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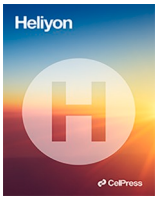

Research article

Investigation of the protective effect of *Lavandula stoechas* against the damage caused by Bisphenol A in the liver tissue of rats

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ABSTRACT

The present study aims to explore the hepatoprotective potential of Lavandula stoechas (LS) against Bisphenol A (BPA)-induced liver toxicity. In this experiment, 32 male rats were utilized and categorized into control, LS, BPA, and BPA + LS groups for the study. Each group received 50 mg/kg of the respective substance. Throughout the 28-day experiment, the control group did not receive any applications. The LS oil was administered intraperitoneally, while BPA was given through oral gavage. At the end of the experiment, rats were anesthetized, and blood was taken from the heart. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TB) values were measured from serum samples. Malondialdehyde (MDA), superoxide dismutase (SOD), total antioxidant status (TAS), total oxidant status (TOS), and oxidative stress index (OSI) measurements were performed in liver tissue. The histological structure was observed using hematoxylin and eosin staining methods. The BPA group showed higher AST levels compared to the control group, but the BPA + LS group exhibited a significant decrease in AST levels compared to the BPA group. Additionally, TB levels were lower in the BPA + LS group compared to the BPA group. MDA levels increased in BPA-treated groups compared to others. The LS-treated groups showed higher SOD levels compared to the control group. Furthermore, an evident increase was noted in the BPA + LS group in comparison to the BPA group. The BPA group exhibited a significant rise in OSI value compared to the control. It was concluded that LS has a protective impact against BPA-induced liver toxicity. The LS-treated groups showed higher SOD levels compared to the control group. Furthermore, a significant increase was noted in the BPA + LS group in comparison to the BPA group. The BPA group exhibited a significant rise in OSI value compared to the control. It was concluded that LS has a protective impact against BPA-induced liver toxicity.

1. Introduction

BPA is a commonly used substance that has negative impacts on living organisms. Its molecular formula is 2,2-bis (4-hydroxyphenyl) propane, and it is a synthetic compound formed by combining two phenol and polycarbonate molecules [1]. BPA is

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commonly used in products such as plastic water bottles, baby bottles, protective coatings in food products, beverage cans, and thermal paper [2]. Substances that cause serious toxic effects, such as BPA and its derivatives, cause concern for scientists, clinicians, and patients [2]. The widespread exposure of humans and animals to BPA in the environment primarily happens through ingestion, inhalation, and skin contact. Nevertheless, the primary route of exposure for living organisms is through dietary intake [3]. Exposure to BPA has been linked to heart disease, irregularities in the development of the brain, weight gain, hypertension, impairment of the thyroid, diabetes, breast cancer, and infertility [4]. BPA interferes with the endocrine system by engaging with estrogen, androgen, and thyroid hormone receptors. Therefore, living organisms experience adverse impacts on their reproductive, nervous, immune, metabolic, and growth systems [5].

Reactive oxygen species (ROS) is a term used for oxygen derivatives that occur as a natural feature of aerobic life. Oxidative stress occurs due to an imbalance between the cellular levels of ROS and the antioxidant defense system. Oxidative stress causes molecular damage [6]. MDA is a stable byproduct of lipid peroxidation induced by ROS and serves as a biological indicator of oxidative stress. Antioxidants are the body's defense systems that clear ROS or prevent ROS production [7]. One of the basic enzymes of the antioxidant defense system is superoxide dismutase (SOD) [8]. The total antioxidant status (TAS) measures the effects of antioxidants in plasma and body fluid, while the total oxidant status (TOS) measures the impact of oxidants [9]. ALT and AST are biomarkers extensively utilized to assess liver damage [10]. Total bilirubin (TB) level is a diagnostic marker in liver-related problems [11].

Liver cells contain high amounts of mitochondria. Liver disorders are related to chronic hepatitis C, steatosis, and oxidative damage of mitochondria. BPA affects the liver by causing oxidative stress. Studies indicate that oxidative stress has the potential to modify the extent of hepatocyte damage and cell death through alterations in signal transduction pathways. BPA exposure at a dose of 250 mg/kg has been reported to cause a significant increase in ALT, AST, Alkaline Phosphatase, lactate dehydrogenase, and MDA levels. In addition, ALT and AST values increased significantly in rats given 25 mg/kg BPA compared to the control group. No significant difference was found at the dose of 10 mg/kg [12]. The histological effects of BPA on the liver were found to be enlarged congested central vein, vacuolar degeneration in hepatocytes, occlusion in hepatic sinusoids, decrease in glycogen count in hepatocytes, increase in the amount of collagen around the vessel in the portal region, irregular nuclei in hepatocytes, and damage to mitochondria [13].

Recently, there has been increased interest in the role and use of natural antioxidants in preventing oxidative stress. Natural antioxidants from fruits and vegetables are known to slow down the oxidative damage process. *Lavandula stoechas* (LS), one of the lavender species, is a well-known plant species due to the medicinal uses of its essential oil content. It is widely used in cosmetics, but it is also used in traditional dishes and herbal teas. The essential oil of LS contains more than 40 substances, such as linalyl acetate, cineole, nerol, borneol, butyric acid, propionic acid, valeric acid, germbulin, tannins, and flavonoids. It has been reported in the literature that LS extract has sedative, antidepressant, antiepileptic, analgesic, antibacterial, and antifungal properties and inhibits anticholinesterase [14]. Ethnobotanical and phytopharmacological studies show that LS treats rheumatic diseases and nephrotic syndromes, prevents spasms, and reduces inflammatory problems [15]. A study has reported that LS has protective effects on the liver and kidneys of mice against oxidative stress [16].

The aim of this study is to examine the histological and biochemical alterations in the liver tissue of male rats exposed to BPA and to assess the protective role of *Lavandula stoechas* against these changes.

2. Material and method

2.1. Experimental animals and experiment plan

Ethics committee approval (Protocol no: 2021/18-2) was obtained from the İnönü University Medical Faculty Experimental Animals Ethics Committee. The care of the animals and all applications were carried out at İnönü University Experimental Animals Research and Production Center as specified in the ethics committee protocol. In the study, 32 Wistar Albino male rats, 10–12 weeks old, weighing 200–250 g, were divided into four groups with 8 rats in each group. The animals were kept in rooms with a temperature of 21±1 °C and a 12-h light/dark cycle throughout the experiment. They were fed ad libitum with normal tap water and standard rat chow. We measured the weights of the live animals at the start and end of our 28-day study.

2.2. Experiment groups

The animals were weighed and divided into four groups with similar mean weights.

Control Group (n: 8): No treatment was administered.

LS Group (n: 8): The intraperitoneal administration of LS (Botalife) was given daily at 50 mg/kg [17].

BPA Group (n: 8): BPA (Sigma 239658) was given daily through oral gavage at a dose of 50 mg/kg/day [18].

BPA + LS Group (n: 8): BPA was administered to rats by oral gavage, and LS was administered intraperitoneally at 50 mg/kg/day.

Research has indicated that liver enzymes can vary depending on the menstrual cycle stages. To mitigate potential confounding variables associated with female hormonal status, male rats were used in our study [19]. We selected the BPA dose for our study based on literature indicating that a 50 mg/kg BPA dosage can lead to liver damage, including hepatic fibrosis, hepatic steatosis, liver tumors, and metabolic syndrome in a short period [18,20,21]. We chose to administer BPA orally because exposure to BPA mainly occurs through ingestion [3]. To avoid exposing the rats to the distinct smell and taste of lavender when it comes into contact with their mouths during administration, we selected *Lavandula stoechas* for the intraperitoneal route. This approach also helps to prevent potential stomach disturbances in the rats, as the oral route was already preferred for BPA. Finally, the intraperitoneal route is generally favored in the literature [22–24].

2.3. Experiment procedure

Rats were given gavage and intraperitoneal injections at a consistent time each day. The applications did not lead to any complications. An anesthetic agent was used to sacrifice the animals at the end of the experiment. Blood was taken by puncturing the heart. Additionally, blood samples underwent centrifugation at 4000 revolutions per minute for 10 min. The serum samples collected were placed into Eppendorf tubes and then stored at a temperature of −80 °C. The liver tissue was then excised, and one-half was preserved in formaldehyde for histological analysis. The other half was placed in a −80 °C freezer for biochemical analysis.

2.4. Biochemical analysis

Tissue and serum samples were allowed to dissolve for 24 h at +4 °C. Tissues were weighed before analysis and placed in screw vials. Tris-HCl pH 7.4 buffers were placed in the tubes by calculating ten times the weight of each tissue. Tissues were homogenized with the help of a ball homogenizer. Homogenized samples were transferred to Eppendorf tubes by vortexing.

ALT value in rat serum was determined by the commercially purchased ALT Elisa rat kit (ELK Biotechnology, Wuhan). Serum AST and total bilirubin values were calculated using the Elisa rat kit (SunRed Biotechnology, China) protocol. Values were measured with an immunoplate reader with Biotek HT Snynergy Gen 5 software.

MDA measurements were performed based on Esterbauer and Cheeseman's methods. In this method, one MDA molecule reacts with two thiobarbituric acid molecules. The test is performed at a pH value of 2–3 at 90–100° for a minimum of 10–15 min. As a result of the reaction, pink pigment is produced. A precipitate is formed from the tissue sample. Values are read at 532 nm after samples have been cooled. The results obtained are calculated in μmol/g unit [25].

SOD enzyme measurement was performed according to the method of Sun et al. [26]. Color change occurs when superoxide anions formed by xanthine/xanthine oxidase reduce nitro blue tetrazolium. The results are given in units per hemoglobin by reading in a spectrophotometer at 50 nm.

TAS and TOS measurements were performed in accordance with the commercially purchased Rel Assay (Rel Assay Diagnostics kit, Mega Medicine, Gaziantep Turkey) protocol and using an immunoplate reader with Biotek HT Snynergy Gen 5 software [27].

2.5. Histopathological analysis

For histopathological analysis, rat liver tissues were cut into small pieces of 34 mm. The pieces were placed in plastic tissue follow-up cassettes and immersed in 10 % formaldehyde for 24 h. Following fixation, the tissues underwent a 24-h wash in running tap water. Subsequently, they were dehydrated in a series of alcohol solutions, cleared in xylene, and finally embedded in paraffin. Paraffin blocks were cut into 5-μm sections using a Leica RM2145 microtome. The general histological structure was examined by applying hematoxylin and eosin staining to the sections. Liver damage was determined by the number of affected areas of inflammation with necrotic, apoptotic, and inflammatory cells in the parenchyma. In order to evaluate the inflamed areas, ten areas were examined at ×20 magnification from each section. The degree of damage was scored as 0 = no affected area, 1 = 1 affected area, 2 = 2 affected areas, and 3 = 3 affected areas. The preparations were inspected using a Leica DFC280 and a Leica Q (Leica Micros Imaging Solution Ltd, Cambridge, UK) image analysis system, and then they were photographed.

2.6. Statistical analysis

The results of the experiment were examined using the IBM SPSS Statistics 28.0 software for statistical analysis. Data are presented as min-max with a median. For all experimental analyses, the conformity of quantitative data to normal distribution for biochemical analyses was evaluated with the Shapiro-Wilk test. Since the experimental data did not show normal distribution according to the study groups ($p > 0.05$), the Kruskal Wallis H test was used to examine the significant difference between the groups. Bonferroni corrected Mann-Whitney U analysis was used for pairwise comparisons in cases with a significant difference between the groups [28]. A p value of <0.05 was considered statistically significant.

Table 1
Biochemical analysis findings in rat serum samples.

Variable	Groups			
	Control	LS	BPA	BPA + LS
ALT (U/L)	5.378 (1.632–9.824)	5.431 (1.426–27.605)	9.61 (5.248–19.275)	7.467 (4.172–14.676)
AST (U/L)	70.634[a] (51.436–89.687)	71.456[a] (36.592–94.341)	86.875[b] (75.321–99.474)	64.778 (43.733–84.956)
TB (nmol/ml)	30.084[b] (28.829–34.731)	29.146 (27.643–31.863)	29.491[b] (27.67–30.953)	28.111 (26.484–32.47)

[a] Significant difference compared to the BPA group for each variable, $p < 0.05$.
[b] Significant difference compared to the BPA + LS group for each variable, $p < 0.05$(Bonferroni corrected Mann-Whitney *U* test after significant Kruskal Wallis test); Data are expressed in median (Minimum–Maximum).

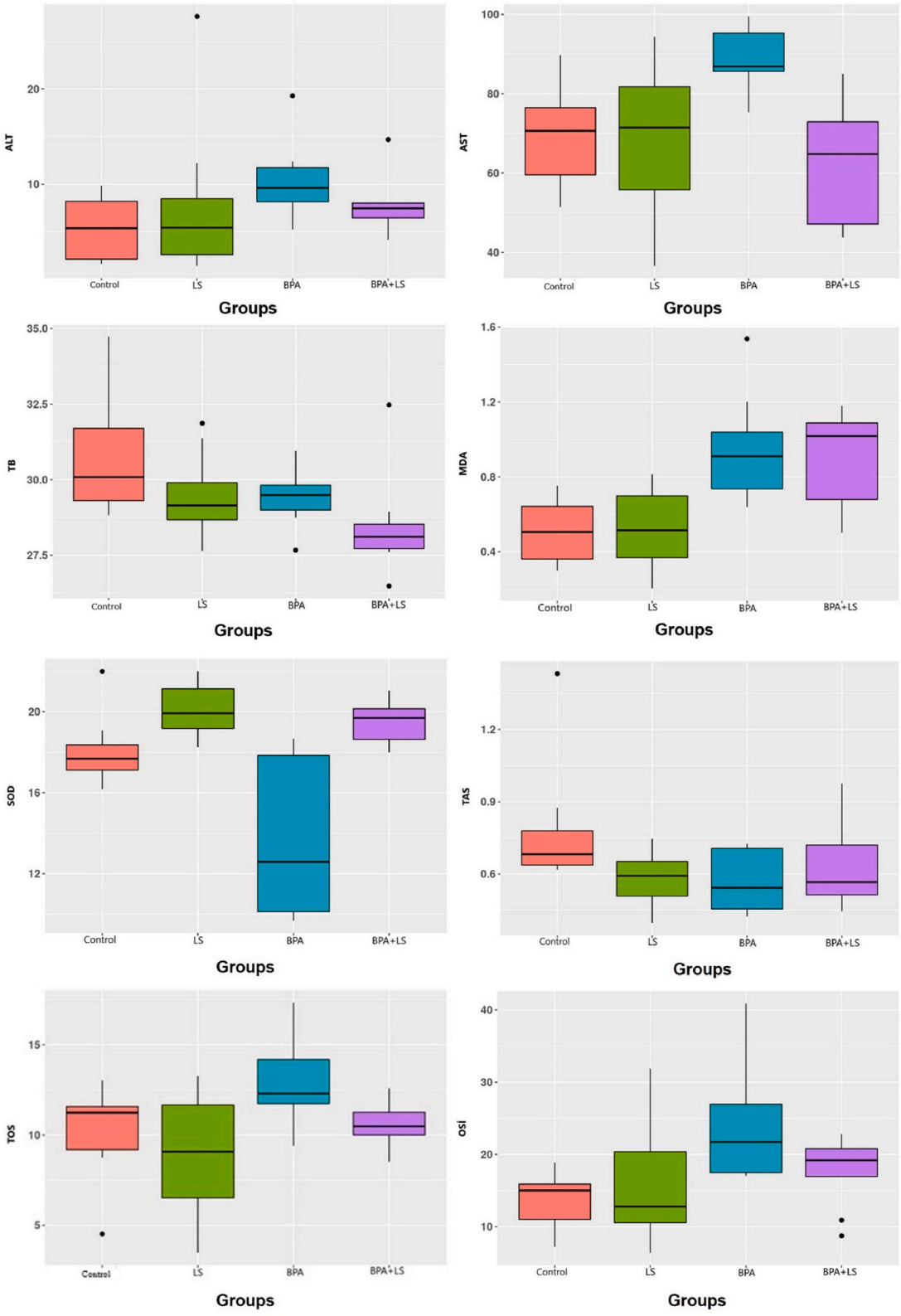

Fig. 1. Tissue and serum analysis box plots.

3. Results

3.1. Rat serum ALT, AST and TB levels

The data presented in Table 1 displays the serum ALT, AST, and TB levels. Upon comparison of the serum samples, no significant difference was observed between the groups in terms of ALT levels. When AST levels were examined, a significant increase was found in the BPA-applied group compared to the control and LS groups. In addition, it was observed that AST levels in the BPA + LS group were significantly decreased compared to the BPA group ($p < 0.05$). When the TB levels between the groups were compared, it was observed that there was a significant decrease in the BPA + LS group compared to the control and BPA groups ($p < 0.05$) (Fig. 1).

3.2. Biochemical analysis findings in rat liver tissue

The results of the biochemical analysis are shown in Table 2. The MDA level showed a significant increase in the BPA-applied groups in comparison to the control and LS groups ($p < 0.05$). Compared to the control group, SOD levels increased in the groups treated with LS. In addition, it was observed that SOD increased significantly in the BPA + LS group compared to the BPA group ($p < 0.05$). There was no significant difference between the groups in TAS and TOS values. The oxidative stress index (OSI) calculated by the TOS/TAS ratio showed a significant increase in the BPA group compared to the control ($p < 0.05$) (Fig. 1).

3.3. Histopathological evaluation

3.3.1. Control Group

In the sections where the hematoxylin-eosin staining method was applied, the classical hexagonal structure consisted of lobules with the vena centralis in the center and the portal areas at the corners. It was observed that hepatocyte cords extended radially from the vena centralis to the periphery of the lobule, and there were sinusoidal capillaries between these cords (Fig. 2 a).

At the corner of each lobule, portal areas containing the portal vein and branches of the hepatic artery and bile canaliculi were seen. The nuclei of hepatocytes were rounded and euchromatic. The cytoplasm was eosinophilic stained. The nuclei of endothelial cells in sinusoids were observed as flat and darkly stained (Fig. 2 b).

3.3.2. LS group

Hematoxylin-eosin staining method was applied in the sections of the liver, similar to the control group; It was observed that the classical hexagonal structure consisted of lobules with the central vein in the center and the portal areas at the corners. It was observed that hepatocyte cords extended radially from the central vein to the periphery of the lobule, and there were sinusoidal capillaries between these cords (Fig. 2 c).

At the corner of each lobule, portal areas containing bile canaliculi with branches of the portal vein and hepatic artery were seen. The nuclei of hepatocytes were round and euchromatic. The cytoplasm was eosinophilic stained. The nuclei of endothelial cells in sinusoids were observed as flat and darkly stained (Fig. 2 d).

3.3.3. BPA group

In the sections where the hematoxylin-eosin staining method was applied, areas with irregular borders were observed in the parenchyma, which differed from the normal histological structure (Fig. 2 e). These areas of inflammation contained inflammatory cells and apoptotic cells.

Another notable discovery was the presence of dead cells with pinkish cytoplasm in various shapes and shrunken nuclei distributed throughout the inflamed areas (Fig. 2 f).

In addition, many eosinophils with their pink-stained cytoplasm in these regions were noted (Fig. 2 g).

Table 2
Biochemical analysis findings in rat tissue samples.

Variable	Groups			
	Control	LS	BPA	BPA + LS
MDA (Tbars g/ml)	0.505[b,c] (0.299–0.753)	0.514[b,c] (0.205–0.814)	0.91 (0.64–1.537)	1.018 (0.502–1.179)
SOD (U/mg protein)	17.676[a,c] (16.174–21.985)	19.924[b] (18.248–21.984)	12.592[c] (9.685–18.654)	19.684 (17.988–21.033)
TAS (TROLOX mmol/L)	0.682 (0.618–1.432)	0.592 (0.397–0.747)	0.544 (0.424–0.726)	0.566 (0.445–0.975)
TOS (umolH_2O_2 Equivelant/L)	11.241 (4.519–13.037)	9.074 (3.481–13.259)	12.296 (9.407–17.333)	10.482 (8.519–12.593)
OSI	15.003[b] (7.224–18.846)	12.797[b] (6.381–31.879)	21.716 (17.034–40.885)	19.191 (8.734–22.812)

[a] Significant difference compared to the LS group for each variable, $p < 0.05$.
[b] Significant difference compared to the BPA group for each variable, $p < 0.05$.
[c] Significant difference compared to the BPA + LS for each variable, $p < 0.05$ (Bonferroni corrected Mann-Whitney *U* test after significant Kruskal Wallis test); Data are expressed in median (Minimum–Maximum).

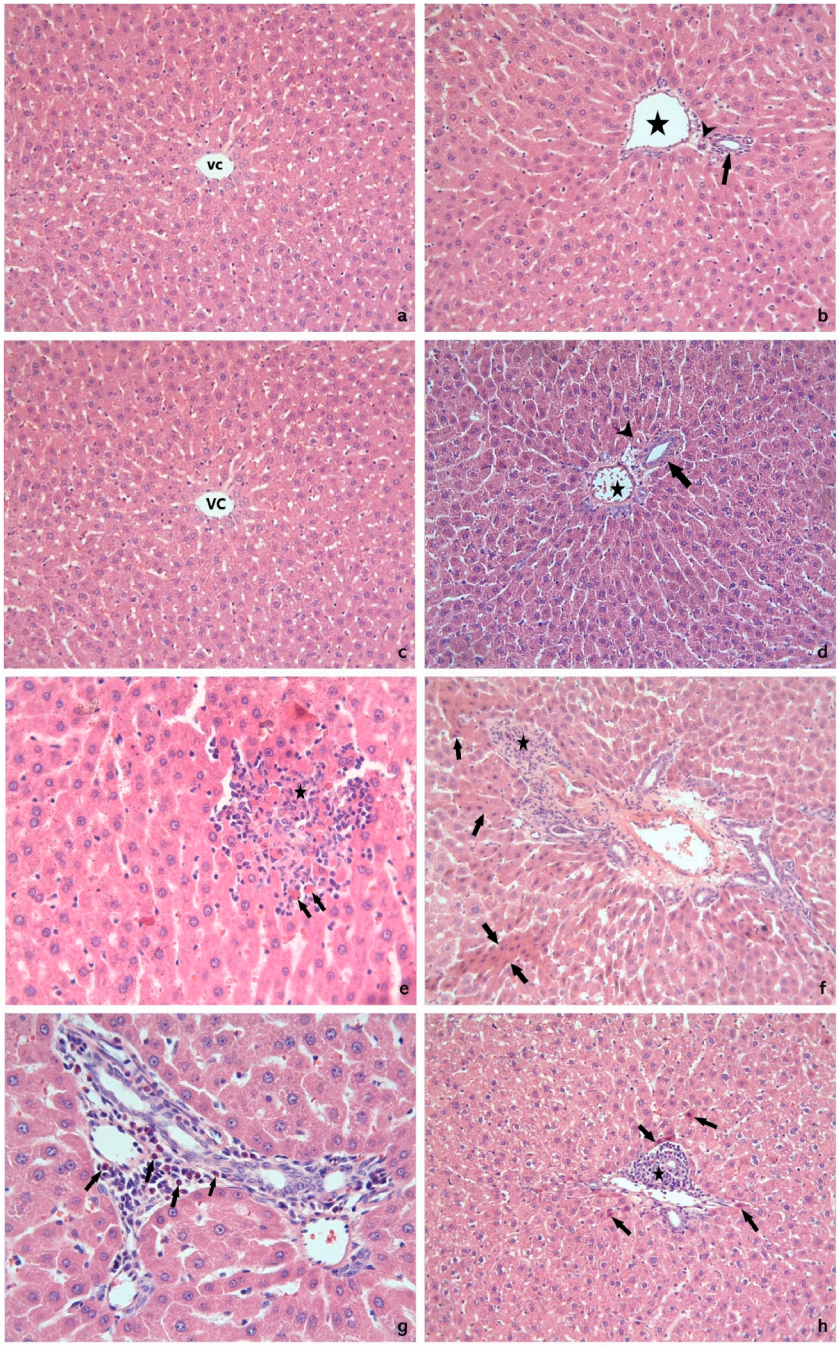

Fig. 2. a: Normal histological appearance of the liver of the control group. VC (vena centralis) H-EX200. b: Control group, portal vein (star), arteria hepatica (arrowhead), and ductus biliaris (arrow). H-EX200. c: Normal histological appearance of LS group liver. VC (vena centralis) H-EX200. d: LS group, portal vein (star), hepatic artery (arrowhead), and bile duct (arrow). H-EX200 e: Area of inflammation containing group BPA, inflammatory cells (star), and apoptotic cells (arrows). H-E; X400. f: BPA group, inflammatory cells (star) in the portal area, and necrotic cells with pycnotic nuclei with eosinophilic cytoplasm (arrows). H-E; x200. g: BPA group, eosinophils (arrows) with pink-stained cytoplasm. H-E; x400. h: BPA + LS group, an area of inflammation with reduced borders (star) and surrounding necrotic cells with eosinophilic cytoplasm and pycnotic nuclei are observed (arrows). H-E; x200.

3.3.4. BPA + LS group

In the sections where the hematoxylin-eosin staining method was applied, areas of inflammation with reduced borders and necrotic cells with a small amount of eosinophilic cytoplasm and pycnotic nuclei were detected around it (Fig. 2 h).

When the histopathological scores between the groups were compared, a significant increase was observed in the BPA group

compared to the Control and LS groups. In contrast, the score was significantly decreased in the BPA + LS group compared to the BPA group. The results of the Histopathological Score are shown in Table 3.

4. Discussion

BPA is an endocrine-disrupting chemical commonly found in our environment. Since it has estrogenic properties, its toxic effects on the reproductive system have been known for a long time, but its impact on the liver has been studied in the last decade [18]. Studies have shown that BPA causes toxicity by causing histopathological and biochemical changes in the liver [29]. Although LS has antioxidant properties and is widely used in traditional medicine, there are limited studies on its medicinal properties. Some of these studies have reported that LS has a protective effect on the liver [17]. After conducting a thorough literature review, we found no studies examining LS's effectiveness in treating organ damage caused by BPA. In our study, we examined the protective effect of 50 mg/kg/day LS against liver toxicity caused by 50 mg/kg/day BPA exposure.

Oral exposure to BPA is known to cause liver damage. In addition, the absorption of high doses of BPA through the skin in humans causes liver damage [30]. Increased serum ALT and AST levels above normal indicate liver damage. Selmi et al. [16] administered 50 mg/kg or lower doses of LS to mice with liver toxicity caused by malathion. As a result of the study, it was observed that the ALT and AST values of the toxic substance applied group increased, and these values decreased when the LS was applied. In our study, the AST level increased in the BPA group compared to the control group. The AST value, which increased with BPA exposure, was determined to decrease significantly in the BPA + LS group. There was no significant change in ALT between the groups. The AST enzyme is also found in other organs besides the liver. Thus, an increase in AST alone may indicate further damage as well as liver dysfunction caused by BPA. Anderson et al. [31] reported that a high increase in AST compared to ALT caused deterioration in liver histology and was associated with cirrhosis. In addition, the significant decrease in the AST value in the BPA + LS group shows the protective effect of LS against liver damage. High levels of bilirubin indicate toxicity in the liver. Poormosavi et al. [32] reported that the TB value increased significantly in rats administered 10 mg/kg BPA. Selmi et al. [16] stated that the TB value decreased in mice administered 50 mg/kg LS in liver damage caused by malathion. In our study, similar to the findings of Selmi et al., LS significantly reduced the TB level against the toxicity of BPA.

MDA value increases in various diseases associated with damage by free radicals. It has been reported in the literature that MDA values in liver tissue increase significantly in BPA exposure [12]. It is also known that LS or other antioxidants provide a decrease in increased MDA levels [12,32]. Similarly, in our study, the MDA level showed a significant increase in the BPA-applied groups compared to the control group. There was no significant effect of LS on the MDA level. This may be due to the presence of more camphor in the LS collected from our country. It is known that excessive intake of this substance may lead to liver toxicity [33]. This may have prevented the lipid peroxidation that LS would prevent.

Toxic substances such as BPA can cause deterioration in SOD activities and decrease these values [18]. Antioxidants provide a protective effect against toxicity by increasing SOD levels [34]. In our study, the SOD value increased significantly in rats given LS compared to the control, similar to previous studies [35]. In addition, it increased significantly in the BPA + LS group compared to the BPA group. Therefore, the increase in the SOD enzyme of LS given groups may be associated with the important role of this enzyme in biological defense systems [36]. Although LS does not affect the MDA level, it may have changed the oxidant-antioxidant balance positively by increasing antioxidant enzymes such as SOD and preventing oxidative stress.

To assess oxidative damage, levels of oxidants and antioxidants are determined using TAS and TOS measurements [37]. In the literature, it has been reported that the TAS value decreases in rats at 10 mg/kg and 50 mg/kg BPA exposure [32,38]. It is also known that antioxidants normalize the TOS level and increase the TAS level [39]. In our investigation, the groups did not show any significant difference in TAS and TOS values in liver tissue. The OSI value, determined by the ratio of these two values to each other (TOS/TAS), increased significantly in the BPA group compared to the control. In the studies, it was observed that while some oxidative stress parameters increased in cases where oxidative stress should occur, TAS and TOS values did not change significantly. Therefore, OSI evaluation may be a more appropriate marker for oxidative stress evaluation [40]. In our study, the increase in OSI value showed that oxidative stress increased in the group given BPA.

At the organelle level of liver tissue, a study reported changes in mitochondrial transmembrane potential and cellular oxidation-reduction in isolated rat hepatocytes when consuming 50 mg/kg of BPA [41]. In an experimental study, it was observed that even low

Table 3
Histopathological score.

Groups	Histopathological score
Control	0 (0–0)
LS	0 (0–0)
BPA	1 (0–3)[a]
BPA + LS	0 (0–1)[b]

[a] Statistically significant difference with the control and LS groups ($p < 0.05$).
[b] Statistically significant difference with the BPA group ($p < 0.05$)(Bonferroni corrected Mann-Whitney *U* test after significant Kruskal Wallis test); Data are expressed in median (Minimum–Maximum).

BPA exposure of 10–20 mg/kg caused blood vessel occlusion, cytoplasmic vacuolization, necrosis, inflammatory cellular infiltration, and bile duct proliferation. In addition, an increase in inflammatory leukocytes around the vena centralis and an increase in irregular areas were observed [42]. Kazemi et al. [43] administered BPA to rats at 5, 25, and 125 mg/kg doses for thirty-five days in their study. While increased nucleus aggregation, inflammatory cell infiltration, and cell necrosis were reported at 5 and 25 mg/kg exposures of BPA, these findings became more pronounced at 125 mg/kg. Exposure to 50 mg/kg of BPA on a daily basis is known to result in hepatic fibrosis, hepatic steatosis, liver tumors, and metabolic syndromes [44]. In this study, we exposed rats to 50 mg/kg BPA daily. Similar to previous studies, our histological findings showed increased apoptotic cells, irregular borders, and inflammatory cells concentrated in the portal area. Kamel et al. [45] detected eosinophils, cells with pycnotic nuclei, vacuolized swollen hepatocytes, and increased sinusoidal areas in the livers of rats exposed to 100 mg/kg BPA. In our study, while eosinophils and cells with pycnotic nuclei were found, no significant change was observed in the size of the sinusoidal area and hepatocytes. In addition, Karabekir et al. [46] reported that histopathological scores in rats given 250 mg/kg of BPA for 2 weeks increased significantly compared to the control group. Al-Griw et al. [47] reported similar findings, noting that histopathological scores in rats given 4 mg/kg of BPA for 2 weeks also increased significantly compared to the control group. Our study yielded comparable results, as we observed a significant increase in histopathological scores compared to the control group after 4 weeks of exposure to 50 mg/kg of BPA. Studies have reported that the findings that occur with BPA exposure may be caused by oxidative stress [43]. The increase in oxidative stress in direct proportion to the histopathological findings in our study supports this view.

Studies have reported that antioxidants have a protective effect against the toxicity of BPA in the liver [48,49]. In an experimental study, when 100 and 200 mg/kg LS was administered to rats, vascular congestion, mild hepatic necrosis, and lymphocyte hyperplasia occurred in the liver [50]. However, Selmi et al. [16] reported that LS administered to mice at 50 mg/kg had a hepatoprotective effect. Despite this information, more studies are needed on the effects of lavender species or LS on the liver. We conducted our study based on the study of Selmi et al. [16]. In our study, similar to this study, it was observed that LS reduced the areas of inflammation in the livers of rats given BPA and decreased cells with eosinophilic cytoplasm and pycnotic nuclei. In addition, it was observed that the histopathological score decreased significantly in rats administered BPA + LS compared to rats administered only BPA. This suggests that LS has a protective effect on the liver against BPA toxicity.

Based on our histological and biochemical analyses, we concluded that LS offers protection from BPA-induced liver injury.

5. Conclusion

It is important to find solutions against toxic substances such as BPA, which modern humans are frequently exposed to. Although lavender and its subspecies, LS, is a plant widely used in traditional medicine, there are few studies in the literature on this subject.

As a result of the biochemical analysis, BPA group showed increased AST levels compared to the control group, but these levels decreased significantly in the BPA + LS group. TB levels were lower in the BPA + LS group. MDA levels increased in BPA-treated groups, while SOD levels increased in LS-treated groups, with a significant increase in the BPA + LS group. The OSI value showed a significant increase in the BPA group compared to the control. Histological findings indicated increased apoptotic cells, irregular borders, and inflammatory cells in the portal area, along with eosinophils and cells with pycnotic nuclei.

In this research, it was observed that LS protects liver tissue by preventing oxidative stress in liver damage caused by BPA. We are confident that the results of this study will enhance the current body of knowledge and offer significant perspectives for upcoming research.

CRediT authorship contribution statement

Merve Aydın: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Conceptualization. **Evren Köse:** Writing – review & editing, Supervision, Conceptualization. **Elif Taşlıdere Karaca:** Visualization, Methodology, Formal analysis. **Kevser Tanbek:** Methodology, Formal analysis, Data curation. **Süleyman Sandal:** Supervision, Project administration.

Ethical statement

Ethics committee approval (Protocol no: 2021/18-2) for the study was obtained from the İnönü University Medical Faculty Experimental Animals Ethics Committee. The care of the animals and all applications were carried out at İnönü University Experimental Animals Research and Production Center as specified in the ethics committee protocol.

Data availability

Data will be made available on request.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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