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Histopathological Study of The Protective Effect of Sesame Oil on Arsenic Induced Hepatorenal Toxicity in Female Rats

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Abstract

This study aims to evaluate the potential of sesame oil to protect female rats from arsenic-induced hepatorenal toxicity. This toxicity arises from the inability of the body to metabolize heavy metals like arsenic, leading to their accumulation in soft tissues. Previous studies suggest that sesame oil, a known antioxidant, may protect against arsenic-induced toxicity in the liver and kidneys. The study included six groups: a control (distilled water) an arsenic model (40 ppm sodium arsenate in drinking water for 6 weeks). Two sesame oil control groups (5 or 2.5 mL/kg by gavage for 6 weeks), and two therapeutic groups that received arsenic for 6 weeks followed by either the high or low doses of sesame oil for another six weeks. The histopathological assessment revealed significant liver and kidney injury in the arsenic-treated group, characterized by renal interstitial fibrosis and tubular necrosis, alongside hepatic necrosis and destruction of the normal cord-like structure of liver cells. In contrast, groups that received sesame oil (5 mL/kg B.W.) as a post-exposure treatment showed a profound reduction in tissue damage. Their liver and kidney morphology were largely restored to a state resembling the healthy controls. The significant results strongly suggest that sesame oil possesses therapeutic properties that protect against the histopathological effects of arsenic toxicity.

Keywords: Sesame oil, Arsenic, and Histopathological.

1. Introduction

Sesame (Sesamum indicum) is nutritionally and medicinally significant due to its high concentration of bioactive lignans and phytoestrogens, including sesamin, sesamolin, sesaminol, and sesamol [1, 2]. These compounds are responsible for potent antioxidants and anti-inflammatory activities, which lead to therapeutic effects such as anti-atherosclerotic and anti- hypertensive actions [3, 4].

A primary mode of action involves scavenging free radicals, thereby inhibiting

the generation of reactive oxygen species (ROS) and reducing lipid peroxidation [5, 6]. In particular, the constituent sesamol demonstrates a wide range of pharmacological properties, such as antimutagenic, chemopreventive, and anti-hepatotoxic effects [7].

Arsenic is a metalloid, the 33rd element in the periodic table, which exhibits properties of both metals and non-metals. Toxicologically, it is classified as a heavy metal [8]. It originates from both natural and anthropogenic sources, contaminating soil, water, and air [9]. The main pathway for human exposure is the consumption of contaminated water, a global health issue affecting over 140 million people due to the natural leaching of inorganic arsenic from the earth's crust [10].

Upon exposure, arsenic induces toxicity primarily by triggering the generation of intracellular reactive oxygen species (ROS). This oxidative stress can directly damage cellular molecules or alter cell signalling pathways and epigenetic modifications, leading to widespread cellular dysfunction [11]. While the toxic mechanisms of arsenic and the protective, antioxidant properties of sesame oil have been individually documented, studies investigating the specific protective role of sesame oil against arsenic-induced tissue damage are limited.

Therefore, this study hypothesizes that sesame oil confers protection against the histopathological suspends induced by arsenic exposure in drinking water.

2. Material and methods

2.1 Preparation and Extraction of sesame oil

A sample of sesame oil was obtained from sesame seeds; the oil sample and its details were specified in the Ministry of Science and Technology. The extract of sesame oil was ready via Uitterhaegen E. method [12].

2.2 Preparation of the dose for sodium arsenate and sesame oil

The sodium arsenate solution was freshly prepared by dissolving sodium arsenate ($Na_2HAsO_4 \cdot 7H_2O$) in distilled water to achieve a concentration of 40 ppm. The solution was provided to the experimental animals through their drinking water for six consecutive weeks, as described by Woods and co-workers [13]. Sesame oil was administered orally using a gastric tube at two dose levels 2.5 mL/kg, and 5 mL/kg body weight (B.W.) respectively. According to the modified protocol, and doses were adjusted weekly according to the body weight of the animals [14].

2.3 Experimental Design

The experiment included six groups, each consisting of ten adult female albino rats. Rats were 8 to10 weeks old and weighed from 180 to 200 grams at the beginning of the study. All animals were housed under standard laboratory conditions temperature 22 ± 2 °C, for 12 hours, light/dark cycle with free access to food and water. The experiment included six groups each group involved 10 female rats as following.

2.3.1 Group 1 (Control).

Rats were administered distilled water.

2.3.2 Group 2

Rats were administered sodium arsenate (40 ppm) in drinking water for six weeks.

2.3.3 Group 3

Rats were treated with sesame oil (5 mL/kg B.W), orally daily by gavage for six weeks.

2.3.4 Group 4

Rats were treated with sesame oil (2.5 mL/kg B.W), orally daily by gavage for six weeks.

2.3.4 Group 5

Rats were administered arsenic (40 ppm sodium arsenate) in drinking water for six weeks. Then treatment by given sesame oil (5 mL/kg B.W), orally daily by gavage for six weeks.

2.3.5 Group 6

Rats were administered arsenic (40 ppm sodium arsenate) in drinking water for six weeks. After that treatment by administered sesame oil (2.5 mL/kg B.W), orally daily by gavage for six weeks.

2.4 Histological Examination

Liver and kidney specimens were fixed in 10 % neutral buffered formalin for 24 hours. Routinely processed into paraffin blocks and sectioned at 5 µm [15]. Tissue sections were then stained with Haematoxylin and Eosin (H&E) for histopathological examination under a light microscope [16].

3. Results

In the control group, the histopathological figures of the liver, kidney were illustrated in figures 1 to 4 those showed normal appearances and normal cytoarchitecture.

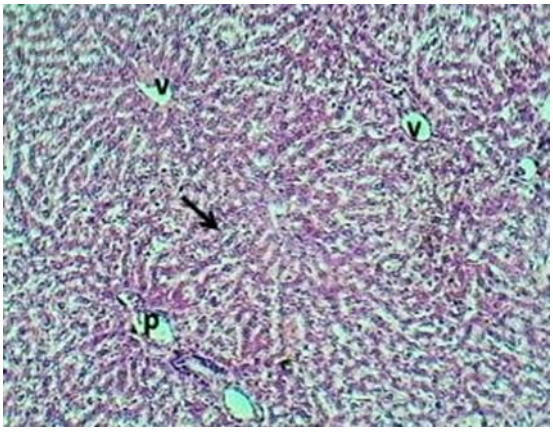

Figure 1: Liver with normal central vein (V), normal portal triad (P), and normally arrangement of cords (arrow). H&E. 100x.

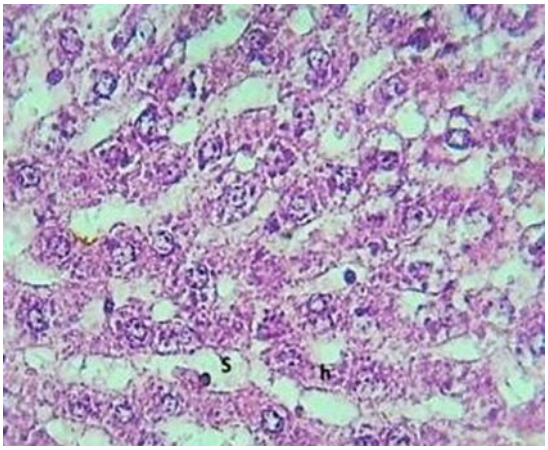

Figure 2: Liver with normally hepatocytes (h) & normal sinusoid (S). H&E. 400x.

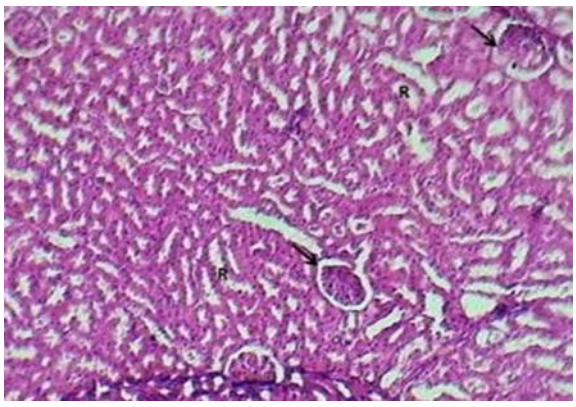

Figure 3: Renal cortex with normal lining cells of renal tubules (R), and normal glomeruli (arrows). H&E. 100x.

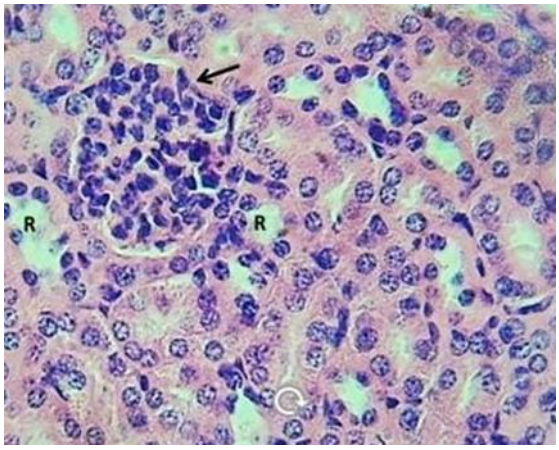

Figure 4: Renal cortex with normal lining cells of renal tubules (R), and normal glomerular cytoarchitecture (arrows). H&E. 400x.

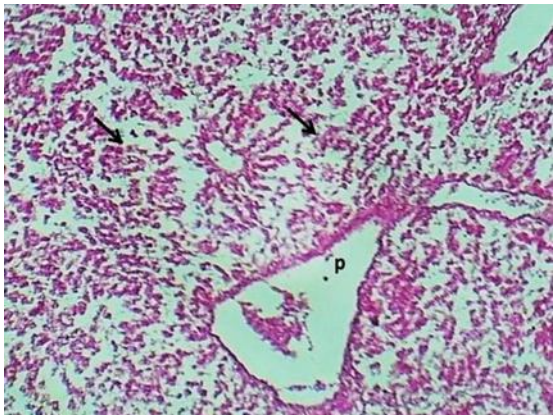

Figure 5: Liver with severe dilation with marked damage of vascular tunics (P), severe necrosis with destruction of hepatic cords and depletion of sinusoids (Arrows). H&E.100x.

Results of group 2 (40 ppm sodium arsenate), the histopathological figures of the liver portal triad showed severe dilation with marked damage of venous tunica, the hepatic lobule revealed marked loss of frame of hepatic lobules associated with severe damage of hepatic cords, severe

necrosis with atrophy and depletion of hepatocytes figure 5 and figure 6.

The histopathological figures of the renal cortex and medulla showed marked interstitial fibrosis with severe necrosis of the lining cells of renal tubules and atrophy and other.

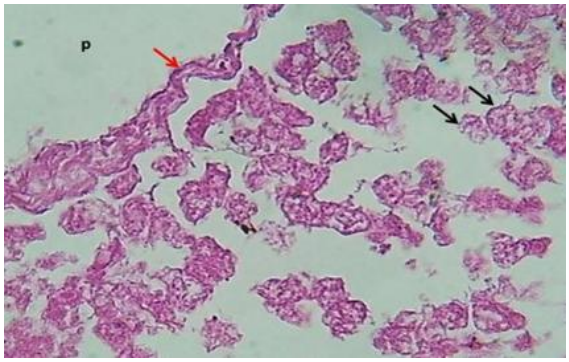

Figure 6: Liver with severe damage of portal vein tunics (P with red arrow), severe necrosis with destruction of hepatic cords and depletion of sinusoids (Black arrows). H&E. 400x.

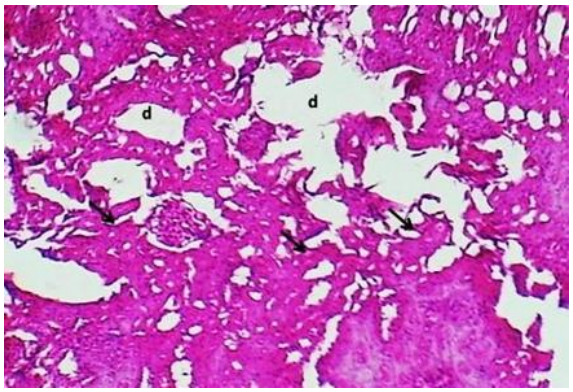

Figure 7: Renal cortex marked tissue depletion (d) with severe interstitial fibrosis (Arrows). H&E. 100x.

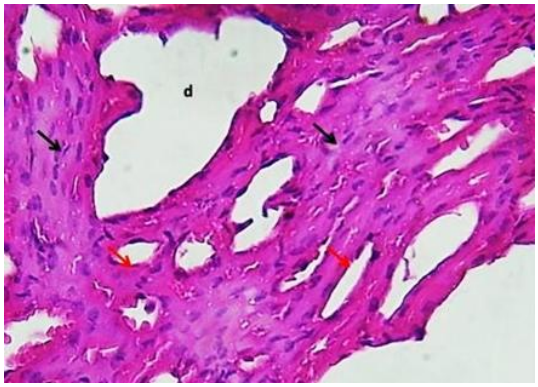

Figure 8: Renal cortex marked interstitial fibrosis (black arrows) with severe necrosis of lining cells of renal tubules with atrophy (Red arrows) and tubular dilation (d). H&E. 400x.

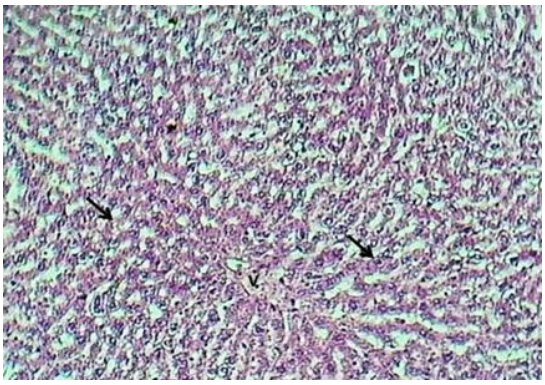

Figure 9: Liver with normal central vein (V) and normally arrangement of cords (arrow). H&E. 100x.

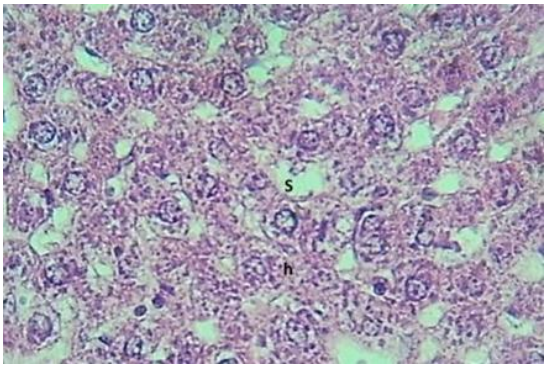

Figure 10: Liver with normal sinusoids (S) and normal hepatocytes (h). H&E. 400x.

Results of group 3 and group 4 (Sesame oil 2.5 mL/kg, 5 mL/kg) were showed histopathological figures of the liver portal triad and hepatic lobules were similar those of control group figure 9 and figure 10. Histopathological figures of the renal cortex showed normal lining cells of almost renal tubules, with little figures of granular and vascular degenerations of few tubules. The glomeruli revealed normal cytoarchitecture figure 11 and figure 12.

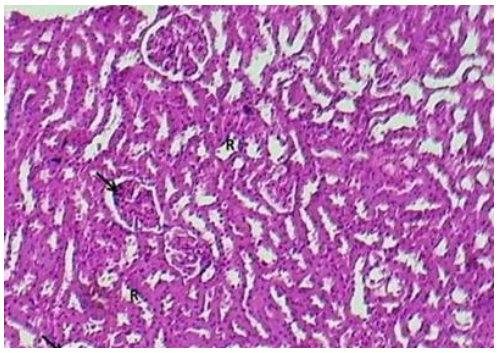

Figure 11: Renal cortex normal lining cells of renal tubules (R), and normal glomeruli (arrows). H&E. 100x.

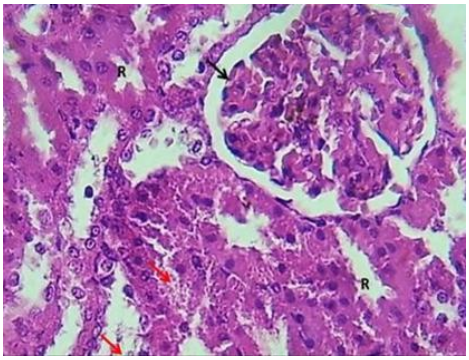

Figure 12: Renal cortex normal lining cells of almost renal tubules (R), with little granular and vascular degeneration (Red arrows) and normal glomerulus (black arrows). H&E. 400x.

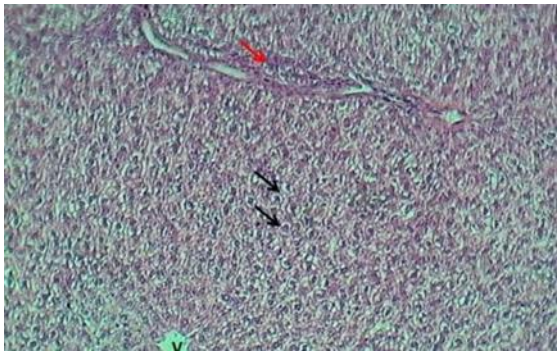

Figure 13: Zonal mild cellular swelling of hepatic cords (Black arrow), portal fibrosis (Red arrow) and normal sinusoid central vein (v). H&E. 100x.

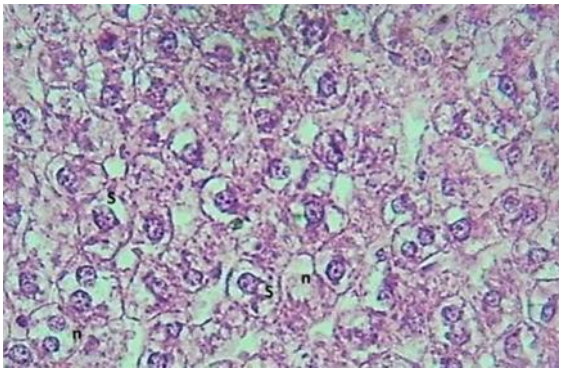

Figure 14: shows mild cellular swelling of hepatic cords (S), with necrosis (n). H&E. 400x.

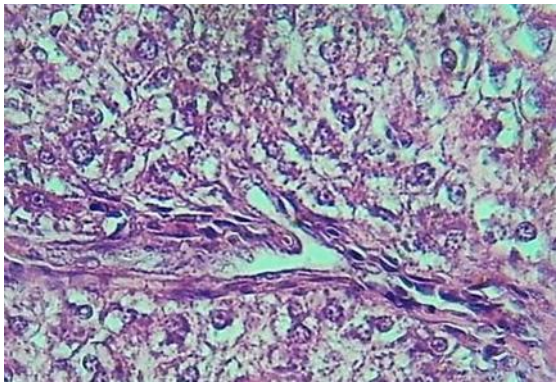

Figure 15: Mild portal fibrosis. H&E. 400x.

Results of group 5 (Arsenic + Sesame oil 2.5mL/ kg), the histopathological figures of the liver lobules showed zonal mild cellular swelling of hepatic cords, normal sinusoids and normal central vein. The portal area revealed mild portal fibrosis with formation of portal fibrous bridges figures 13, 14 and 15. The histopathological figures of the kidneys were similar those of control group figure16.

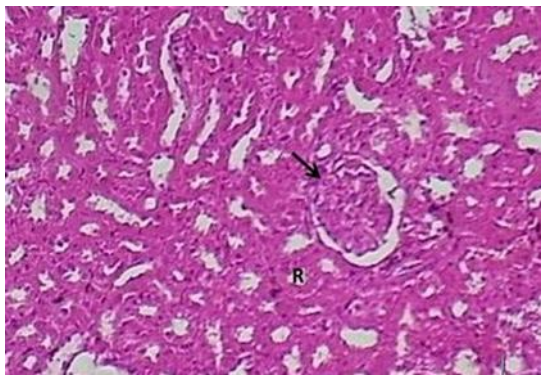

Figure 16: Cortex shows normal glomeruli (Arrow) and normal lining cells of renal tubules. H&E. 200x.

Results of group 5 (Arsenic + Sesame oil 5mL/ kg), histopathological figures of the liver and kidneys were similar those of control group figure 17 to figure 20.

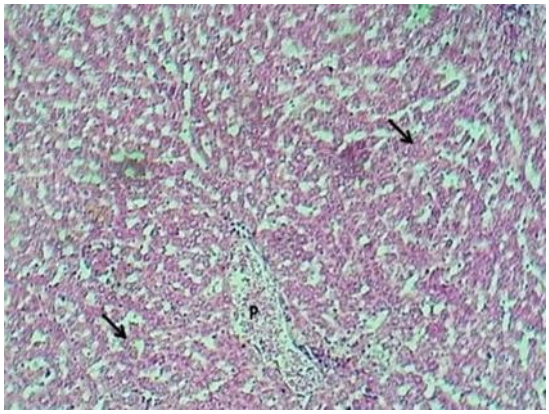

Figure 17: Normal arrangement of hepatic cords (black arrow), normal sinusoid and portal vein (p). H&E.100.

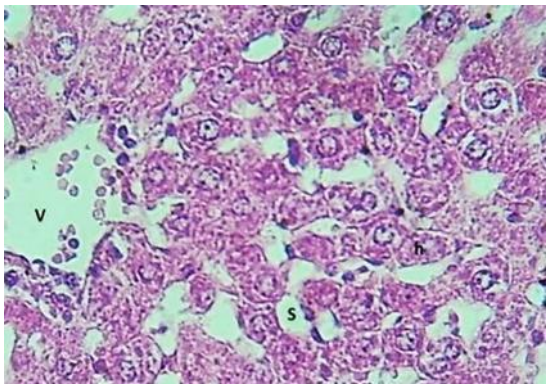

Figure 18: Normal hepatocytes (h), normal sinusoid (S) and central vein (V). H&E. 400x.

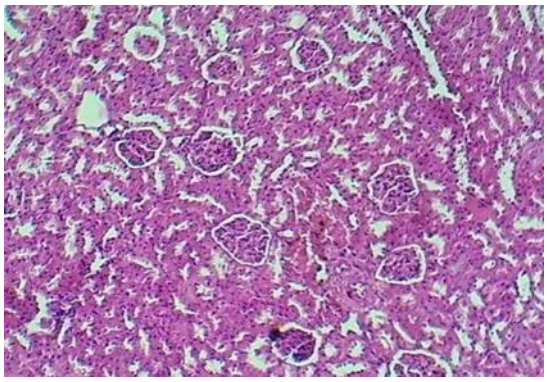

Figure 19: Normal glomeruli, and normal lining cells of renal tubules. H&E. 100x.

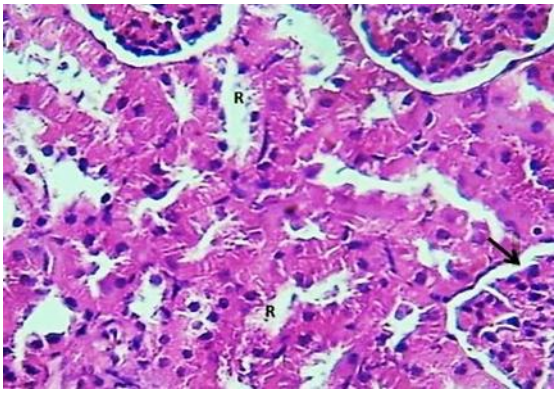

Figure 20: Normal glomeruli (Arrow)m and normal lining cells of renal tubules (R). H&E, 400x.

4. Discussion

Histopathological alterations observed in the present study are consistent with findings from previous in vivo investigations on arsenic toxicity. Shangloo et al. [17], demonstrated that sodium arsenite administered in drinking water induced dose-dependent damage in the liver and kidneys of albino rats.

The liver of exposed animals exhibited a progression of lesions, from mild central venous dilatation and portal hemorrhage at a lower dose (50 mg/kg) to severe architectural distortion, necrosis, cytoplasmic vacuolation, and mononuclear infiltrates at a higher dose (100 mg/kg).

Similarly, renal tissues showed disrupted architecture, eosinophilic casts, and mononuclear infiltration, contrasting with the normal histology seen in controls. Research has shown that arsenic exposure induces significant degenerative changes in the liver and kidneys. Studies in mice exposed to lower concentrations (30-300 ppb) have reported hepatic necrosis and cytoplasmic blebbing, with the kidneys showing severe necrosis and tubular degeneration at higher doses [18]. These histopathological alterations, which include hepatic sinusoidal expansion, hepatocellular necrosis, and renal tubular necrosis with glomerular contraction, confirm the susceptibility of these organs to arsenic toxicity.

The damage mechanism is fundamentally rooted in oxidative stress, where arsenic accumulation in tissues leads to free radical generation and a disruption of the cellular antioxidant balance [19]. This process is further supported by evidence of arsenic-induced alterations in antioxidant gene expression and oxidative DNA damage [20]. With chronic exposure potentially causing epigenetic modifications like DNA methylation.

These collective mechanistic insights strongly substantiate the causal relationship between arsenic exposure and the observed hepatorenal pathology. The current investigation validates that sesame oil offers considerable protection against liver and kidney damage induced by arsenic. This aligns with the findings of Al- Jbouri and Al-Zahra [21]. That confirmed the non-

toxic nature of sesame oil by observing nearly normal histological structures in the livers and kidneys of female rats given a 0.5 mL dose. According to their research, these protective effects stem from sesame oil's dense nutritional profile; the seed is roughly 50 % oil, which is rich in essential amino acids, unsaturated fats, and powerful antioxidants.

These components work to alleviate oxidative stress, which in turn reduces tissue damage and may offer a defence against chronic illnesses [22]. The hepatoprotective and Reno protective effects of sesame oil observed in this study are consistent with previous research on its efficacy against heavy metal toxicity.

Azab [23] demonstrated that sesame oil (5 mL/kg) mitigated lead-induced hepatotoxicity in albino mice. While lead acetate exposure alone caused severe hepatic damage-including hepatocyte enlargement, pyknotic nuclei, necrosis, and inflammatory infiltration-concurrent administration with sesame oil largely normalized liver architecture. Similarly documented the protective role of sesame oil in lead-exposed kidney tissue, noting a significant reduction in histological damage, inflammatory infiltration, and tubular dysfunction [24, 25].

The protective mechanism identified across these studies is attributed to sesame oil's capacity to ameliorate oxidative stress and suppress pro-inflammatory pathways. Sesame oil has been shown to possess free radical scavenging properties and to protect against oxidative stress-induced toxic injuries.

Many researchers have investigated its role in attenuating hepatic damage. Consequently, its potential to mitigate hepatic injury has been the focus of numerous studies. Chiang et al. established that sesamin effectively ameliorated lead and lipopolysaccharide induced acute liver injury in rats by inhibiting proinflammatory cytokines and nitric oxide production [24].

This protective effect occurs through the suppression of multiple signalling pathways, including c-Jun N-terminal kinase, p38 MAPK, cyclooxygenase-2, inducible nitric oxide synthase, and GADD45b [23]. There is increasing evidence that inflammation and oxidative stress act together in causing kidney injury. Recent findings highlight the role of Nrf2 signalling in modulating the inflammatory response and protecting the kidneys from oxidative damage.

Plant-derived Nrf2 activators like curcumin have been shown in human studies to be both safe and health-promoting. These activators exert antioxidant and anti- inflammatory effects,

making them potentially effective in treating or delaying renal disease [26].

After CCl_4 administration, Nrf2 levels significantly decreased; however, co-administration of sesame oil restored Nrf2 levels [27]. A limitation of the study is the complex composition of sesame oil, which contains multiple bioactive substances. This complexity makes it difficult to determine which specific components are responsible for its observed protective effects.

5. Conclusion

This study confirms that sesame oil provides significant hepatic and renal protection against arsenic-induced toxicity in female rats. Histopathological findings revealed that sesame oil, especially at 5 mL/kg body weight, markedly reduced tissue damage and restored the normal architecture of the liver and kidneys.

These effects are attributed to its antioxidant and anti-inflammatory compounds, particularly sesamol and sesamin, which act by scavenging reactive oxygen species (ROS) and activating cellular defence pathways. Therefore, sesame oil represents a safe and promising natural agent for reducing hepatorenal toxicity caused by heavy metal exposure.

6. References

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