Journal of Health and Biology
https://journalhb.org/
JHB
SPBH

Original Article

Study of the protective effect of alcoholic extract of flax seeds against thioacetamide-induced hepatotoxicity in male albino rats

Karrar Hussein Al-Kuraiti[1], Mahmood N. Hammood[2] and Farah Jawad Al-Masoudi[3]

[1] Ministry of Education, General Directorate of Education in Karbala, Iraq
E-mail: karrarhussain886@gmail.com

[2]Ministry of Education, General Directorate of Education in Karbala, Iraq
E-mail: mahmood_neamah@karbala.edu

[3]Department of Biomedical Engineering, College of Engineering, Kerbala University, Kerbala, Iraq
Email: farah.j@uokerbala.edu.iq

DOI: https://doi.org/10.71428/JHB.2026.0215

Abstract

The current study aims to investigate the role of flaxseed extract versus hepatotoxicity stimulated by thioacetamide in male white rats by examining some modifications. Liver tissue was examined for enzymes and antioxidants, urea, and creatinine. In this experiment, 25 male albino rats were divided into five groups: the control group (G1) and the treatment group (G2). They were injected with thioacetamide at a dose of 300 mg/kg for a month. The third, fourth, and fifth groups (G3, G4, G5) were dosed daily with the alcoholic extract of flax seeds at doses of 400 mg/kg, 600 mg/kg, and 800 mg/kg, respectively, and then injected with thioacetamide (300 mg/kg), while continuing to be dosed with the alcoholic extract of flax seeds. The samples of tissue and blood were collected after completion of the experiment, and changes in liver tissue, liver enzymes (AST, ALT, ALP, LDH), antioxidants (MDA, GSH), urea, and creatinine were measured. The results showed changes in liver tissue with an increase in the levels of liver enzymes (AST, ALT, ALP, LDH), malondialdehyde, urea, and creatinine, and a decrease in the level of glutathione after treatment with thioacetamide. Treatment with the alcoholic extract of flax seeds led to a significant improvement in liver tissue, a decrease in the levels of liver enzymes, malondialdehyde, urea, and creatinine, and an increase in the level of glutathione. We conclude that the alcoholic extract of flax seeds plays a protective role against hepatotoxicity resulting from treatment with thioacetamide.

Keywords: flax seeds, hepatotoxicity, thioacetamide

1. Introduction

The liver is a vital organ. It is the most substantial gland in the human anatomy, situated in the upper right quadrant of the abdomen. It has a weight of roughly 1.5 to 2 (kg) and plays a major role in performing many vital functions that contri bute to regulati ng the body's work, iincluding the metaboliism of nutri ents such as carbohydrates, fats and prote ins, the producti on of clotting factors, the regulati on of the i mmune system, the bi otransformation of chemi cals and drugs and their detoxification, the storage of v itamins, the producti on of bi le and other important functions [1]. The use of experimental models to induce hepatotoxicity is of great importance for studying pathophysiology. They furnish significant evidence in preclinical investigations, enhancing the understanding of hepatoprotective strategies against

Received: June 5, 2026. Accepted: September 7, 2026. Published: September 23, 2026

various natural and synthetic toxic agents. Numerous chemical substances, including thioacetamide (TAAi), carbon tetrachloride, dimethylnitrosamine, diethylnitrosamine, aflatoxin B1, among others, have been employed in animal models to induce both acute and chronic liver damage [2].

Thioacetamide (TAA) is a white, crystalline, water-soluble organosulfur compound with the molecular formula C2H5NS. It was first discovered as a hepatotoxic agent in rats by Fitzhugh and Nelson in 1948. It is extensively utilized in animal research to provoke hepatic damage and fibrosis. It is utilized in laboratory and industrial settings, metallurgy, fungicides, insecticides, pharmaceuticals, as well as in the paper and leather sectors. It is extensively utilized in the pharmaceutical and chemical industries as a source of sulfide ions in lieu of hydrogen sulfide. Its consumption results in hepatic encephalopathy, metabolic acidosis, centrilobular necrosis, and liver fibrosis. It is detrimental to the liver, harmful to the kidneys, and a potential carcinogen. [3,4]. The hepatotoxic thioacetamide (TAA) is administered either orally or via intraperitoneal injection to induce liver injury in rodents. This is dose- and time-dependent, as thioacetamide undergoes biotransformation to thioacetamide sulfoxide, which is further metabolized to a toxic metabolite, thioacetamide disulfoxide. These metabolites are capable of modifying cellular macromolecules, leading to oxidative stress and acute central hepatic necrosis [5]. The biotransformation of thioacetamide into its secondary metabolites via the CYP450 pathway produces reactive radicals in hepatocytes, which leads to oxidative stress and tissue damage. Its metabolites also produce lipid peroxides. TAA causes liver damage through lipid peroxidation and oxidative stress, two processes responsible for the secretion of cytokines, prostaglandins, and growth factors that promote fibrosis and liver injury. Therefore, TAA is closely associated with oxidative stress in a mouse model [6].

Liver diseases are a public health concern because conventional treatments for these diseases have limited outcomes and associated side effects. Therefore, the use of complementary and alternative herbal medicine has attracted research interest for new, plausible hepatoprotective agents capable of improving or reversing liver injury with minimal side effects. Over the years, this research has gained momentum with several studies focusing on the hepatoprotective potential of botanical medicines [7]. The history of treatment with medicinal plants dates back to the ancient times of mankind. The connection between man and his search for medicines in nature goes back to the distant past. There is abundant evidence of this from various sources: written documents, preserved artifacts, and even original plant medicines. Awareness of the use of medicinal plants is attributed to long years of struggle against diseases, thanks to which man learned to search for medicines in seeds, bark, fruits, and other parts of plants. Contemporary science has confirmed their effectiveness and has included in modern pharmacological treatment a group of medicines of plant origin that were known to ancient civilizations and used throughout the ages. Awareness of the development of ideas related to the use of medicinal plants, in addition to the development of awareness, has increased the ability of doctors and pharmacists to meet the challenges that have emerged with the spread of diseases with the aim of facilitating human life [8].

Flax (Linum usitatissimum L.) is a dicotyledonous plant of the Linaceae family with bluish flowers. It is an annual herbaceous plant found widely in many countries and is one of the oldest fiber crops. It has been cultivated in India and China for 5,000 years and in Egypt and Samaria for 10,000 years. Flax has been used as a seed and fiber. Flax fibers (which are three times stronger than cotton) are used in the linen industry and in various textile industries due to their natural straightness. The very long flax fibers are also used in the manufacture of decorative fabrics, stiff threads, ropes, and tires.[9]. Flax seeds are a

natural food rich in biologically active substances. Flaxseed oil contains about 53% alpha-linolenic acid (ALA), making it the richest plant source of this compound, and 19% oleic acid. Due to its high ALA content, flaxseed oil has a fatty acid ratio of 6:3, which is about 0.3:1. Thanks to its anti-inflammatory and anti-proliferative properties, ALA has an anticancer effect on the human body, preventing the development and metastasis of malignant tumors. ALA extracted from flax seeds also has a positive effect on blood lipid levels, as it has been found to significantly reduce plasma total cholesterol, low-density lipoprotein (LDL) cholesterol, and very-low-density lipoprotein (VLDL) cholesterol [10]. Consuming ground flaxseeds significantly reduces body weight and hyperlipidemia and improves liver enzymes. They are regarded as strong antioxidants and have a preventive role against steatohepatitis and liver fibrosis in a mouse model. These include alpha-linolenic acid, fiber, and phytoestrogens in lignins that impact hepatic estrogen receptors, reportedly protecting liver cells from harm. Flaxseed is rich in water-soluble fibers that are powerful antioxidants. They boost insulin sensitivity and reduce inflammatory responses in many of the chronic diseases by about 30%.[11,12]. The current study aims to determine the palliative role of flaxseed extract against thioacetamide-induced hepatotoxicity by studying some histological and biochemical changes in male albino rats.

2. Materials and methods

2.1. Animal models

There are 25 of animals were brought from an animal house in Hillah city, weighing between 150 and 250 grams, and were placed in plastic cages with iron covers, designated for raising laboratory animals. The floor of the cages was covered with sawdust, taking care to change it from time to time. Water and food were provided, consisting of animal feed (ad libitum), purchased from local markets. Then, they were left under suitable ventilation conditions, at room temperature (25 C°), as well as suitable humidity, with a natural light and dark period, in order to acclimatize.

2.2. The design of the experiment

There are 25 experimental animals divided into 5 groups.

1- The control **(G1)** was given normal saline only**.**

2- Treatment group **(G2)**: Thioacetamide at a dose of 300 mg/kg for a month.

3- The first preventive group **(G3)**: The alcoholic extract of flax seeds was given (400 mg/kg) in the morning, followed by an injection of TAA (300 Mg/Kg) daily for a month.

4- The second preventive group **(G4)**: The alcoholic extract of flax seeds was given (600 mg/kg) in the morning, followed by an injection of TAA (300 Mg/Kg) daily for a month.

5- The third preventive group **(G5)**: The alcoholic extract of flax seeds was given (800 mg/kg) in the morning, followed by an injection of TAA (300 Mg/Kg) daily for a month**.**

2.3. Preparation of alcoholic extract

Flax seeds were obtained from a herbal shop in Karbala Governorate. After obtaining the seeds, they were washed thoroughly with water and left to dry for a week. Afterwards, the herbs were placed in a grinder dedicated to grinding herbs to obtain a fine powder. The method of Chera et al. (2022)[13] was used. To prepare the alcoholic extract, 50 grams of dry flax seed powder was weighed and added to 250 ml of 70% ethyl alcohol, which was used as a solvent in preparing the extract. The mixture was then placed in a Soxhlet device for the extraction process. The process lasted for four hours. After completion of the extraction process, the extract was concentrated to obtain a dry powder that could be dosed to animals after dissolving it in distilled water.

2.4. Liver Toxicity Induction

Liver damage is induced in male white rats by intraperitoneal injection of **t**hioacetamide (TAA) at a dose of 300 mg/kg/day, because **t**hioacetamide is a typical hepatotoxic substance due to its effect on protein synthesis, RNA and DNA activity, and

gamma-glutamyl transpeptidase activity. Its metabolites are responsible for nucleolar enlargement, increased nuclear volume, intracellular calcium ion concentration, and altered cell permeability. It also inhibits mitochondrial activity, leading to centrolobular necrosis, protein degradation, and lipid peroxidation. In addition, it impairs the urea cycle and the activity of transaminase enzymes [14].

2.5. Specimen collection

After starving the animals for a period of 12 hours, they are anesthetized using chloroform. After anesthetizing them, about 5 mL of blood is withdrawn and placed in special test tubes for laboratory tests later. Then the animals are dissected to extract the required organs (liver) in order to conduct histological tests on them.

2.6. Measurement of Liver Enzymes

Notable decline. Automated or semi-automated analyzers are used to assess the levels of liver enzymes in serum, following the principle of spectrophotometric analysis. Along with this, photometry serves as the gauge of the absorption of light within the spectrum of visible light, ultraviolet light, and infrared light. The concentration of a material in a liquid or solution can be found using this unit of measurement [15].

2.7. Measurement of Antioxidant

The activity level of antioxidants (glutathione and malondialdehyde) in the blood serum of male albino rats was estimated according to the methods described in the following references [16-18].

2.8. Measurement of Urea and Creatinine

The concentrations of urea and creatinine in the serum of male albino rats were assessed according to the methodologies outlined in the subsequent references.[19,20].

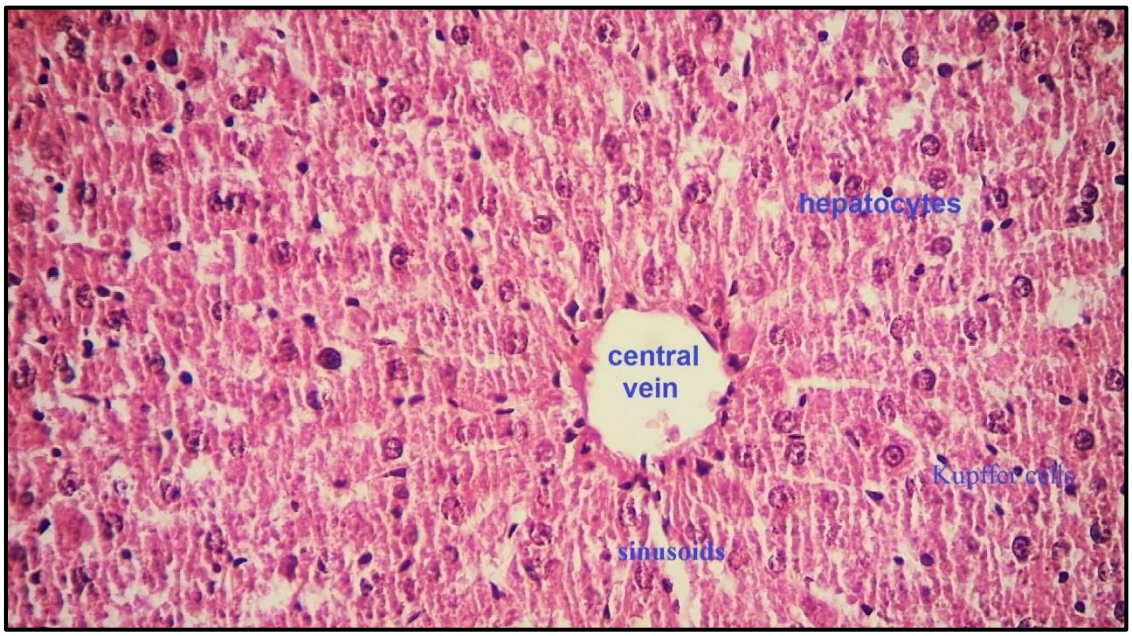
2.9. Statistical analysis

Statistical analysis was conducted for a 5x5 replicate experiment according to the Revised Least Significant Difference (L.S.D.) test at the probability level ($p \leq 0.05$) using the Statistical Package for the Social Sciences (SPSS) version 26 [21].

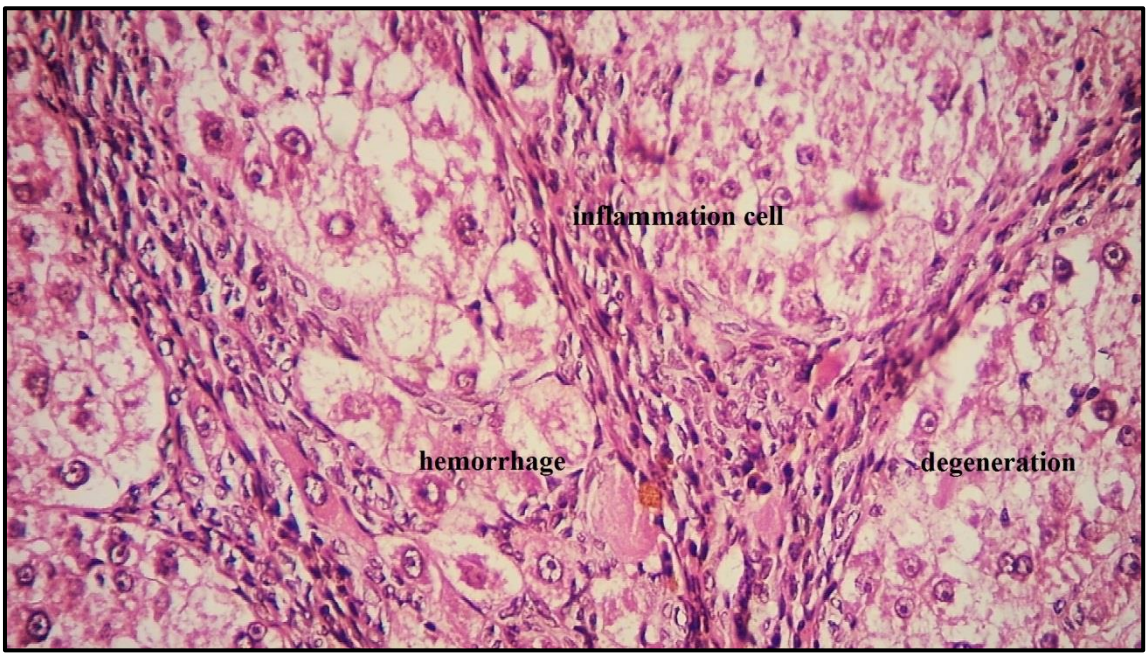
3. Results

3.1. Liver Tissues

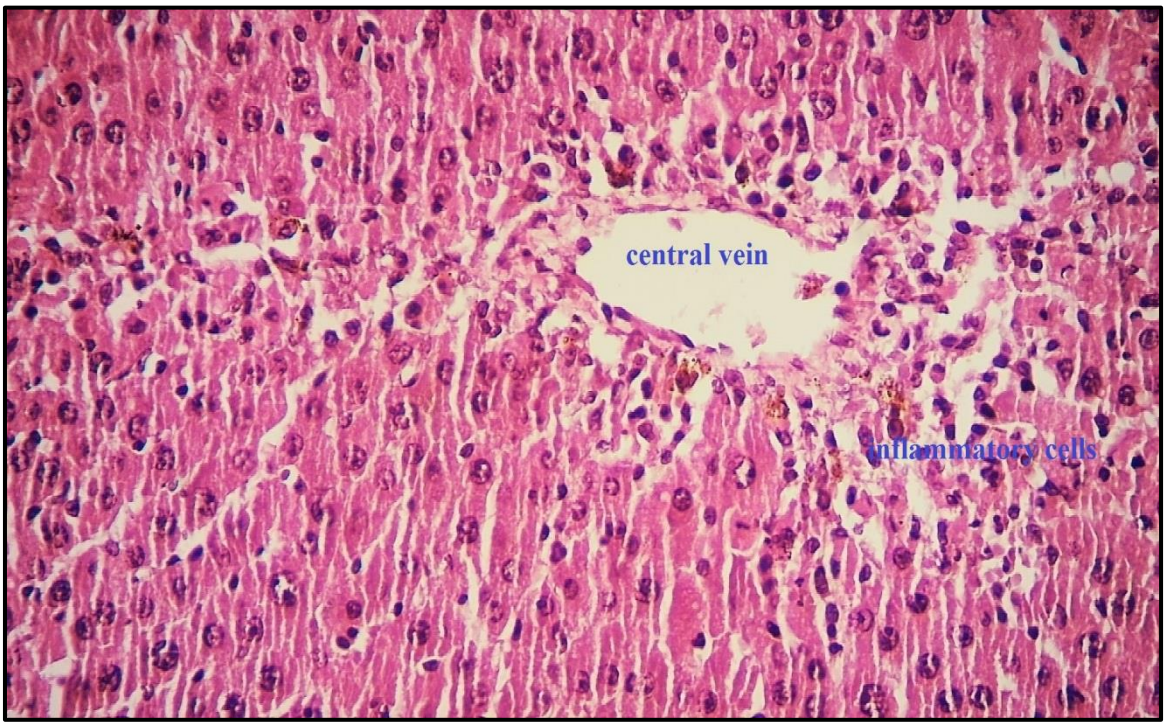
The section (G1) shows the control group: The normal shape of liver cells with sinusoids, as well as the central vein and the presence of Kupffer cells as well. The section (G2) shows the treatment group that treated with thioacetamide; bleeding was observed in the tissue. The segment also exhibited inflammation in certain regions of the tissue and degeneration of the hepatic cells compared to the normal portion (G1). The section (G3) shows the first preventive group, showing mild inflammation opposite (G1) normal section. The section (G4) shows the second preventive group, and the section (G5) shows the third preventive group, showing regular sinusoids and liver cells in a normal state, and a central vein with kupffer cells in a normal state, opposite (G2) with treatment(G2).



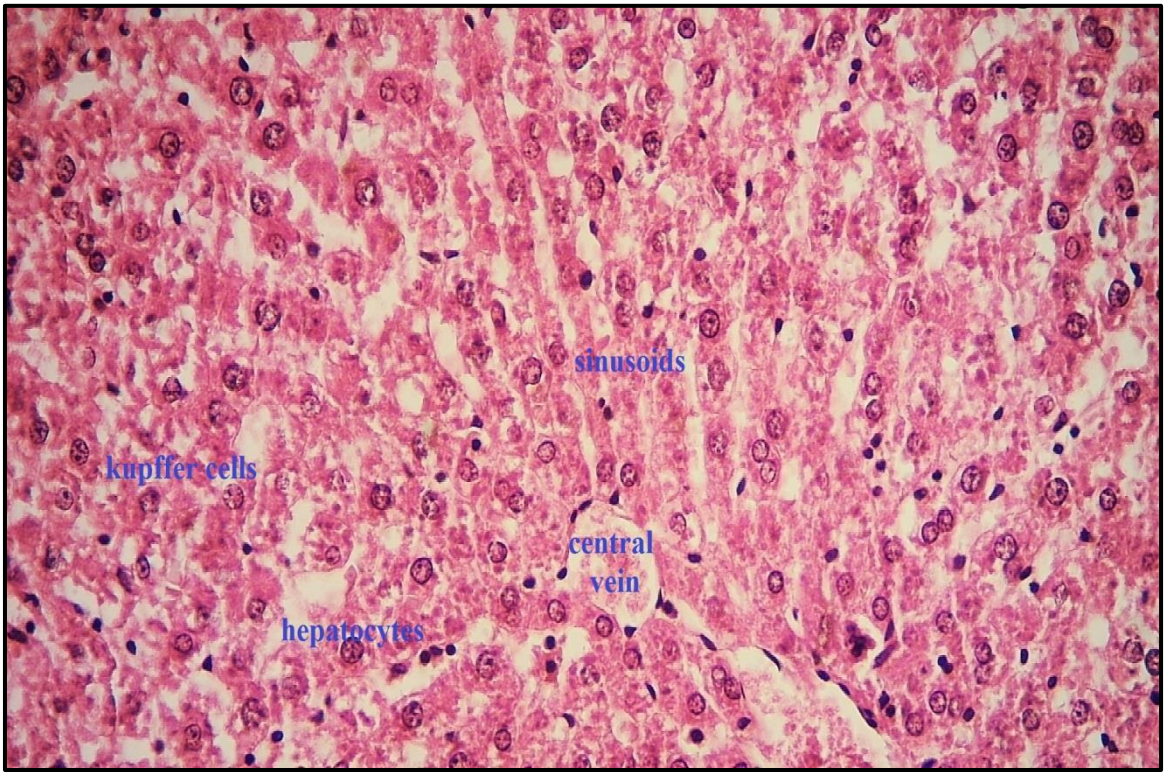
The section shows the normal control (G1)(400X) H&E.



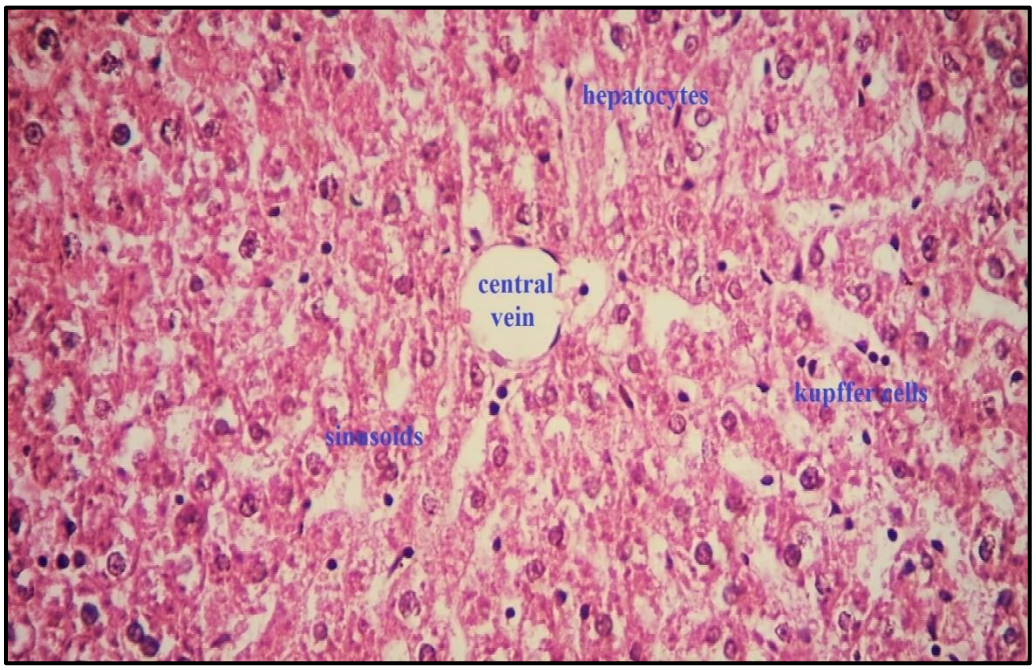
The section shows the treatment group (G2)(400X) H&E.



The section shows the first preventive group (G3)(400X) H&E.



The section shows the second preventive group (G4)(400X) H&E.



The section shows the third preventive group (G5)(400X) H&E.

3.2. Livre Enzymes

Table (1) appears a critical increase in liver enzymes, as AST (110.40 ± 3.187), ALT (61.40 ± 1.887), ALP (256.20 ± 3.541), and LDH (409.60 ± 5.938) in the group treated with TAA, which induces liver toxicity, compared to the control group AST (61.20 ± 1.960), ALT (32.40 ± 1.288), ALP (175.40 ± 2.315), and LDH (206.20 ± 4.067), whilst a significant reduction at first preventive group that was dosed a dosage of **400**mg/kg of the extract AST (90.20 ± 1.655), ALT (49.60 ± 0.939), ALP (239.60 ± 1.990) and LDH (324.60 ± 7.711) compared to the group treated with TAA, which induces hepatotoxicity. A significant decrease ($P<0.05$) was observed in the second preventive group, which was dosed at a dosage of **600**mg/kg of the extract, in AST (77.80 ± 2.905), ALT (41.80 ± 1.393), ALP (220.40 ± 1.720), and LDH (316.80 ± 4.294) compared to the group treated with TAA, which induces hepatotoxicity. Also, a significant decrease ($P<0.05$) in the third preventive group, which was dosed at a dosage of **600**mg/kg of the extract, was observed in AST (73.20 ± 2.131), ALT (40.60 ± 0.927), ALP (221.20 ± 1.772), and LDH (310.80 ± 4.259), which were lower than those in the group treated with TAA, which induces liver toxicity.

3.3. Antioxidants

Table (2) appears a critical increase in malondialdehyde (MDA) (21.30 ± 1.161) in the group treated with TAA, which induces liver toxicity, compared to the control group (12.50 ± 0.836), whilst a critical reduction was found in the first preventive group that received an administration of the alcoholic extract of flax seeds at a dosage of (400 mg/kg) (17.77 ± 0.620) and a significant decrease ($P<0.05$) in the second preventive group that was dosed at a dosage of **600**mg/kg of the extract (13.62 ± 0.859) and also a significant decrease ($P<0.05$) in the third preventive group that was dosed at a dosage of **800**mg/kg of the extract (13.34 ± 0.709) compared to the group treated with TAA, which induces toxicity. The liver showed significant differences ($P<0.05$) between the first preventive group and the second and third preventive groups, and no significant difference ($P>0.05$) between the second and third preventive groups.

Table (2) indicated a critical reduction at glutathione (GSH) (6.58 ± 0.916) in the group treated with TAA, which induces liver toxicity, compared to the control group (13.46 ± 1.063), whilst a significant increase was found in the first preventive group that was dosed with the alcoholic extract of flax seeds at a

dosage of (400 mg/kg) (9.75 ± 0.510) and a significant increase (P<0.05) in the second preventive group that was dosed at a dosage of **600**mg/kg of the extract (11.85 ± 1.293) and also a significant increase (P<0.05) in the third preventive group that was dosed at a dosage of **800**mg/kg of the extract (12.55 ± 0.668) compared to the group treated with TAA, which induces liver toxicity, with no critical difference (P>0.05) between the first and second preventive groups and between the second and third preventive groups.

From the results of the first and second tables, we find that TAA causes a disturbance in liver functions, as it causes an increase in liver enzymes and malondialdehyde, as well as a decrease in glutathione. However, flax seeds play a role in improving liver functions, as they may play a role in reducing liver functions and malondialdehyde, and an increase in glutathione.

3.4. Urea and Creatinine

Table (3) explained a critical increase at urea (48.77 ± 1.586) in the group treated with TAA, which induces liver toxicity, compared to the control group (25.04 ± 2.054), whilst a notable decline was found at first preventive group that was dosed with the alcoholic extract of flax seeds at a dosage of (400 mg/kg) (37.95 ± 1.358) and a notable decline (P<0.05) in the second preventive group that was dosed at a dosage of **600**mg/kg of the extract (34.20 ± 1.715) and also a notable decline (P<0.05) in the third preventive group that was dosed at a dosage of **800**mg/kg of the extract (34.46 ± 1.138) compared to the group treated with TAA, which induces liver toxicity.

The results of Table (3) explained a critical increase at creatinine level (3.01 ± 0.585) in the group treated with TAA, which induces liver toxicity, compared to the control group (0.83 ± 0.059), Whilst a critical reduction was found at first preventive group, which received an administration of the alcoholic extract of flax seeds at a dosage of (400 mg/kg) (1.79 ± 0.466), and a notable decline (P<0.05) in the second preventive group, which was dosed at a dosage of **600**mg/kg of the extract (1.05 ± 0.149), and also a notable decline (P<0.05) in the third preventive group, which was dosed at a dosage of **800**mg/kg of the extract (0.94 ± 0.249) compared to the group treated with TAA, which induces liver toxicity.

Table (1) shows the liver enzymes.

Standards / Groups	AST (U/L)	ALT (U/L)	ALP (U/L)	LDH (U/L)
Control(G1)	61.20 ± 1.960 **D**	32.40 ± 1.288 **D**	175.40 ± 2.315 **D**	206.20 ± 4.067 **C**
TAA 300/mg/kg(G2)	110.40 ± 3.187 **A**	61.40 ± 1.887 **A**	256.20 ± 3.541 **A**	409.60 ± 5.938 **A**
Extract(400mg/kg) +TAA(G3)	90.20 ± 1.655 **B**	49.60 ± 0.939 **B**	239.60 ± 1.990 **B**	324.60 ± 7.711 **B**
Extract(600mg/kg) +TAA(G4)	77.80 ± 2.905 **C**	41.80 ± 1.393 **C**	220.40 ± 1.720 **C**	316.80 ± 4.294 **B**
Extract(800mg/kg) +TAA(G5)	73.20 ± 2.131 **C**	40.60 ± **0**.927 **C**	221.20 ± 1.772 **C**	310.80 ± 4.259 **B**

Means ± Std.E

Different letters in the vertical direction represent substantial differences between the groups.

Table (2) explains antioxidants

Standards / Groups	MDA (mg/dl)	GSH (mg/dl)
Control(G1)	12.50 ± 0.836 **C**	13.46 ± 1.063 **C**
TAA 300/mg/kg(G2)	21.30 ± 1.161 **A**	6.58 ± 0.916 **A**
Extract(400mg/kg) +TAA(G3)	17.77 ± 0.620 **B**	9.75 ± 0.510 **B**
Extract(600mg/kg) +TAA(G4)	13.62 ± 0.859 **C**	11.85 ± 1.293 **BC**
Extract(800mg/kg) +TAA(G5)	13.34 ± 0.709 **C**	12.55 ± 0.668 **C**

Means ± Std.E
Different letters in the vertical direction represent substantial differences between the groups.

Table (3) shows urea and Creatinine.

Standards / Groups	Urea (mg/dl)	Creatinine (mg/dl)
Control(G1)	25.04 ± 2.054 **C**	0.83 ± 0.059 **B**
TAA 300/mg/kg(G2)	48.77 ± 1.586 **A**	3.01 ± 0.585 **A**
Extract(400mg/kg) +TAA(G3)	37.95 ± 1.358 **B**	1.79 ± 0.466 **B**
Extract(600mg/kg) +TAA(G4)	34.20 ± 1.715 **B**	1.05 ± 0.149 **B**
Extract(800mg/kg) +TAA(G5)	34.46 ± 1.138 **B**	0.94 ± 0.249 **B**

Means ± Std.E
Different letters in the vertical direction represent substantial differences between the groups.

4. Discussion

Histological sections revealed that thioacetamide-induced hepatotoxicity resulted in changes in liver tissue, consistent with a study by Goel et al.(2025)[22]. Macrophages cause tissue damage through antiproliferative and cytotoxic activities, resulting from the release of reactive oxygen species, reactive nitrogen species, and pro-inflammatory cytokines (IFN-γ and TNF-α) [23]. Treatment with an alcoholic extract of flax seeds improved liver tissue and reduced tissue damage, in line with research by Al-Ani et al. (2017) [24]. Flax seeds play a role in reducing cell necrosis and degeneration, preventing inflammatory cell infiltration and hemorrhage, and helping to reduce DNA fragmentation. Flax seeds and their components may act as signaling molecules that modulate the expression of genes involved in the production of the pro-inflammatory cytokine TNF-α and apoptosis, thereby improving biological activities and health [25].

The present results demonstrated that thioacetamide-induced hepatotoxicity resulted in elevated liver enzymes. This is in line with research by Alamri (2024)[26]. TAAs promote hepatocellular necrosis and inflammation, which makes liver enzymes in the blood work harder. This is commonly used as a biomarker of liver injury, as the enzymes are present in the cytoplasm of cells during necrosis and inflammation and then leak into the bloodstream, causing elevated serum enzyme levels [27]. Treatment with flaxseed alcohol extract led to a big reduction in liver enzyme levels, in line with research by Yari et al. (2016) [28]. Flax seeds are known as a functional food due to their beneficial nutritional properties. In addition to omega-3, flax seeds contain a high percentage of fiber, lignans, easily digestible protein, and antioxidants. Among the benefits of flax seeds are inhibiting hepatic genes that break down glucose and fat and stimulating the oxidation of fatty acids. This leads to preventing inflammation and hepatic necrosis, thus preventing the leakage of liver enzymes into the bloodstream [29].

The present results explain that thioacetamide-induced hepatotoxicity resulted in an increase in malondialdehyde levels and a decrease in glutathione levels. This agrees with the findings of Mousa et al. (2019)[30]. TAA promotes lipid peroxidation and liver fibrosis. Therefore, it is logical to assume that TAA causes cell damage by inhibiting the activity of antioxidant enzymes. This confirms the role of oxidative stress in the mechanisms of liver fibrosis and cirrhosis [31]. Oxidative stress occurs when the excessive production of reactive oxygen species exceeds the capacity of antioxidant defenses to scavenge them, leading to oxidative damage to macromolecules such as proteins, lipids, and nucleic acids. Unregulated oxidative stress has been implicated in countless diseases [32,33]. Treatment with alcoholic extract of flax seeds resulted in a significant decrease in malondialdehyde levels and an increase in glutathione levels, which was in agreement with the findings of Musazadeh et al.(2021)[34]. Flax has a preventive and therapeutic role thanks to its phytochemical composition consisting of substances with anti-inflammatory and antioxidant effects. Flax seeds have anti-inflammatory activity by increasing antioxidant activity as well as by reducing the activity of NF-κB, RNS, and ROS [13].

The present results demonstrated that thioacetamide-induced hepatotoxicity resulted in elevated urea and creatinine levels, consistent with the findings of Shaikh Omar(2018)[35]. Kidney tissue is harmed by thioacetamide, which is toxic to the kidneys. It results in cell death in the terminal section of the proximal renal tubules, collagen deposition in the renal medulla, and fibrin deposition in the renal tubules. This impairs renal function and causes severe tubular epithelial cell death, along [36]. Treatment with alcoholic extract of flax seeds resulted in a significant decrease in urea and creatinine levels, consistent with the results of a study by Al Za'abi et al. (2021)[37]. Flax seeds are rich in alpha-linolenic acid, which has anti-inflammatory properties. This component has been

found to be partly responsible for the beneficial kidney-protective effects by acting as an antagonist of platelet-activating factor receptors. This factor contributes to the inflammatory response to progressive glomerulonephritis [38].

5. Conclusion

From the results of the study, we conclude that thioacetamide has a harmful effect on the structure of liver tissue, as well as on liver enzymes and antioxidants, and leads to impaired kidney function. The study found that the alcoholic extract of flax seeds has a significant protective role, as it improved liver tissue, has anti-inflammatory and antioxidant properties, and also has an anti-nephrotoxic effect.

Conflict of interest: NIL

Funding: NIL

6. References

1. Zhang H, Xu J. Unveiling thioacetamide-induced toxicity: Multi-organ damage and omitted bone toxicity. Human \& Experimental Toxicology. 2024;43:09603271241241807. doi:10.1177/09603271241241807 PubMed PMID: 38531387.

2. Ezhilarasan D. Molecular mechanisms in thioacetamide-induced acute and chronic liver injury models. Environmental Toxicology and Pharmacology. 2023;99:104093. doi:https://doi.org/10.1016/j.etap.2023.104093

3. El-Hameed SA, Ibrahim I, Awadin W, El-Shaieb A. Thioacetamide: Definition, Exposure, Hepatic and Renal Toxicity. Mansoura Veterinary Medical Journal. 2023;24(4):3.

4. Sepehrinezhad A, Shahbazi A, Sahab Negah S, Joghataei MT, Larsen FS. Drug-induced-acute liver failure: A critical appraisal of the thioacetamide model for the study of hepatic encephalopathy. Toxicology Reports. 2021;8:962–70. doi:https://doi.org/10.1016/j.toxrep.2021.04.011

5. Sharawy MH, El-Awady MS, Makled MN. Protective effects of paclitaxel on thioacetamide-induced liver fibrosis in a rat model. Journal of Biochemical and Molecular Toxicology. 2021;35(5):e22745.

6. Kundu A, Gali S, Sharma S, Kacew S, Yoon S, Jeong HG, et al. Dendropanoxide Alleviates Thioacetamide-induced Hepatic Fibrosis via Inhibition of ROS Production and Inflammation in BALB/(C) Mice. International journal of biological sciences. 2023;19(9):2630–47. doi:10.7150/ijbs.80743. PubMed PMID: 37324954.

7. Ugwu CE, Suru SM. Medicinal plants with hepatoprotective potentials against carbon tetrachloride-induced toxicity : a review. Egyptian Liver Journal. 2021;11:1–26. doi:10.1186/s43066-021-00161-0

8. Petrovska BB. Historical review of medicinal plants' usage. Pharmacognosy Reviews. 2012 Jan;6(11):1–5. doi:10.4103/0973-7847.95849 PubMed PMID: 22654398.

9. Saleem MH, Ali S, Hussain S, Kamran M, Chattha MS, Ahmad S, et al. Flax (Linum usitatissimum L.): A Potential Candidate for Phytoremediation? Biological and Economical Points of View. Plants. 2020;9(4). doi:10.3390/plants9040496

10. Nowak W, Jeziorek M. The Role of Flaxseed in Improving Human Health. Healthcare. 2023;11(3). doi:10.3390/healthcare11030395

11. Hendawi MY, Alam RTM, Abdellatief SA. Ameliorative effect of flaxseed oil against thiacloprid-induced toxicity in rats: hematological, biochemical, and histopathological study. Environmental Science and Pollution Research. 2016;23:11855–63.

12. Sorour HA, Salem MA, Abdelmaksoud DA, Abd Elgalil MM. The Impact of High Fat Diet and Flaxseed on Liver Histology, Histochemistry and Morphometry in Ovariectomized Albino Rat. Egyptian Journal of Histology. 2022;45(1):68–89.

13. Chera EI, Pop RM, Pârvu M, Soritău O, Uifălean A, Cătoi FA, et al. Flaxseed Ethanol Extracts' Antitumor, Antioxidant, and Anti-Inflammatory Potential. Antioxidants. 2022;11(5):892.

14. Akhtar T, Sheikh N. An overview of thioacetamide-induced hepatotoxicity. Toxin Reviews. 2013;32(3):43–6.

15. Lala V, Zubair M, Minter D. Liver function tests. StatPearls. 2023.

16. Muslih B, Mizil YO, Al-Nimmer MS. Detection the level of peroxynitrite and related with antioxidant status in the serum of patients with acute myocardial infarction. NationalJChemistry. 2001;4:625–37.

17. Moron MS, Depierre JW, Mannervik B. Levels of glutathione, glutathione reductase and glutathione S-transferase activities in rat lung and liver. Biochimica et biophysica acta (BBA)-general subjects. 1979;582(1):67–78.

18. Marklund S, Marklund G. Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase. European journal of biochemistry. 1974;47(3):469–74.

19. Chaney AL, Marbach EP. Modified Reagents for Determination of Urea and Ammonia. Clinical Chemistry. 1962 Apr 1;8(2):130–2. doi:10.1093/clinchem/8.2.130

20. Larsen K. Creatinine assay by a reaction-kinetic principle. Clinica Chimica Acta. 1972;41:209–17. doi:https://doi.org/10.1016/0009-8981(72)90513-X

21. Moder K. Alternatives to F-test in one way ANOVA in case of heterogeneity of variances (a simulation study). Psychological Test and Assessment Modeling. 2010;52(4):343.

22. Goel R, Mishra R, Kumar N, Imsong N, Singh N, Gaur P, et al. Hepatoprotective effect of diosmetin against thioacetamide-induced liver injury via modulating Bax/NF-κB/caspase-3/Nrf-2/PPARϒ signaling pathway in rats. Naunyn-Schmiedeberg's Archives of Pharmacology. 2025. doi:10.1007/s00210-025-04293-7

23. Golbar HM, Izawa T, Wijesundera KK, Bondoc A, Tennakoon AH, Kuwamura M, et al. Depletion of hepatic macrophages aggravates liver lesions induced in rats by thioacetamide (TAA). Toxicologic Pathology. 2016;44(2):246–58.

24. Al-Ani IM, Abired AN, Mustafa BE, Wahab ENA, Azzubaidi MS. Effect of flaxseed extract on the liver histological structure in streptozotocin induced diabetic rats. IIUM Medical Journal Malaysia. 2017;16(1).

25. Diab KA, Ibrahim NE, Fahmy MA, Hassan EM, Omara EA. Inhibitory activity of flaxseed oil against CdCl2 induced liver and kidney damage: Histopathology, genotoxicity, and gene expression study. Toxicology Reports. 2020;7:1127–37. doi:https://doi.org/10.1016/j.toxrep.2020.08.023

26. Alamri ZZ. Protective and therapeutic effects of apigenin on thioacetamide - induced hepatotoxicity in male rats : physiological and morphological study. Egyptian Liver Journal. 2024. doi:10.1186/s43066-024-00318-7

27. Abdou SE, Taha NM, El-Wahab A, Mandour A, Lebda MA, El Hofi HR, et al. Antifibrotic Effect of Curcumin on Thioacetamide Induced Liver Fibrosis. Alexandria Journal of Veterinary Sciences. 2015;45.

28. Yari Z, Rahimlou M, Eslamparast T, Ebrahimi-Daryani N, Poustchi H, Hekmatdoost A. Flaxseed supplementation in non-alcoholic fatty liver disease: a pilot randomized, open labeled, controlled study. International journal of food sciences and nutrition. 2016;67(4):461–9.

29. Khodadadi N, Sadeghi A, Poustchi H, Abbasi B, Nilghaz M, Melekoglu E, et al. Effectiveness of flaxseed consumption and fasting mimicking diet on anthropometric measures, biochemical parameters, and hepatic features in patients with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): a randomized controlled clinical t. Nutrition & Diabetes. 2024;14(1):93.

30. Mousa AA, El-Gansh HAI, Eldaim MAA, Mohamed MAEG, Morsi AH, El Sabagh HS. Protective effect of Moringa oleifera leaves ethanolic extract against thioacetamide-induced hepatotoxicity in rats via modulation of cellular antioxidant, apoptotic and inflammatory markers. Environmental Science and Pollution Research. 2019;26(31):32488–504.

31. Bashandy SAE, Ebaid H, Abdelmottaleb Moussa SA, Alhazza IM, Hassan I, Alaamer A, et al. Potential effects of the combination of nicotinamide, vitamin B2 and vitamin C on oxidative-mediated hepatotoxicity induced by thioacetamide. Lipids in Health and Disease. 2018;17(1):29. doi:10.1186/s12944-018-0674-z

32. Stefanello ST, Hartmann DD, Amaral GP, Courtes AA, Leite MTB, da Silva TC, et al. Antioxidant protection by β-selenoamines against thioacetamide-induced oxidative stress and hepatotoxicity in mice. Journal of Biochemical and Molecular Toxicology. 2017 Dec 1;31(12):e21974. doi:https://doi.org/10.1002/jbt.21974

33. Yameny A, Fekry T. Oxidative Stress and Malignancy: The Central Role of Reactive Oxygen Species (ROS) in Cancer. Biobacta Journal of Biochemistry and Molecular Biology, (2026); 3(1):1-10. https://doi.org/10.71428/BJBMB.2026.0101

34. Musazadeh V, Jafarzadeh J, Keramati M, Zarezadeh M, Ahmadi M, Farrokhian Z, et al. Flaxseed Oil Supplementation Augments Antioxidant Capacity and Alleviates Oxidative Stress: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Evidence-Based Complementary and Alternative Medicine. 2021;2021(1):4438613.

35. Shaikh Omar AM. The potential protective influence of flaxseed oil against renal toxicity induced by thioacetamide in rats. Saudi Journal of Biological Sciences. 2018;25(8):1696–702. doi: https://doi.org/10.1016/j.sjbs.2016.09.021

36. Lim J youn, Jung WW, Kim W, Moon KS, Sul D. Nephrotoxicity evaluation and proteomic analysis in kidneys of rats exposed to thioacetamide. Scientific Reports. 2022;12(1):6837. doi:10.1038/s41598-022-11011-3

37. Al Za'abi M, Ali H, Ali BH. Effect of flaxseed on systemic inflammation and oxidative stress in diabetic rats with or without chronic kidney disease. PLoS One. 2021;16(10):e0258800.

38. HUSSIEN ZG, AZIZE RA, AL-MOUSAWI AT. The effect of Flaxseed (Linum Usitatissimum L) consumption in biochemical parameters of rats. International Journal of Pharmaceutical Research. 2020;12(2).