of rats treated with lead acetate exhibited loss of the radial distribution of sinusoids from the liver's central vein as well as distortion of the liver's parenchyma. There was a noticeable necrosis of hepatocytes that looked highly esinophilic and some had pyknotic nuclei. The bright, foamy cytoplasm of the hepatocytes, which had many vacuole-like gaps, gave them a huge appearance. Numerous liver cells suffered damage and lost their distinctive appearance. Others had extreme cytoplasmic vacuolation, which is so widespread in certain cells that only very little pieces of the cytoplasmic mass remain. Kupffer cell hyperactivation was noted. The portal blood sinusoids, and central veins all had significant dilatation and congestion. Multifocal to widespread coagulative necrosis was seen in certain places. Infiltrations of inflammatory cells were seen in the portal veins. These alterations are run parallel to those obtained by Abdelhamid *et al.*, 2020 who mentioned that the micrograph of lead acetate group shows either hydropic degeneration (which caused some sinusoidal occlusion) or necrosis of hepatocytes, and leukocytic infiltration of the portal area.

Our study found that the ingestion of *Trigonella foenumgraecum L* seeds and\or *Curcuma longa* prevent the histological alterations induced by lead acetate. These results run parallel to the results of previous studies **(**Botsoglou *et al.*, 2010, and Das, 2014**).** The livers of rats treated with extract of fenugreek seeds showed a significant attenuation from CCl4-induced liver damage as evident from normal hepatocytes with well-defined nuclei. The improvement of histological changes in the liver are well correlating with the biochemical estimations. These results suggest that the extract of fenugreek seeds has potential clinical applications for treating liver disorders (Botsoglou *et al.*, 2010, and Das, 2014).

Treatment of rats with lead acetate simultaneously with curcumin could partially improve the biochemical, and histopathological alterations induced by lead acetate that may be due to antioxidant, anti-inflammatory, and immunomodulatory effects of curcumin that able to minimize the lead acetate induced oxidative damage in rats (Abdelhamid *et al.*, 2020).

Curcumin has anti-inflammatory and antioxidant properties with a potent ability to inhibit reactive oxygen species formation (Biswas *et al*., 2005). The apparent protective effects of curcumin against lead induced toxicity were attributed to its scavenging and chelating properties or its capacity to induce detoxifying enzymes by upregulation of the Keap1/Nrf2/ARE pathway (nuclear factor erythroid 2-related factor2/antioxidant response elements) (García-Niño and Pedraza-Chaverri 2014). Curcumin is considered as a natural Nrf2 activator which regulates the biosynthesis of glutathione, involved in the regulation of the expression of several cytoprotective genes that antagonize oxidative and inflammatory damage (Ali *et al.* 2018, Al Basher *et al.* 2020) and re-established ALAD activity in the blood and different organs (Mice Flora *et al.*, 2013). Moreover, curcumin has suppressive effect on the formation of ROS and stimulatory effect on endogenous antioxidant activity by its free radical scavenging property (Hismiogullari *et al.*, 2015) which attributed to its unique conjugated structure that shows typical radical-trapping ability as a chain-breaking antioxidant since it includes two methoxylated phenols and an enol form of β- diketone (Masuda et al. 2001). Additionally, curcumin reduces LPO via interference with oxidation processes by removal of excess of O2 and H2O2 through restoring the reduced CAT activity (Waseem et al. 2014).

6. Conclusion

It can be concluded that lead acetate significantly affected both the histological structure and function of the liver. Lead acetate hepatotoxicity can be avoided by consuming *Trigonella foenumgraecum L* seeds and/or *Curcuma longa.* According to the current study, *Trigonella foenumgraecum L* seeds and *Curcuma longa* may prevent the hepatotoxicity caused by lead acetate. These findings imply that *Trigonella foenumgraecum L* seeds and/or *Curcuma longa* may find use in clinical settings to treat liver diseases.

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