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Histopathological and Functional Changes of the Possible Protective Effects of Aqueous Extract of Fenugreek Seeds (Trigonella Foenum-Graecum) on Ibuprofen-Induced Hepato-Renal Toxicity in Male Local Rabbits

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Abstract:

The study aimed to evaluate the protective role of aqueous extract of fenugreek seeds against ibuprofen-induced hepatic and renal damage in 24 adult male rabbits. They were divided into: control group; ibuprofen group (40 mg/kg); fenugreek extract group (100 mg/kg); and a group treated with ibuprofen + fenugreek extract (40 and 100 mg/kg, respectively). Histological examinations showed liver damage in the ibuprofen group, including central vein congestion, mononuclear cell infiltration, Kupffer cell activation, and portal vein congestion. The renal tissue showed glomerular shrinkage, Bowman's capsule dilation, peritubular hemorrhage, and leukocyte infiltration. Liver enzymes (ALP, AST, ALT) and urea, creatinine, and uric acid levels were elevated, indicating hepatic and renal damage, more pronounced in the ibuprofen group. The fenugreek-treated group maintained tissue structure and function, indicating a protective role against ibuprofen-induced damage.

Keywords: Aqueous extract، fenugreek seeds، ibuprofen، liver and kidney tissues، male rabbits.

دراسة التغيرات النسيجية والوظيفية للتأثيرات الوقائية المحتملة للمستخلص المائي لبذور الحلبة (*Trigonella foenum-graecum*) على السمية الكبدية– الكلوية المستحدثة بالأيبوبروفين في ذكور الأرانب المحلية

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الملخص:

هدفت الدراسة إلى تقييم الدور الوقائي للمستخلص المائي لبذور الحلبة ضد التلف الكبدي والكلوي الناجم عن الأيبوبروفين في 24 أرنب ذكر بالغ. قُسِّمت المجموعات إلى: مجموعة ضابطة؛ مجموعة الأيبوبروفين (40 ملغم/كغم)؛ مجموعة مستخلص الحلبة (100 ملغم/كغم)؛ ومجموعة عولجت بالأيبوبروفين + مستخلص الحلبة (40 و100 ملغم/كغم على التوالي). أظهرت الفحوصات النسيجية تلفًا في الكبد في مجموعة الأيبوبروفين، شمل احتقان الوريد المركزي، وتسلل الخلايا وحيدة النواة، وتنشيط خلايا كوبفر، واحتقان الأوردة البابية. وأظهر النسيج الكلوي انكماش الكبيبات، واتساع محفظة بومان، ونزفًا قرب الأنابيب، وارتشاح خلايا دم بيضاء. كما ارتفعت إنزيمات الكبد (ALP، AST، ALT) ومستويات اليوريا والكرياتنين وحمض البوليك، مما يشير إلى تلف كبدي وكلوي والتي كانت أكثر وضوحًا في مجموعة الأيبوبروفين. حافظت المجموعة المعالجة بمستخلص الحلبة على بنية ووظيفة الأنسجة، مما يشير إلى دور وقائي ضد التلف الناجم عن الأيبوبروفين.

الكلمات المفتاحية: المستخلص المائي، بذور الحلبة، الأيبوبروفين، أنسجة الكبد والكلى، ذكور الأرانب.

1. Introduction

Plants play an important role in the diet, as they are considered food and a natural source of treatment for various diseases, due to their chemical composition, which is highly beneficial and important from a physiological point of view for humans and animals. Most current studies focus on the use of plant extracts to find a role for antioxidants in preventing damage caused by many chemical reactions involving unstable free radicals in animal tissues. Among these medicinal plants is fenugreek, which is rich in natural antioxidants. The fenugreek plant has antioxidant properties that protect organs from damage and reduce the risk of disease (Club & Branch, 2013). One of these organs is the liver, which is one of the largest organs in the body, weighing approximately 1.5 kg and performing many vital functions necessary for maintaining the body's internal balance (Naruse et al., 2007). These functions include removing toxins, drugs and harmful substances from the blood, as well as playing a role in glucose production, blood clotting and urea production, which is subsequently excreted in urine. It also contributes to the regulation of amino acid levels and the production of many important proteins such as albumin and clotting proteins. Furthermore, the liver plays a key role in producing bile. It also acts as a biological filter, contributing to the removal of foreign particles and toxic

substances from the bloodstream (Wang et al., 2025). Due to the variety of its vital functions and its constant exposure to toxic substances, the liver is particularly susceptible to imbalance in the body. Despite its high capacity for regenerating its cells and restoring its functional mass within a relatively short period of time when damaged, increased cellular damage can lead to what is known as liver failure due to liver cell damage (Husaema et al., 2025; Ramirez-Mejia, 2024). On the other hand, the kidneys play a role in maintaining physiological balance. This includes filtering the blood to remove metabolic waste products such as urea and creatinine, regulating fluid and electrolyte balance, and eliminating drugs and toxins through the urinary excretion process (Ferguson et al., 2008; Alsaeh et al., 2025). Therefore, any dysfunction in kidney function can lead to serious disturbances in the body's various functions and can even threaten human life (Al-Shukri et al., 2026). Urea and creatinine are two of the most important metabolic by-products filtered by the kidneys, so any increase in these substances in the blood is a sign of kidney tissue dysfunction. This change may be due to the inability of the Malpighian corpuscles to eliminate these substances, causing them to accumulate in the blood (Reynolds, 1982). Non-steroidal anti-inflammatory drugs are among the most commonly used medications. ibuprofen is one of the most widely used, and is used to treat many acute and chronic conditions such as rheumatoid arthritis, osteoarthritis, dysmenorrhoea, and to relieve pain after surgery (Ngo & Bajaj, 2024; StatPearls Publishing, 2024). It is also prescribed as an analgesic, antipyretic, and anti-inflammatory agent, and has been used for many years by patients with arthritis (Ershad et al., 2018). However, excessive use of ibuprofen can lead to adverse effects. However, it may lead to drug poisoning, which can cause many negative side effects, including renal and hepatic toxicity, as well as some skin disorders (Gooch et al., 2007).

1.1 Objectives of the study:

Fenugreek is a medicinal herb used since ancient times in traditional medicine and food in several countries. Its seeds are notable for their content of a variety of bioactive compounds such as alkaloids, saponins, flavonoids, dietary fibres, and antioxidants. In light of the widespread use of flavonoids in the treatment of diseases, this study aimed to evaluate the protective effect of fenugreek seeds in reducing pathological tissue and functional changes in the liver and kidneys resulting from ibuprofen poisoning in male rabbits, by examining their ability to minimise tissue damage and protect liver and kidney tissue from the toxic effects of this drug.

2. Materials and Methods:

2.1 Chemicals used:

Ibuprofen (400 mg) was obtained from Bristol Laboratories Ltd. Bristol Laboratories Ltd. Unit 3, Canalside, Northbridge Road, Berkhamsted, HP4 1EG) from a local pharmacy in the city of Khoms, Libya. To prepare the ibuprofen solution according to the method of McQuay & Moore (2007), one ibuprofen tablet was dissolved in 4 ml of distilled water, and then administered orally at a dose of 40 mg/kg using a syringe.

2.2 The plant used in the study:

The plant used in the study was fenugreek seeds, chosen based on a review of previous studies and its importance in the medical field. It was purchased from a local herbalist's market in Khoms, Libya.

2.3 Preparation of the aqueous fenugreek extract:

The aqueous extract was prepared according to the method of Handa (2008) with some modifications, by mixing 25 g of fenugreek seed powder in 250 mL of boiling distilled water (at a ratio of 1:10). The mixture was stirred to cool using a shaker for 24 hours. The solution was then filtered using Whatman No. 2 filter paper. This process was repeated to obtain the required quantity, after which the extract was stored in a bottle and refrigerated at 4°C until use.

2.4 Test Animals:

The study used 24 male local rabbits, weighing between 800–1200 g and aged 11–19 months, obtained from local markets. They were housed in special metal cages under laboratory conditions at 25 ± 2°C, and provided with water and food ad libitum. The experiment lasted for one month .

2.5 Experimental Design:

Group 1 (Control): The animals were provided with water and food only, without any treatment.

Group 2 (Ibuprofen): Ibuprofen was administered at a dose of 40 mg/kg.

Group 3 (Fenugreek Seed Water Extract): The animals were administered fenugreek seed water extract at a dose of 100 mg/kg.

Group 4 (Ibuprofen + aqueous fenugreek seed extract): The animals were administered a 40 mg/kg dose of ibuprofen and a 100 mg/kg dose of aqueous fenugreek seed extract.

2.6 Histological Studies :

The animals were sacrificed and dissected; sections of the liver and kidneys were taken and placed in a fixative solution (10% formalin) until histological processing began. After fixation, small sections were taken from each organ (liver and kidneys) for processing.

2.6.1 Histological Preparations :

Animal tissues were prepared by subjecting them to a series of processes according to the method described by Azab et al. (2022), as follows: dehydration, impregnation,

embedding, sectioning, and staining. Tissue processing and examination were performed at the Histology Department of Zliten Teaching Hospital.

2.7 Blood sampling :

At the end of the experiment, blood was drawn from the marginal ear vein using a special medical syringe (El-Rawi et al., 2013), The blood was collected in clean, dry glass tubes free of anticoagulants, and centrifuged at 3000 rpm for 15 minutes to obtain serum, which was then stored in a freezer at -20°C.

2.8 Biochemical Analyses:

Liver function enzymes (ALP, AST, and ALT) were measured, as well as serum levels of creatinine, urea, and uric acid.

2.9 Statistical Analysis:

The results were statistically analyzed using SPSS-25, Results were expressed as the mean ± standard error of the mean (SEM), with 95% confidence intervals provided. The P-value was used, with statistical significance indicated if $P < 0.05$.

3. Results

Histological Study: The results of the histological examination of the animal groups treated with ibuprofen and the aqueous extract of fenugreek seeds revealed histological changes in liver and kidney tissues when compared with each other and with the control group (untreated).

3.1 Histological Changes in the Livers of Male Rabbits:

3.1.1 Histological changes in the livers of male local rabbits in the control group:

Figure 1 shows micrographs of histological sections from the livers of male rabbits in the control group, which have a normal histological structure where the hepatocytes appear polygonal, with homogeneous cytoplasm and large nuclei. The figure shows micrographs of liver tissue sections from male rabbits in the control group, which exhibit a normal histological structure: the hepatocytes appear polygonal with homogeneous cytoplasm and large, centrally located nuclei, arranged in longitudinally parallel hepatic bands separated by sinusoids containing Kupffer cells. It also contains a central vein lined with simple squamous epithelium located in the center of the hepatic lobule, as shown in Figure (1).

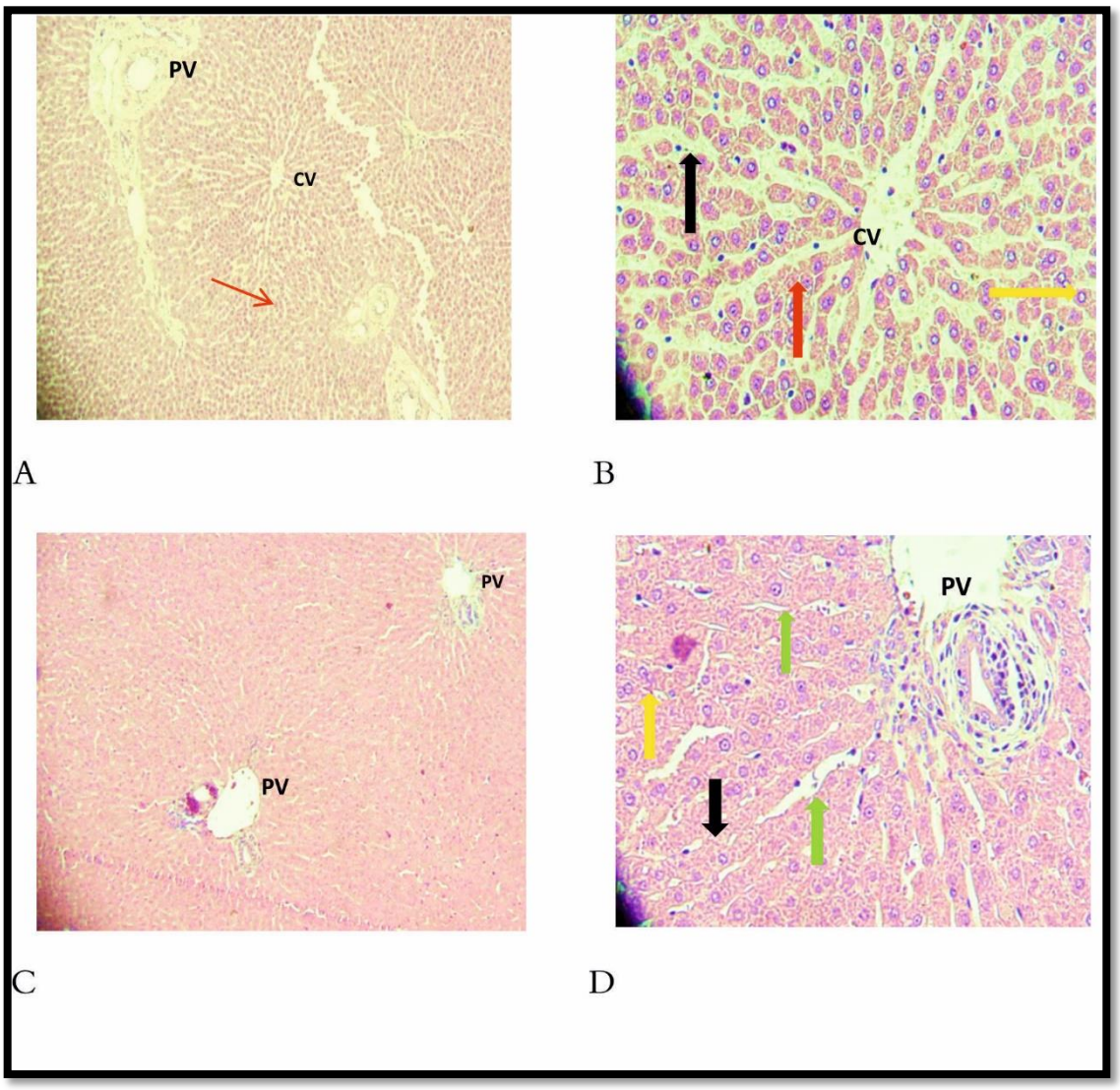


Figure (1): Histological sections of the liver of male rabbits in the control group. A: Central vein (CV), hepatic portal vein (PV), blood sinusoid (red arrow), (100X; H&E), B: Central vein (CV), sinusoid (red arrow), Kupffer cell (black arrow), binucleated hepatocyte (yellow arrow), (400X; H&E). C: Portal vein (PV), (100X; H&E), D: Portal vein (PV), sinusoid (green arrow), binucleated hepatocyte (yellow arrow), Kupffer cell (black arrow), (400X; H&E).

3.1.2 Histological Changes in the Livers of Male Rabbits Treated with Fenugreek Seed Water Extract:

Microscopic examination of liver tissue from male rabbits treated with fenugreek seed water extract revealed the presence of normal hepatocytes with large, polygonal, centrally located nuclei, arranged in rectangular hepatic bands separated by sinusoids containing Kupffer cells, while others contain a few red blood cells. They also contain a central vein in the center of the hepatic lobule lined with simple squamous epithelium, as shown in Figure (2).

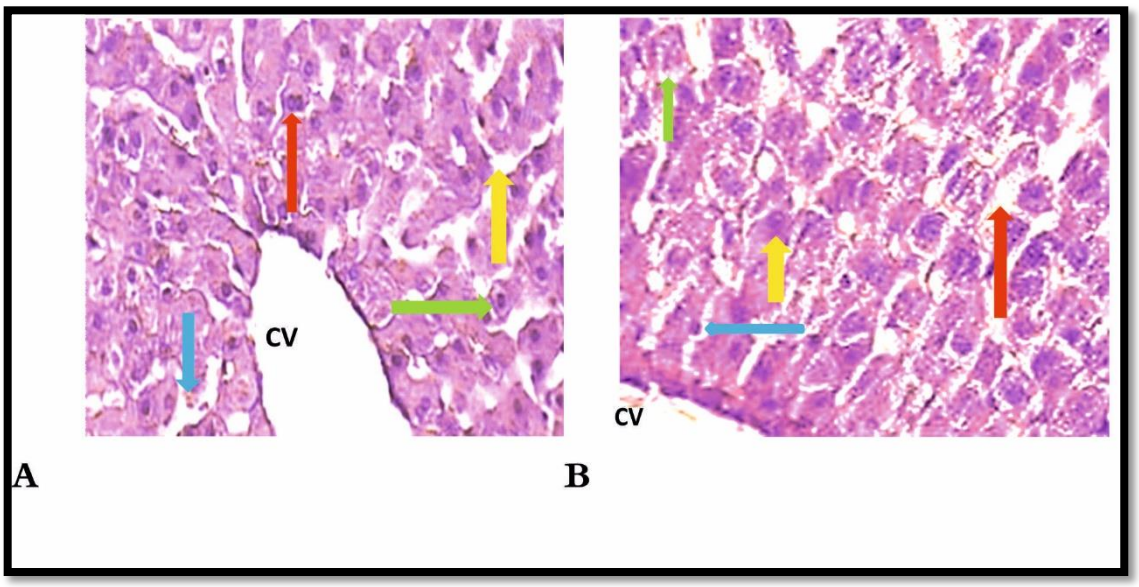


Figure (2): Tissue section from a group of male rabbits treated with an aqueous extract of fenugreek seeds. A: Central vein (CV), sinusoid (yellow arrow), binucleated hepatocyte (red arrow), hepatocyte nucleus (green arrow), Kupffer cell (blue arrow), (400X; H&E). B: Central vein (CV), sinusoid (red arrow), binucleated hepatocyte (green arrow), hepatocyte nucleus (yellow arrow), Kupffer cell (blue arrow), (1000X; H&E).

3.1.3 Histological changes in the livers of male rabbits treated with ibuprofen:

Histological sections of the livers of male rabbits treated with ibuprofen revealed swollen hepatocytes with central nuclei, along with dilation, congestion, and clotted blood in the central vein, and increased thickness of the central vein endothelium in some hepatic lobules, as well as dilation and increased numbers of sinusoids containing active Kupffer cells, in addition to leukocyte infiltration in some areas of the liver tissue near the central vein and in the portal area. We also observe congestion with the presence of clotted blood in the hepatic portal vein and an increase in its wall thickness, along with fibrosis in the hepatic portal vein region (Figure 3).

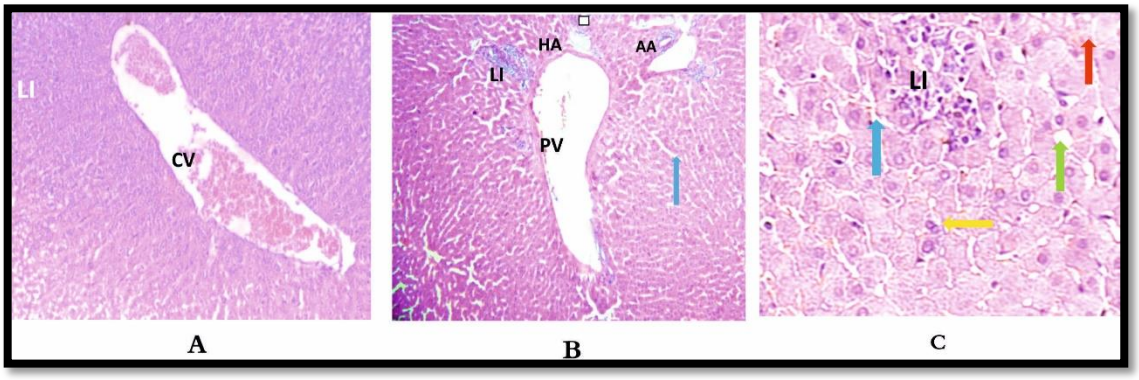


Figure (3): Histological sections of the livers of male rabbits treated with ibuprofen. Image A: Dilated central vein congested with clotted blood (CV), leukocyte infiltration (LI), B: Dilatation and congestion

of the portal area and portal vein (PV), dilatation of the sinusoids (blue arrow), leukocyte infiltration near the portal vein (LI), increased thickness of the bile ducts (AA), increased thickness of the hepatic artery (HA) (red arrow), C: Leukocyte infiltration (LI), dilation of the sinusoids containing red blood cells the presence of binucleated hepatocytes (yellow arrow), the presence of fatty infiltration and cytoplasmic vacuoles in hepatocytes (green arrow), and an active Kupffer cell (blue arrow).

3.1.4 Histological changes in the livers of male rabbits treated with ibuprofen and aqueous fenugreek seed extract:

In this group, microscopic examination of the tissue sections revealed histological improvement in the liver compared to the ibuprofen-only group: A, B, and C, where hepatocytes regained their normal shape in regular, orderly rows, while the central vein was observed to have somewhat regained its normal size, with slight infiltration of white blood cells (Figure 4).

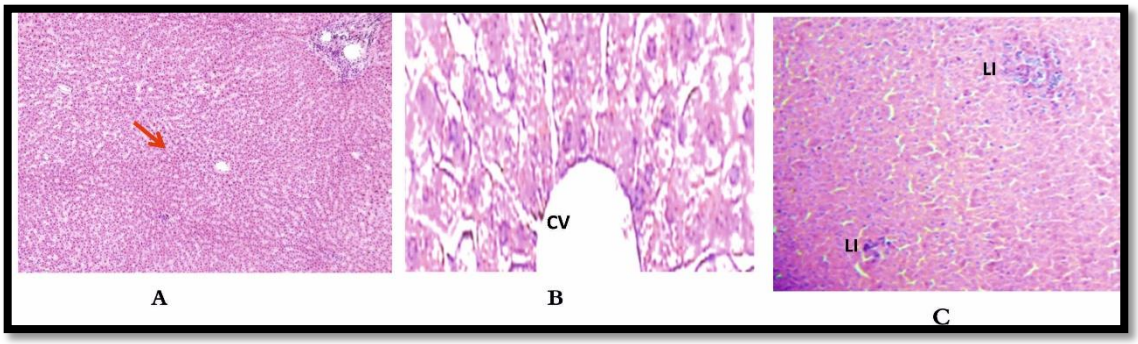


Figure (4): shows an improvement in liver tissue, where the liver tissue has regained its normal size (red arrow), while the hepatocytes have retained their longitudinally parallel shape in the form of hepatic bands; however, we observe the presence of some inflammatory cells in certain areas of the liver tissue (A, B, and C) (100X; A & 400X; B & 100X; C).

3.2 Histological Changes in Male Rabbit Kidneys:

3.2.1 Histological Structure of Male Rabbit Kidneys in the Control Group:

Renal histological examination of the cortical region in the control group revealed a normal structure of the glomeruli and renal tubules, which appear lined by columnar cells lined by simple squamous cells, characterized by a thick wall with an internal lumen (Figure 5).

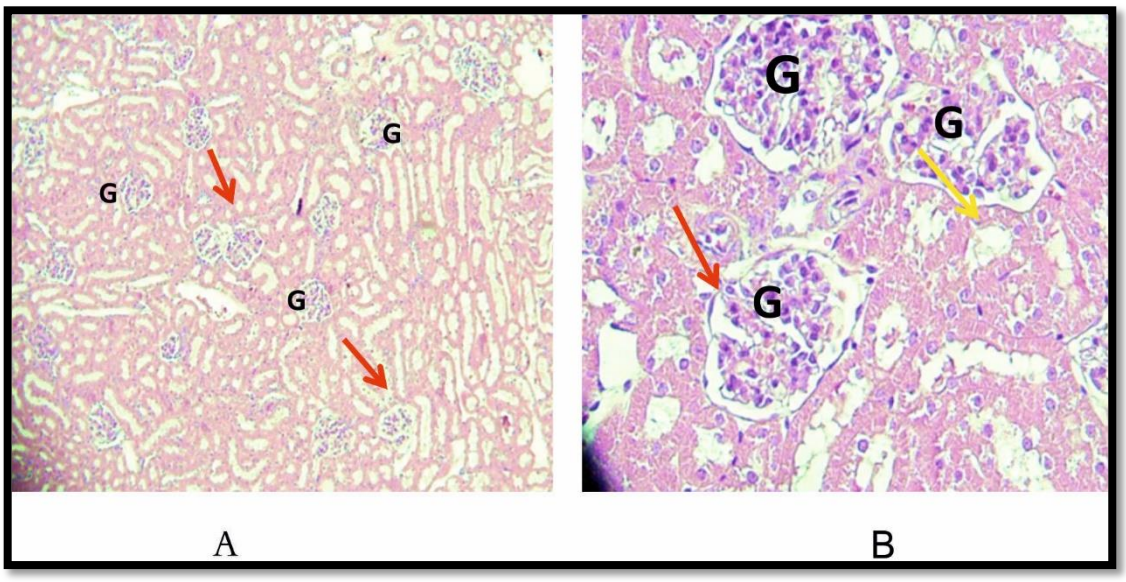


Figure (5): shows a histological section of the renal cortex in the control group, where normal Malpighian corpuscles are observed, each surrounded by a Bowman's capsule and lined by simple squamous epithelium (red arrow), and a Malpighian corpuscle (G), with the presence of normal renal tubules having a thick wall and an internal lumen (yellow arrow). (100X; A, 400X; B, H&E).

3.2.2 Histological changes in the kidneys of male rabbits administered an aqueous extract of fenugreek seeds:

Histological examination of the renal cortex revealed the presence of normal, regularly shaped glomeruli, similar to those found in the control group. The examination also showed that each glomerulus of Bowman's capsule was lined with a simple squamous epithelium, as well as thick-walled urinary tubules, each containing an internal lumen free of any protein deposits; some of the renal tubules also contained red blood cells (Figure 6).

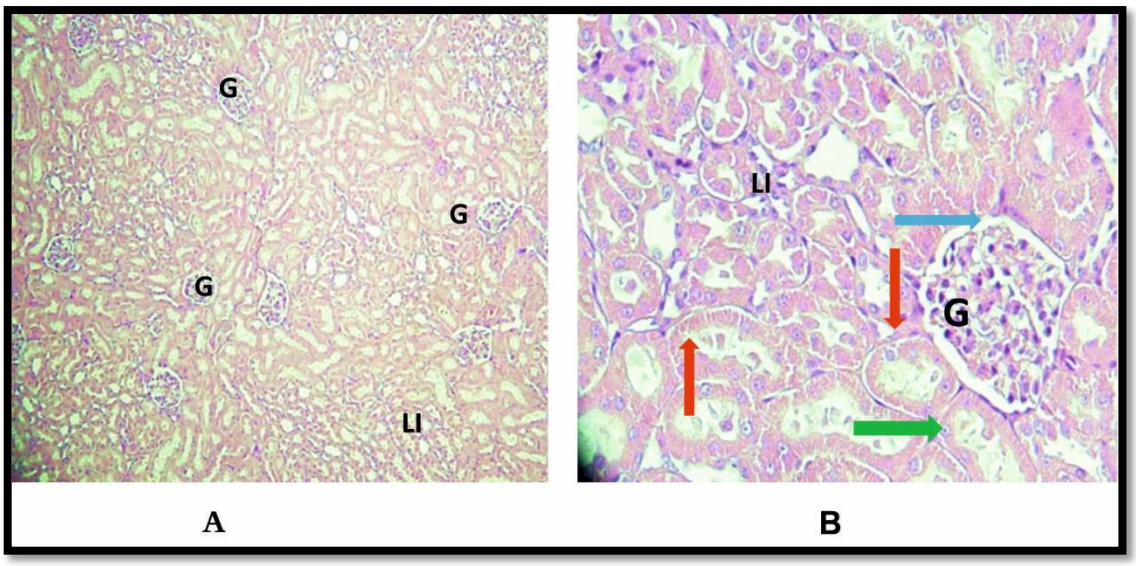


Figure (6): Tissue in the cortical layer containing normal, regularly shaped Melbius bodies, each surrounded by a Bowman's capsule and lined with simple squamous epithelium (G) (blue arrow). The adjacent renal tubules have thick walls (green arrow) and contain an internal lumen (red arrow), with mild infiltration of white blood cells between the urinary tubules (LI). (100X; A, 400X; B, H&E).

3.2.3 Histological Changes in the Kidneys of Male Rabbits Treated with Ibuprofen:

Microscopic examination of the kidneys of male rabbits administered ibuprofen alone revealed clear histological changes in the cortical region, where congestion with severe hemorrhage in the renal tissue was observed, along with dilation of the renal tubules and atrophy and shrinkage of the glomeruli, accompanied by infiltration and invasion of (Figure 7).

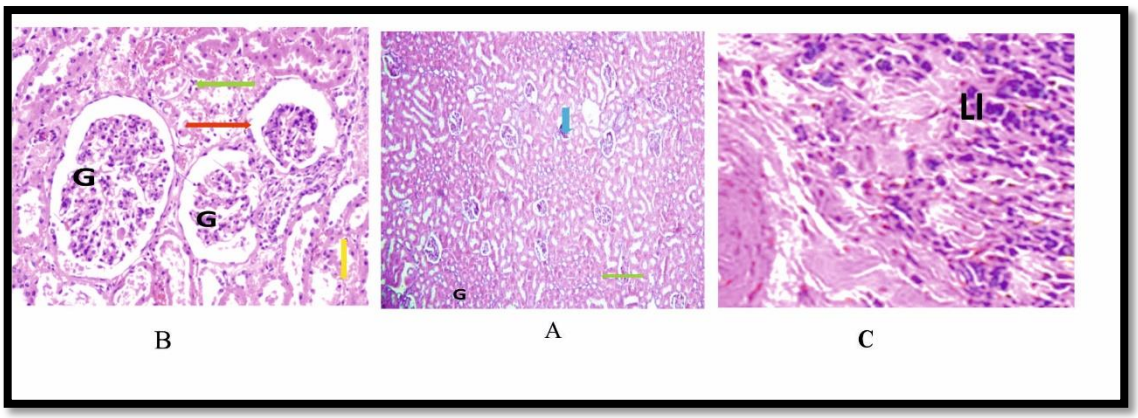


Figure (7): shows sections of the renal cortex in the ibuprofen-treated group, where A and B reveal hemorrhage in the renal tissue, particularly in the blood vessels near the Malpighian corpuscles (green arrow), dilatation of Bowman's capsule (red arrow), dilation and dissolution of the renal tubules (yellow arrow), infiltration of inflammatory cells (LI), and clear atrophy and shrinkage of the renal glomeruli (G) (blue arrow), as well as infiltration of white blood cells (LI). (100X; A & 400X; B & 400X; C).

3.2.4 Histological changes in the kidneys of male rabbits in the ibuprofen and fenugreek seed aqueous extract groups:

Microscopic examination of the cortical layer of the kidneys of rabbits administered ibuprofen with the aqueous extract of fenugreek seeds indicated a clear improvement throughout the renal tissue, with the presence of regular Melbigi bodies and intact renal tubules, along with minimal leukocyte infiltration in some areas (Figure 8).

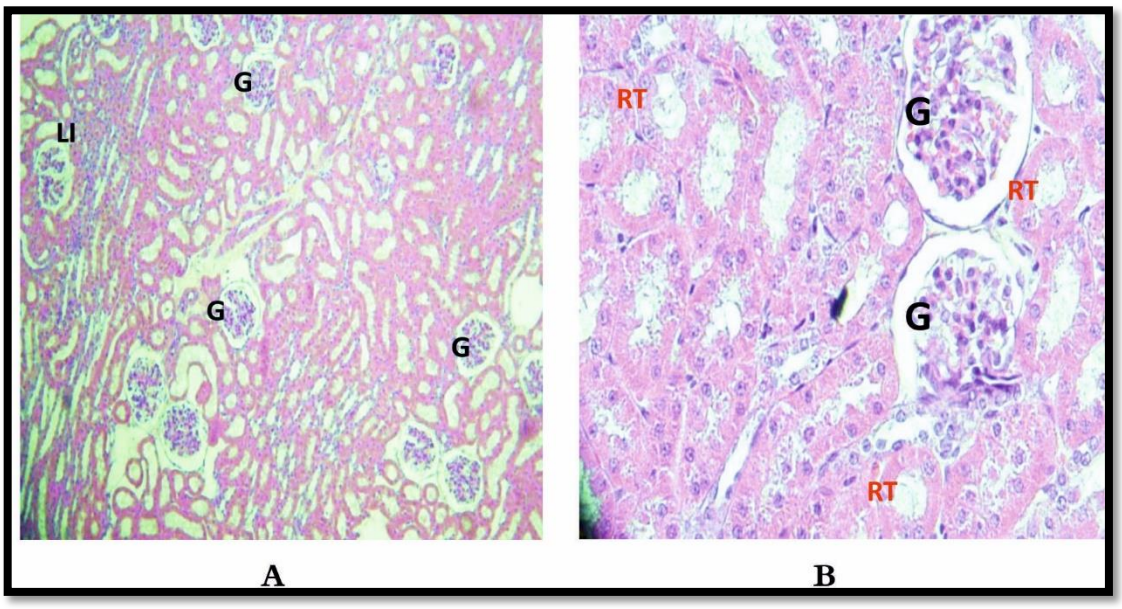


Figure (8): Tissue section of the renal cortex of male rabbits that received ibuprofen and fenugreek seed aqueous extract together, where the sections show improvement and regularity of the glomeruli as well as regularity of the renal tubules (RT) with the presence of some white blood cell infiltration (LI), (100X: A. 400X: B, H&E).

3.3 Biochemical parameters of selected liver and kidney functions:

Table (1): Biochemical parameters of selected liver and kidney functions.

The variables:	**Groups**			
	Control	Fenugreek seeds	Ibuprofen	Ibuprofen + Fenugreek seeds
(ALT, U/L)	3.07±29.50	4.07±35.50	*6.69±54.00	#2.99±35.00
(AST, UL)	3.03±33.00	3.11±30.00	*4.84±43.00	#2.76±34.00
(ALP, UL)	7.59±86.50	8.14±97.50	*9.92±125.00	#7.15±102.00
Urea (mg/dl)	3.11±37.33	3.29±43.83	*5.61±61.8	#4.40±39.45
Creatinine (mg/dl)	0.06±0.68	0.05±0.70	*0.18±1.30	#0.08± 0.80
Uric acid (mg/dl)	0.42±3.88	0.52±3.98	*0.93±4.96	#0.36±2.96

*Statistically significant change (P<0.05) compared to the control group; # Statistically significant change (P<0.05) compared to the ibuprofen group.

3.3.1 Serum ALT activity :

The results in Table 1 show that treatment of rabbits with 40 mg/kg ibuprofen resulted in a statistically significant increase (P<0.05) in serum ALT activity (54.00±6.69) compared to the control group (29.50±3.07). Meanwhile, the group treated with 100 mg/kg of the aqueous extract and ibuprofen (35.00 ± 2.99) showed a significant decrease (P < 0.05) in ALT enzyme activity when compared to the ibuprofen group, while there was no significant difference (P<0.05) in enzyme activity between the fenugreek seed group (35.50±4.07) and the control group (29.50±3.07).

3.3.2 Serum AST Activity :

The results showed a significant increase (P<0.05) in AST enzyme activity in the ibuprofen group (43.00±4.84) compared to the control group (33.00±3.03). The group receiving the 100 mg/kg aqueous extract and ibuprofen showed a significant decrease (P<0.05) in enzyme activity (34.00±2.76) when compared to ibuprofen alone, The study did not show any significant differences (P<0.05) in AST enzyme activity in the fenugreek seed group alone (30.00±3.11) when compared to the control group (33.00±3.03).

3.3.3 Serum ALP activity :

The results showed a significant increase (P<0.05) in ALP activity in the ibuprofen group (125.00±9.92) compared to the control group (86.50±7.59), while the results showed a significant decrease (P<0.05) in enzyme activity in the ibuprofen + aqueous extract group (102.5±7.15), and the results indicated a significant increase (P<0.05) in enzyme activity in the aqueous extract group (97.50±8.14) compared to the control group. The results indicated a statistically significant increase (P<0.05) in enzyme activity in the aqueous extract group (97.50±8.14) compared to the control group (86.00±7.59).

3.3.4 Serum Urea Concentration :

The results showed a statistically significant increase (P<0.05) in serum urea concentration in the ibuprofen group (61.8±5.61) compared to the control group (37.33±3.11). Meanwhile, the results indicated that the aqueous extract group combined with ibuprofen (39.45 ± 4.40) showed a statistically significant decrease (P < 0.05) compared to the ibuprofen group (61.8 ± 5.61). The results also showed a significant increase in urea (P<0.05) in the aqueous extract group (43.83±3.29) compared to the control group (37.33±3.11).

3.3.5 Serum Creatinine Concentration :

The results indicate a significant increase (P<0.05) in serum creatinine concentration in the ibuprofen group (1.30±0.18) compared to the control group (0.68±0.06). The ibuprofen and aqueous extract group (0.80 ± 0.08) showed a

significant decrease (P < 0.05) compared to the ibuprofen group. The aqueous extract group (0.70 ± 0.05) showed no significant difference (P < 0.05) compared to the control group (0.68 ± 0.06).

3.3.6 Serum uric acid concentration :

The results showed a significant increase (P<0.05) in serum uric acid concentration in the ibuprofen group (4.96±0.93) compared to the control group (3.88±0.42). Meanwhile, the aqueous extract plus ibuprofen group (2.96 ± 0.36) showed a significant decrease (P < 0.05) compared to the ibuprofen group. No significant difference (P<0.05) was observed in the aqueous extract group (3.90±0.52) compared to the control group (3.88±0.42).

4 Discussion :

This study was conducted to investigate the major histological and functional changes resulting from excessive ibuprofen administration and the protective effect of fenugreek seed aqueous extract on the liver and kidneys of adult male rabbits. The study results indicated clear histological changes in the group administered 40 mg/kg ibuprofen compared to the control group, These changes included disorganized and irregular liver cells, along with dilation and clotted blood in the central veins of the liver tissue. The cytoplasm of the liver cells also contained vacuoles of various sizes, and there was narrowing of the sinusoids with the presence of some red blood cells in some of them, in addition to the infiltration of inflammatory cells in some areas of the liver tissue, particularly in regions near the central vein and in the portal area, as well as congestion and clotted blood in the portal vein, thickening of its wall, and thickening of the hepatic artery. as well as histological examination of the liver in this study, which revealed the presence of binucleated hepatocytes. These changes were in contrast to the control group, which showed no changes in liver tissue. This study was consistent with that of (Aziz et al., 2018), in which male white Wistar rats were administered 40 mg/kg ibuprofen, leading to congestion in the portal veins, leukocyte infiltration in some tissue areas, and congestion of blood vessels near the portal tract. Another study in which gerbils were administered 40 mg/kg of ibuprofen for 5 days also demonstrated changes in liver tissue, including leukocyte infiltration and an increase in hepatocyte size; furthermore, the hepatocytes were arranged irregularly with the presence of binucleated hepatocytes, and these changes were observed in this Another study in which rats were administered 40 mg/kg of ibuprofen for 5 days also demonstrated changes in liver tissue, including leukocyte infiltration and an increase in hepatocyte size; the hepatocytes were arranged irregularly, with the presence of binucleated hepatocytes. These changes were observed in this study (Bhatti et al., 2024). These pathological histological changes are attributed to oxidative stress resulting from the activation of metabolic pathways generated in response to toxic compounds, which cause liver tissue damage (Donati et al., 2016). The presence of infiltrating inflammatory cells can be explained by degenerative changes in liver tissue that led to the release of chemotactic factors, thereby causing the infiltration of these cells—such as neutrophils and monocytes—to defend the body (Jaeschke et al., 1999). Inflammation is part of a complex biological response through which the body

eliminates pathogens and other factors to initiate the healing process (Ferrero-Miliani et al., 2007).

The current study also revealed that in the ibuprofen group (40 mg/kg), there was a decrease in the renal cortex and an increase in the Bowman's capsule, with haemorrhaging in the nearby vessels and infiltration of white blood cells between the renal tubules, as well as the presence of deposits in the cytoplasm of the cells that line the renal tubules. These changes were not observed in the control group, which exhibited normal characteristics. This study is consistent with the study by Akinola et al. (2003), which examined the effect of ibuprofen on renal development. The study found that ibuprofen (22 mg/kg) for 15 days caused shrinkage of the glomeruli and expansion of the Bowman's capsule in the treated group, unlike the control group which showed no tissue changes.

This study also showed an improvement in liver function and tissue in the water extract group and the ibuprofen group compared to the ibuprofen group alone, with significant reductions in liver enzyme activity and liver fibrosis. The liver cells also appeared more organised with large central nuclei and slight infiltration of white blood cells. These results are consistent with several studies, including Rezq (2016) and Algridi & Azab (2021), which used the alcoholic extract of fenugreek seeds to combat toxicity. The study of aluminium chloride in male rats indicated an improvement in liver tissue by reducing liver fibrosis and restoring the shape and size of liver cells. In another study, the effectiveness of the active compounds found in fenugreek seeds was tested using methanol against carbon tetrachloride (CCl4) poisoning. The study showed an improvement in liver tissue with mild fibrosis when compared with the carbon tetrachloride group, which is consistent with the results of this study (Das, 2014). Similarly, in this study, the aqueous extract of fenugreek seeds played a significant role in maintaining the biological structure of the kidneys, as evidenced by histological sections in the group that received the aqueous extract with ibuprofen showing improvement in the renal tubules with the presence of some inflammatory cells, until the Kupffer cells became regular and restored their natural shape with the presence of red blood cells between the tubules. This study concurred with the study by Mbarki et al. (2017). A study was conducted to evaluate the role of fenugreek seed extract in inhibiting renal fibrosis in diabetic rats. The study revealed that, upon histological examination of the sections, an improvement in the renal tubules was observed through a reduction in AGEs formation in the renal tubule (Shivam & Gupta, 2026).

This study demonstrated changes in liver and kidney function followed by clear histological changes in the ibuprofen group compared to the control group; these changes include elevated activity of the liver enzymes AST, ALT, and ALP, and these results are consistent with a number of studies (Garba et al., 2012; Gola et al., 2016; Dodiya et al., 2011). A study conducted on Wistar rats administered 40 mg/kg of ibuprofen for 30 days also showed a statistically significant increase ($P < 0.05$) in the levels of the liver enzymes AST, ALT, and ALP, which is fully consistent with the results of the current study (Abbass and Abed, 2017). A study by Panchal et al. (2022), in which male Wistar rats were treated with 400 mg/kg ibuprofen for 5 days,

showed a statistically significant increase ($P < 0.05$) in the activity of the liver enzymes AST, ALT, and ALP compared to the control group, and these results were consistent with the current study .

The results of the current study showed a significant increase in the concentrations of urea, creatinine, and uric acid in the ibuprofen group compared to the control group; these results were consistent with the study conducted by (Aprioku et al. 2014). As this study showed, there was a significant decrease in the biochemical indicators of urea, creatinine, and uric acid levels, which affects kidney function. This study agrees with the study by Mbarki et al. (2017).

5 Conclusions :

Based on the results of this study, changes were observed in the liver and kidney, which were characterized by liver fibrosis, central vein congestion with clotted blood, and infiltration of white blood cells in some tissue areas. Additionally, there was renal papillary atrophy with dilation of the Bowman's capsule and the presence of deposits in the cytoplasm of the cells that line the renal tubules. Furthermore, elevated levels of liver enzymes, urea, creatinine, and uric acid were observed in the ibuprofen-treated group compared to the control group. In this study, it was found that the function of liver and kidney tissues improved in the group that was given the water extract of fenugreek seeds with ibuprofen, as the liver and kidney tissues regained their biological structure and function compared to the ibuprofen only group. This is because the fenugreek seed extract plays a significant role in preventing oxidative stress and inhibiting free radicals due to its antioxidant properties.

6 Recommendations :

-Do not exceed the recommended dosage of ibuprofen as indicated in the drug information leaflets, and do not take these medications without consulting the treating physician or a pharmacist.

-Leave a time gap between recommended doses to avoid the accumulation of toxins, and use it for the shortest possible time.

-Take foods rich in natural antioxidants, including fenugreek seed extract, which is effective in preventing many types of cancer.

-Increase awareness and health education about the importance of herbal medicine to reduce the side effects of chemical drug treatments.

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