EXPERIMENTAL STUDY

The effects of rose oil on liver damage in an experimental model of obstructive jaundice

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ABSTRACT

BACKGROUND: This study investigates the effects of Turkish rose oil (Rosa damascena) on liver damage in rats with experimentally induced obstructive jaundice.

METHODS: A total of 40 Wistar-Albino rats were divided into three groups: Sham (control), Obstructive Jaundice (OJ), and Rose Oil treatment (RO). Obstructive jaundice was induced by bile duct ligation in the OJ and RO groups. The RO group received 100 mg/kg of oral Turkish rose oil daily for seven days.

RESULTS: Biochemical analysis showed significantly elevated levels of liver and biliary injury markers, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT), in the OJ group. These markers were significantly reduced in the RO group. Additionally, oxidative stress markers such as malondialdehyde (MDA) and myeloperoxidase (MPO) were lower in the RO group compared to the OJ group. Although levels of antioxidant enzymes, including glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD), were higher in the RO group, the differences were not statistically significant. Interestingly, C-reactive protein (CRP) levels were unexpectedly higher in the RO group than in the OJ group, possibly due to the study duration or dosing protocol. Histopathological examination revealed significant portal inflammation, bile duct proliferation, polymorphonuclear leukocyte (PMNL) infiltration, necrosis, and fibrosis in the OJ group. Conversely, the RO group showed substantial reductions in these pathological features, including milder bile duct proliferation and necrosis ($p<0.001$). Additionally, connective tissue expansion and collagen deposition were significantly lower in the RO group compared to the OJ group.

CONCLUSION: The anti-inflammatory and hepatoprotective effects of Turkish rose oil, previously reported in the literature, were demonstrated in this study for the first time through oral administration. The findings highlight its potential in mitigating acute liver damage caused by obstructive jaundice. However, some unexpected biochemical results (e.g., elevated CRP and MDA levels) may be attributed to the short study duration, limited sample size, and lack of dose variation. Overall, Turkish rose oil emerges as a promising natural agent with significant hepatoprotective and anti-inflammatory properties. These results suggest that it may serve as a potential therapeutic option for liver damage associated with obstructive jaundice. Further studies are warranted to investigate varying dosages, longer treatment durations, and larger sample sizes to better understand its therapeutic potential.

Keywords: Turkish rose oil; Rosa damascena; essential oil; obstructive jaundice; liver; rat.

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INTRODUCTION

Biliary obstructive jaundice (BOJ) remains a significant concern in hepatobiliary medicine, despite advances in knowledge, technology, surgical techniques, and healthcare infrastructure. This condition can lead to multi-organ complications, with the liver being particularly vulnerable to damage. The primary cause of its pathophysiological changes is endotoxemia, which induces elevated cytokine levels through the activation of macrophages, monocytes, and endothelial cells. This cascade initiates an uncontrollable inflammatory response, potentially leading to multi-organ failure and respiratory distress syndrome, driven by the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin 6 (IL-6).[1]

Tissue damage associated with BOJ is linked to oxidative injury to cell membranes, necrosis, and lipid peroxidation (LP). An imbalance between reactive oxygen species (ROS) and the antioxidant defense system results in tissue damage and a decline in the antioxidant defense capacity in BOJ. Consequently, organs become more vulnerable to ROS-induced injury.[2,3] Glutathione (GSH) plays a critical role in non-enzymatic defense against oxygen radicals, while glutathione peroxidase (GSH-Px) contributes to enzymatic antioxidant protection. Malondialdehyde (MDA), a byproduct of LP, serves as a marker of oxidative stress. Tissues affected by LP exhibit elevated levels of MDA and myeloperoxidase (MPO).[3,4] In jaundiced rats, the activity of key enzymes, including GSH-Px, catalase (CAT), and superoxide dismutase (SOD), which are responsible for eliminating ROS from tissues, is decreased. Consequently, the compromised function of the antioxidant defense system increases susceptibility to tissue damage.[3,5]

Histopathologically, BOJ induces liver fibrosis, characterized by proliferation of biliary canal epithelial cells, hepatocyte necrosis, and activation of satellite cells. Liver fibrosis and damage result from the cytotoxic effects of accumulated bile acids, released inflammatory cytokines, and oxygen radicals. Studies have reported that proliferation of bile duct epithelium and hepatocytes begins 48 hours after the onset of jaundice, peaking on the fifth day. Changes occurring within the first seven days after jaundice onset are classified as acute cholestatic injury.[6]

The liver plays vital roles in metabolism, biosynthesis, excretion, secretion, and detoxification, making it a multifunctional organ. Most liver diseases are marked by increased liver cell death and impaired regeneration. Unlike most other organs, the liver has the capacity to regenerate new cells in response to even extensive cellular loss. However, when cell loss exceeds a critical threshold, regeneration is impaired, leading to liver failure and death.[7] A biliary obstruction presents two mechanical challenges. First, the enterohepatic circulation is disrupted, as substances secreted into the bile cannot reach the gastrointestinal tract. Second, blockage of the extrahepatic biliary tree increases pressure within the main ducts, hindering bile excretion and potentially causing bile reflux. In addition to altering the metabolism of bilirubin and bile salts and disrupting the enterohepatic circulation, biliary obstruction also leads to several other significant changes in the liver's essential functions.

BOJ can now be promptly treated using advanced techniques such as endoscopic retrograde cholangiopancreatography (ERCP). However, due to delays in scheduling, patients often wait approximately one week before undergoing the procedure. Numerous recent experimental studies have been conducted to prevent or minimize liver damage that may occur during this waiting period.[8-11]

Studies on rose oil and its extracts have reported a wide range of effects,[12] including treatment of eye disorders,[13] anti-inflammatory,[14-17] antioxidant,[18,19] anticancer,[20] antimicrobial,[21,22] antispasmodic,[23] antidepressant,[24] hypnotic,[25] constipation prevention/laxative,[26] neuroprotective,[27] hepatoprotective,[28,29] antitussive,[30,31] bronchodilator,[32,33] analgesic,[25,34] anticonvulsant,[35] anti-Human Immunodeficiency Virus (anti-HIV),[36] antidiabetic,[37] antiulcer,[38] anti-aging,[19] antilipase,[39,40] antisolar,[41] and cardiovascular protective effects.[42,43]

A review of the literature revealed no studies investigating the effects of Turkish rose oil on liver damage induced by BOJ. This study aims to evaluate the protective effects of Rosa damascena (Isparta Rose), which holds Geographical Indication (GI) in our region, on liver damage in rats with experimentally induced BOJ. Our primary parameters include pro-inflammatory cytokines, lipid peroxidation markers, antioxidant enzyme activity, and histopathological changes.

MATERIALS AND METHODS

This study was conducted in accordance with the Animal Research: Reporting In Vivo Experiments (ARRIVE) 2.0 guidelines and was approved by the Local Committee on Animal Research of Burdur Mehmet Akif Ersoy University (Decision date and number : 26.08.2021-800). This study was supported by the Süleyman Demirel University Scientific Research Coordination Unit under Project Number TTU-2021-8425.

A total of 40 Wistar-Albino rats, weighing between 150-200 grams and aged 10-12 weeks, were included in the study. The sample size was determined through power analysis. Rats in the experimental groups were housed in an environment maintained at an average temperature of 22°C, with humidity levels between 55-60%, and a 12-hour light-dark cycle. They were provided with standard pellet feed and tap water ad libitum. Feed was withheld 12 hours prior to surgery, while access to water was allowed up to two hours before the procedure. No antibiotics were administered before or after surgery.

Pure rose oil was generously provided by the Gülbirlik-

Rosense company. Gas Chromatography/Mass Spectrometry (GS/MS) analysis identified a total of 40 different compounds, primarily consisting of citronellol (24.05%), geraniol (13.53%), phenylethyl alcohol (3.17%), trans-geranyl acetate (4.17%), and methyl eugenol (2.25%), as well as long-chain hydrocarbons such as nonadecane (12.41%) and heneicosane (5.73%).

The rats were randomly divided into three groups as follows:

Group 1 (Sham): This group consisted of 10 rats that underwent laparotomy with exposure of the bile duct but without any additional intervention. The incision was closed, and rats were fed ad libitum with tap water and standard pellet feed.

Group 2 (BOJ): This group included 15 rats in which the bile duct was ligated and transected during laparotomy. The rats were then fed ad libitum with tap water and standard pellet feed for seven days.

Group 3 (RO): This group included 15 rats in which the bile duct was ligated and transected during laparotomy. In addition to ad libitum access to tap water and standard pellet feed, the rats received a daily oral dose of 100 mg/kg/day of pure rose oil (RO). The RO was administered sublingually using an automatic pipette to accommodate the small volume (in the microliter range) and to enhance absorption. Treatment continued for seven days.

Surgical Procedure

Anesthesia was induced in all three groups via intraperitoneal injection of 50 mg/kg ketamine hydrochloride and 25 mg/kg xylazine hydrochloride. Once general anesthesia was achieved, the shaved abdominal areas of the restrained rats were surgically prepared with a 10% povidone-iodine solution. The abdominal skin was covered with a sterile surgical drape, exposing the abdominal wall. A vertical 2 cm incision was made on the anterior abdominal wall. After completion of the surgery, the abdominal walls of each animal was sutured with 4/0 polypropylene suture material according to standard procedures. The rats were placed in a warm environment postoperatively to allow the anesthetic effects to wear off, while being monitored in room air without supplemental oxygen. Once the anesthetic effect had fully subsided, the rats were returned to their cages.

In the BOJ group, a total of three rats died (one within the first 24 hours and two on postoperative day 1) and were excluded from the study. In the RO group, two rats died on postoperative days 5 and 6, respectively, and were also excluded from the study.

Postoperative Treatment

Throughout the experimental period, all groups were provided standard pellet feed and tap water ad libitum, except during the preoperative fasting period. No additional drug treatment was administered to the Sham and BOJ groups. However, the RO group received a single daily oral dose of 100 mg/kg of pure Turkish rose oil (Gülbirlik-Rosense®) for seven days. As there were no previous studies using oral pure rose oil, the dosage of 100 mg/kg/day was determined based on data from studies involving oils of other aromatic plants.[28,29,44-47] Rats were monitored for postoperative clinical signs such as icterus in the sclera and skin, and changes in urine color.

Sample Collection

On the seventh day of the experiment, all rats were anesthetized via intraperitoneal injection. Following blood collection via intracardiac puncture, the animals were euthanized by cervical dislocation, and liver samples were harvested. Blood samples were placed in yellow-capped tubes for biochemical analysis and in purple-capped ethylenediaminetetraacetic acid (EDTA) tubes for enzyme-linked immunosorbent assay (ELISA) using rat-specific kits.

Liver tissues obtained for ELISA studies were weighed and homogenized in a glass container at a ratio of 1:9 (g:mL) with phosphate buffer solution (PBS) at a pH of 7.2-7.4. Following homogenization, the samples were subjected to sonication in a separate glass beaker immersed in an ice-filled container. The homogenates were then centrifuged at 5000 rpm for 10 minutes at +4°C, and the resulting supernatants were stored at -20°C until further analysis. The remaining portion of the liver tissue was fixed in 10% buffered formalin solution for histopathological examination.

Measurement of Cytokine and Tissue Enzyme Levels

Previously centrifuged samples stored at -20°C were thawed on the day of analysis, then vortexed, and homogenized. The absorbance values of cytokines interleukin-6, interleukin 8 (IL-8), and tumor necrosis factor alpha in rat plasma, as well as enzymes malondialdehyde, myeloperoxidase, superoxide dismutase, glutathione peroxidase, and catalase in liver tissue homogenates, were spectrophotometrically measured at a wavelength of 450 nm using an ELISA microplate reader, following the manufacturer's instructions.

Histopathological Analysis

Liver samples were collected during necropsy and fixed in 10% buffered formalin solution. Tissue processing was carried out using a fully automated tissue processor (Leica ASP300S; Leica Microsystem, Nussloch, Germany), and the samples were embedded in paraffin. Three serial sections, each 5 microns thick, were cut using a Leica 2155 fully automated rotary microtome. The sections were then stained using hematoxylin and eosin (HE), Azan trichrome, and Picro Sirius Red staining methods to evaluate connective tissue development, and examined under a light microscope. Histopathological examination included the evaluation of bile duct prolifera-

tion, necrosis, portal inflammation, polymorphonuclear leukocyte (PMNL) infiltration, and fibrosis. Each parameter was scored on a scale from 0 to 4 as follows: (0) absent, (1) mild, (2) moderate, (3) severe, and (4) very severe.[48] Microphotographs were captured using the Database Manual CellSens Life Science Imaging Software System.

Statistical Analyses

Data were transferred to IBM SPSS version 23 (IBM Inc., Chicago, IL, USA) for statistical analysis. Prior to analysis, the dataset was reviewed for entry errors and checked to ensure all parameters were within the expected range. Descriptive statistics were calculated, including means and standard deviations for continuous variables, and counts (n) and percentages (%) for categorical variables. Relationships between categorical variables were assessed using the Chi-square test. Normality of continuous variables was assessed using the Kolmogorov-Smirnov test, and homogeneity of variances was evaluated using Levene's test. One-way Analysis of Variance (ANOVA) was used for comparisons among three groups, and the Kruskal-Wallis H test was applied when the assumption of normality was not met. For the statistical analysis of histopathological scores, Duncan's test was performed. Post-hoc analyses were conducted when differences were observed. A significance level of $p<0.05$ was considered for all analyses.

RESULTS

Statistical Evaluation of Blood and Tissue ELISA Studies

No statistically significant differences were observed in the mean values of IL-6, IL-8, and TNF-α among the groups (p=0.082, p=0.604, and p=0.321, respectively). The mean C-reactive protein (CRP) value was 0.40±0.05 in both the Sham and BOJ groups, and 0.47±0.06 in the RO group. A statistically significant difference was found among the groups regarding CRP levels (p=0.002). It was noted that the mean CRP level in the RO group was significantly higher compared to both the Sham and BOJ groups.

No statistically significant differences were found among the groups in MDA levels (p=0.321). Similarly, no statistically significant differences were observed in the mean values of SOD and GSH-Px among the groups (p=0.170 and p=0.198, respectively). However, a statistically significant difference was observed in CAT levels among the groups (p=0.010), with the mean CAT value in the Sham group being significantly higher than in the GY group. No statistically significant differences were found in MPO levels among the groups (p=0.775). The statistical analysis results of the ELISA method are presented in Table 1.

A statistically significant difference was observed in the mean aspartate aminotransferase (AST) values among the groups (p=0.011). The mean AST values in both the BOJ and RO groups were significantly higher compared to the Sham group (p=0.030 and p=0.002, respectively). No statistically significant difference was found in the mean alanine aminotransferase (ALT) values among the groups (p=0.058). A statistically significant difference was observed in mean alkaline phosphatase (ALP) values among the groups (p=0.037), with the mean ALP in the RO group being significantly higher than in the Sham group (p=0.004). A statistically significant difference was also found in mean gamma-glutamyl transpeptidase (GGT) values among the groups (p=0.001). The mean GGT values in the BOJ group were significantly higher compared to the Sham group (p=0.002). Statistically significant differences were observed in the mean total bilirubin values among the groups (p=0.001). The mean total bilirubin levels in the BOJ group were significantly higher than those in the Sham group (p<0.001). The statistical analysis results of the biochemical markers are presented in Table 2.

Table 1. Statistical analysis of enzyme-linked immunosorbent Assay (ELISA) results among groups

	Sham	BOJ	RO	p
	Mean±SD			
IL-6	0.57±0.06	0.53±0.12	0.62±0.11	0.082
IL-8	0.64±0.07	0.59±0.19	0.63±0.11	0.604
TNF-α	0.57±0.09	0.54±0.14	0.61±0.09	0.321
CRP	0.40±0.05	0.40±0.05	0.47±0.06	0.002*
MDA	0.56±0.11	0.51±0.11	0.50±0.08	0.321
SOD	0.57±0.21	0.60±0.20	0.62±0.18	0.170
GSH-Px	1.14±0.17	1.24±0.17	1.14±0.07	0.198
CAT	1.25±0.15	1.09±0.16	1.05±0.12	0.010*
MPO	0.70±0.15	0.68±0.11	0.66±0.09	0.775

Data are presented as mean ± standard deviation (SD). One-way Analysis of Variance (ANOVA) or Kruskal-Wallis H test was used. *p<0.05. IL-6: Interleukin-6; IL-8: Interleukin-8; TNF-α: Tumor Necrosis Factor-Alpha; CRP: C-Reactive Protein; MDA: Malondialdehyde; SOD: Superoxide Dismutase; GSH-Px: Glutathione Peroxidase; CAT: Catalase; MPO: Myeloperoxidase.

Table 2. Statistical analysis of biochemical markers among groups

	Sham	BOJ	RO	p
AST	160.70±136.72	455.67±311.60	326.90±131.53	**0.011***
ALT	79.78±77.17	181.28±144.78	114.05±37.46	0.058
ALP	319.40±16.27	422.08±135.38	419.85±92.65	**0.037***
GGT	10.00±7.12	60.25±57.64	33.77±26.46	**0.001***
Total Bilirubin	0.16±0.04	3.53±3.73	2.79±2.38	**0.001***

Data are presented as mean ± standard deviation (SD). One-way Analysis of Variance (ANOVA) or Kruskal-Wallis H test was used. *p<0.05. AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; ALP: Alkaline Phosphatase; GGT: Gamma-Glutamyl Transferase.

Pathological Findings

During necropsy, the livers in the Sham group appeared normal. However, in the BOJ and RO groups, the livers were enlarged and exhibited pale coloration. These changes were more pronounced in the BOJ group.

Histopathological examination of liver samples stained with HE revealed normal tissue architecture in the Sham group. In the BOJ group, severe hyperemia and mild inflammatory cell infiltration were observed. The most prominent observation in this group was bile duct hyperplasia and increased connective tissue surrounding the ducts. Additionally, marked hepatocyte degeneration and necrotic changes were observed in certain areas of the liver. Notably, a reduction in these histopathological changes was observed in the group treated with RO (Fig. 1).

Histopathological analysis revealed statistically significant differences in bile duct proliferation, necrosis, portal inflammation, PMNL infiltration, and fibrosis among the groups (p<0.001). All of these parameters were significantly higher in the BOJ group compared to the RO group (p<0.001). The statistical analysis results of the histopathological scores are presented in Table 3.

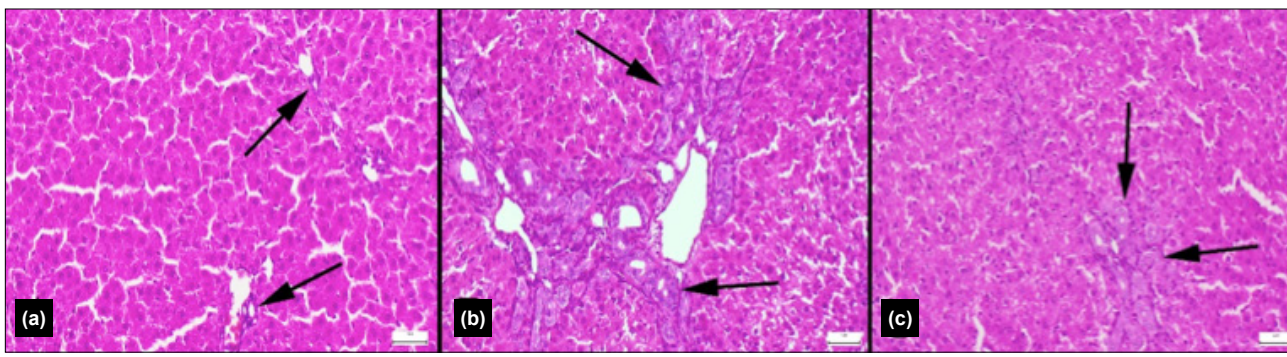

Figure 1. Histopathological appearance of the livers and bile ducts between the group. **(a)** Normal bile ducts (arrows) in control group. **(b)** Severely proliferated bile ducts (arrows) in BOJ group. **(c)** Decreased bile duct proliferations (arrows) in RO group, HE, Scale Bars=50µm.

Table 3. Statistical analysis of histopathological scores among groups

	Sham	BOJ	RO	All Groups	Sham vs. BOJ	Sham vs. RO	BOJ vs. RO
	Mean±SD			p			
Bile duct proliferation	0.1±0.3	3.8±0.5	2.0±0.6	<0.001	<0.001	<0.001	<0.001
Necrosis	0	2.8±0.8	0.8±0.7	<0.001	<0.001	0.007	<0.001
Portal inflammation	0.2±0.4	3.2±0.7	1.2±0.4	<0.001	<0.001	<0.001	<0.001
PMNL infiltration	0.2±0.4	3.4±0.5	1.4±0.5	<0.001	<0.001	<0.001	<0.001
Fibrosis	0	3.8±0.5	1.6±0.5	<0.001	<0.001	<0.001	<0.001

Data are presented as mean ± standard deviation (SD). One-way Analysis of Variance (ANOVA) or Kruskal-Wallis H test was used. *p<0.05. PMNL: Polymorphonuclear Leukocytes.

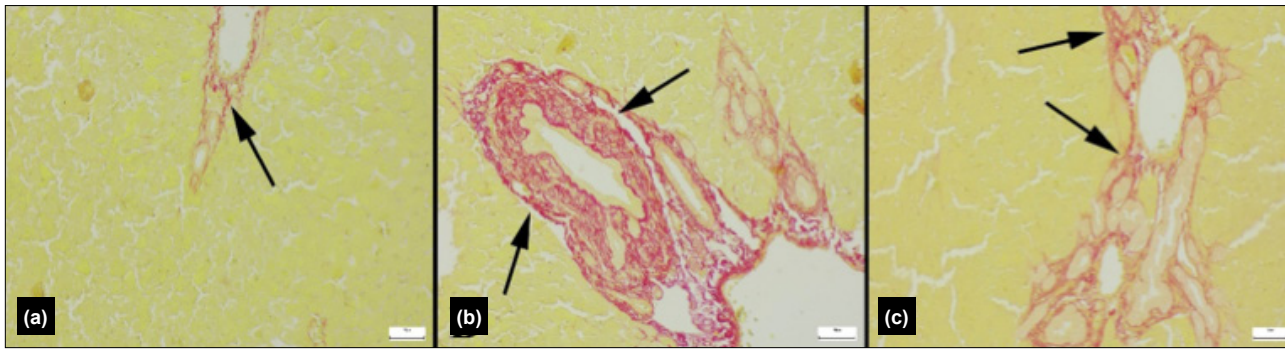

Figure 2. Microscopical appearance of fibrous tissue of the livers between the group. **(a)** Normal and slight fibrous tissue (arrow) in control group. **(b)** Markedly increased fibrous tissue (arrows) in BOJ group. **(c)** Decreased fibrous tissue proliferation (arrows) in RO group, Picro sirius red, Scale Bars=50μm.

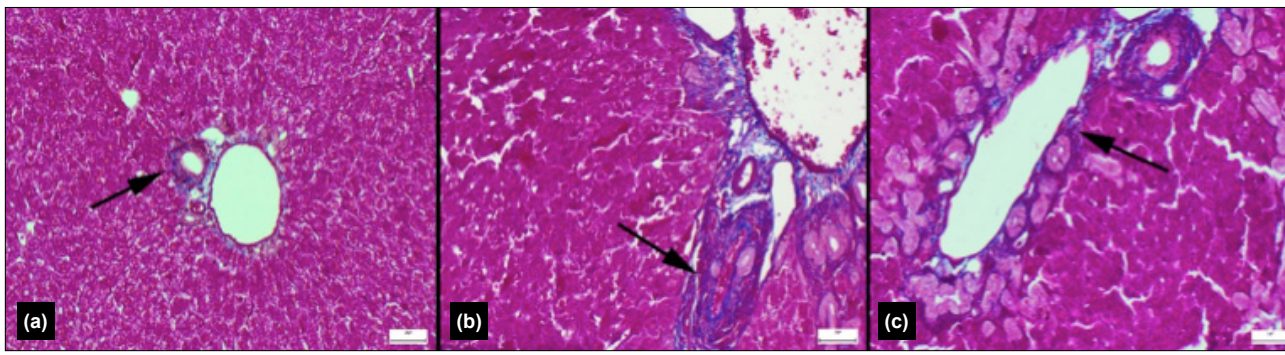

Figure 3. Microscopical appearance of collagen between the group. **(a)** Normal and slight collagen (arrow) in control group. **(b)** Markedly increased collagen (arrows) in BOJ group. **(c)** Decreased collagen (arrows) in RO group, Picro sirius red, Scale Bars=50μm.

Results of Picro Sirius Red and Azan Trichrome Staining

Collagen was stained red with Picro Sirius Red, while it appeared blue in Azan Trichrome staining, allowing for the assessment of connective tissue and collagen accumulation. Evaluation of increased connective tissue showed that in the Sham group, the presence of collagen and connective tissue was very slight and thin, In contrast, both the BOJ and RO groups exhibited increased collagen deposition, with the increase being notably more pronounced in the BOJ group compared to the RO group (Figures 2 and 3).

DISCUSSION

In a Taiwan-based experimental study, induced BOJ in rats was associated with notable elevations in IL-1, IL-6, and TNF-α levels in the blood, which activated the nuclear factor-kappa B (NF-κB) pathway in hepatocytes, leading to hepatocellular damage accompanied by ROS.[49] Similarly, a study conducted in the Netherlands showed an initial rise in plasma IL-6 levels in mice with induced BOJ, followed by a rapid decline. However, from the 12th day onward, a significant increase in IL-6 levels was noted. They also observed fluctuations in plasma TNF-α levels, likely due to the intermittent nature of its production and its short half-life, which may account for variable results.[50] Another study by Castell et al.[51] highlighted a contrast in the half-lives of IL-6 in plasma versus tissue following recombinant IL-6 injection: IL-6 was undetectable in plasma at 20 minutes, while it remained detectable in liver tissue samples collected at the same time. However, in our study, no statistically significant differences were observed in the mean values of IL-6, IL-8, and TNF-α among the groups. This lack of significance may be attributed to the short half-lives of these cytokines, their measurement in plasma rather than in tissue samples, and the relatively brief duration of the experiment.

CRP, an acute-phase reactant, has been reported to increase in obstructive jaundice, as noted by Padillo et al..[52] In our study, a statistically significant difference in CRP levels was found among the groups (p=0.002), with the RO group showing significantly higher mean CRP levels than the Sham group. Although a reduction in CRP was expected due to RO's potential to reduce liver damage and inflammation, the RO group unexpectedly exhibited higher CRP levels, not only compared to the Sham group but also to the BOJ group. The anticipated reduction in CRP due to RO's effect was not observed. It is possible that the application of RO influenced CRP production centrally in the liver, resulting in the elevated CRP levels observed in the RO group.

Enzymes such as GSH-Px, CAT, and SOD play key roles in

cellular defense against oxygen radicals. MDA, a byproduct of lipid peroxidation, serves as a marker of oxidative stress (48,49). However, our study did not reveal a statistically significant difference in MDA levels among the groups. Despite this, MDA levels were lower in the RO group compared to the BOJ group. This observation might become significant with a larger sample size, longer experimental duration, and adjusted rose oil dosage. Similarly, no significant difference was observed in mean GSH-Px levels among the groups. Although not statistically significant, the higher SOD levels in the RO group may indicate potential support for antioxidant mechanisms. A significant difference was found in CAT levels among the groups, with the mean CAT level in the Sham group being notably higher than in the RO group. Furthermore, although not statistically significant, CAT levels in the BOJ group were lower compared to the control group. This trend may suggest that cholestasis-induced inflammation could suppress antioxidant enzyme activity, potentially reaching significance in studies with larger sample sizes. MPO levels did not show significant differences among the groups in our study. However, the lower MPO levels observed in the RO group compared to both the control and BOJ groups may indicate the antioxidant potential of rose oil. Increasing the sample size, extending the duration of the study, or adjusting the rose oil dosage could help strengthen these findings.

In a study by Saxena et al.,[28] the protective effect of rose flower extract against acetaminophen-induced toxicity in rats was investigated. Rats that received 2 g/kg of acetaminophen orally were administered rose water at doses of 250, 500, and 1000 mg/kg. Acetaminophen toxicity led to alterations in AST, ALT, ALP, lactate dehydrogenase (LDH), albumin, bilirubin, creatinine, liver lipid peroxidation, and glutathione levels. The rose flower extract demonstrated protective effects against acetaminophen-induced liver damage, potentially through antioxidant mechanisms.[27] In our study, a statistically significant difference was observed in mean AST values among the groups (p=0.011), with AST levels in both the BOJ and RO groups being notably higher than in the Sham group. Mean ALT values did not differ significantly among the groups (p=0.058), although ALT levels in the BOJ and RO groups were noticeably higher compared to the control. These findings indicate liver damage, as reflected by increased AST and ALT levels in the BOJ and RO groups, likely due to obstructive jaundice. The lower values in the RO group suggest a protective effect of rose oil, consistent with its reported anti-inflammatory and hepatoprotective properties in the literature. The lack of statistical significance in ALT levels may be attributed to high variability; larger sample sizes may help reveal more definitive differences. A significant difference was observed in mean ALP values among the groups (p=0.037). Mean ALP levels were notably higher in the RO group compared to the control. Although not statistically significant, the RO group had lower ALP levels than the BOJ group. This lack of significance between the BOJ and RO groups may be due to high variability. As expected, ALP levels were significantly elevated in both the BOJ and RO groups compared to the control group, likely due to the induced obstruction. A modest positive effect of rose oil was observed in the RO group, despite the lack of statistical significance, suggesting a potential anti-inflammatory effect on the bile ducts, as reported in previous literature.

In our study, significant differences were also found in GGT levels among the groups (p=0.001). Rats in the BOJ group exhibited significantly higher GGT values compared to the Sham group, while the RO group showed lower GGT levels than the BOJ group. This finding suggests that rose oil may help reduce biliary tract inflammation, aligning with prior research. Similarly, a significant difference in total bilirubin levels was observed across the groups (p=0.001). Rats in the BOJ group had markedly elevated total bilirubin levels compared to the Sham group. Meanwhile, the RO group exhibited lower total bilirubin levels than the BOJ group, suggesting a potential liver-protective effect of rose oil against biliary tract and liver damage.

Dadkhah et al.[46] conducted a study in which sepsis was induced in rats, and Rosa damascena essential oil was administered orally at doses of 50 and 100 mg/kg for 14 days. They found that oral administration of RO led to reductions in portal inflammation, neutrophil infiltration, granular degeneration, and macrophage infiltration, effects comparable to those of indomethacin.[45] In another study by Davoodi et al.,[47] rats were given Rosa damascena hydroalcoholic extract and simvastatin after being fed a high-fat diet for two weeks to induce non-alcoholic fatty liver disease. After eight weeks, significant reductions in steatohepatitis and necrosis were observed in the groups treated with simvastatin and rose extract compared to the high-fat diet group.[46] In our study's pathological examinations, livers in the Sham group exhibited a normal appearance. However, the BOJ and RO groups displayed enlarged, pale-colored livers, with these changes being particularly pronounced in the obstructive jaundice group. These findings suggest a potential protective effect of rose oil against liver damage.

Histopathological analysis of HE-stained liver samples revealed normal tissue architecture in the Sham group. In contrast, the BOJ group exhibited notable changes, including bile duct hyperplasia, increased connective tissue around the ducts, severe vascular congestion, mild inflammatory cell infiltration, hepatocyte degeneration, and localized necrosis. Interestingly, the RO group showed reduced histopathological alterations, supporting the liver-protective properties of RO. Collagen-specific staining revealed minimal collagen in the Sham group, while both the BOJ and RO groups exhibited increased connective tissue and collagen deposition. This increase was more pronounced in the BOJ group, highlighting the protective effect of rose oil against liver fibrosis. Bile duct proliferation was nearly absent in the control group, severe in the BOJ group, and mild to moderate in the RO group. Statistical analysis revealed a significant relationship in

bile duct proliferation among the groups ($p<0.001$), indicating increased proliferation due to BOJ, which was mitigated by RO treatment. Necrosis was absent in the control group but ranged from moderate to severe in the TS group, and from absent to mild/moderate in most rats in the GY group. Statistical analysis showed a significant relationship between necrosis and group ($p<0.001$), indicating increased necrosis in obstructive jaundice, which was attenuated by rose oil. Portal inflammation ranged from absent to mild in the Sham group, was severe to moderate in the BOJ group, and mild to moderate in the RO group. Statistical analysis indicated a significant relationship in portal inflammation among the groups ($p<0.001$), reflecting severe inflammation due to BOJ, which was alleviated by RO treatment. PMNL infiltration was mostly absent in the Sham group, severe in the BOJ group, and mild to moderate in the RO group. Statistical analysis showed a significant relationship in PMNL infiltration among the groups ($p<0.001$), demonstrating increased infiltration due to BOJ, which was reduced by RO application. Fibrosis was absent in the Sham group, severe in the BOJ group, and mild to moderate in the RO group. Statistical analysis showed a significant relationship between fibrosis and the groups ($p<0.001$), suggesting its development in obstructive jaundice and its mitigation by rose oil.

CONCLUSION

In conclusion, oral administration of Turkish rose oil resulted in a statistically significant reduction in elevated biochemical markers, portal inflammation, bile duct proliferation, PMNL infiltration, and necrosis, all indicators of acute liver damage caused by biliary obstructive jaundice. Based on these findings, Turkish rose oil appears to be effective in reducing tissue damage and inflammation, consistent with the benefits previously reported for rose oils and extracts from other regions. Its application in the treatment of liver damage caused by biliary obstructive jaundice represents a novel therapeutic approach. Further studies are needed to more thoroughly evaluate the effectiveness of rose oil in this context, particularly at varying dosages and durations.

Ethics Committee Approval: This study was approved by the Burdur Mehmet Akif Ersoy University Animal Research Local Ethics Committee (Date: 26.08.2021, Decision No: 800).

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DENEYSEL ÇALIŞMA - *ÖZ*

Deneysel tıkanma sarılığı modelinde gül yağının karaciğer hasarı üzerine etkileri

AMAÇ: Bu çalışmada, deneysel olarak tıkanma sarılığı oluşturulmuş sıçanlarda Türk gül yağının (Rosa Damascena) karaciğer hasarı üzerindeki etkileri değerlendirildi.

GEREÇ VE YÖNTEM: Çalışma kapsamında 40 Wistar-Albino sıçanı, Sham (kontrol), tıkanma sarılığı (TS) ve gül yağı tedavisi (GY) olmak üzere üç gruba ayrılmıştır. TS ve GY gruplarında safra yolları bağlanarak tıkanma sarılığı oluşturulmuş, GY grubuna ek olarak 7 gün boyunca günlük 100 mg/kg oral Türk gül yağı uygulanmıştır.

BULGULAR: Biyokimyasal incelemelerde, TS grubunda aspartat aminotransferaz (AST), alanin aminotransferaz (ALT), alkalin fosfataz (ALP), gama glutamil transferaz (GGT) gibi karaciğer ve safra yolu hasar enzimlerinin anlamlı derecede arttığı, GY grubunda ise bu değerlerin belirgin şekilde azaldığı görülmüştür. Ayrıca, oksidatif stres belirteçlerinden malondialdehit (MDA) ve miyeloperoksidaz (MPO) düzeylerinin TS grubuna göre GY grubunda daha düşük olduğu tespit edilmiştir. Antioksidan enzimlerden glutatyon peroksidaz (GSH-Px) ve süperoksit dismutaz (SOD) seviyeleri GY grubunda daha yüksek bulunmasına rağmen, bu değişiklikler istatistiksel anlam taşımamıştır. C-reaktif protein (CRP) seviyeleri, TS grubuna kıyasla GY grubunda beklenenden daha yüksek ölçülmüş ve bu durumun çalışma süresi ve doz tasarımı ile ilişkili olabileceği öne sürülmüştür. Histopatolojik incelemeler, TS grubunda karaciğerde belirgin portal inflamasyon, safra duktusu proliferasyonu, polimorfonükleer lökosit (PMNL) infiltrasyonu, nekroz ve fibrozis bulgularının olduğunu göstermiştir. GY grubunda bu histopatolojik bulguların belirgin şekilde azaldığı, örneğin safra duktusu proliferasyonu ve nekrozun daha hafif seviyelerde izlendiği tespit edilmiştir ($p<0.001$). Ayrıca, bağ dokusu ve kollajen artışının TS grubuna göre GY grubunda daha düşük olduğu görülmüştür.

SONUÇ: Türk gül yağının literatürde bildirilen antienflamatuvar ve hepatoprotektif etkileri, bu çalışmada literatürde olmayan şekilde ilk defa oral olarak verilerek gül yağının koruyucu etkileri gözlemlenmiştir. Özellikle tıkanma sarılığına bağlı akut karaciğer hasarını azaltmada etkinliği gösterilmiştir. Ancak, bazı biyokimyasal parametrelerde (ör. CRP ve MDA) beklenmeyen sonuçlar, deney süresinin kısa olması, örneklem büyüklüğünün sınırlılığı ve gül yağı dozlarının çeşitlendirilememesiyle açıklanabilir. Sonuç olarak, Türk gül yağı, karaciğer hasarını azaltıcı ve inflamasyonu önleyici etkileri ile öne çıkan bir doğal ürün olarak değerlendirilmiştir. Bu çalışmanın bulguları, Türk gül yağının tıkanma sarılığına bağlı karaciğer hasarında umut verici bir tedavi seçeneği olabileceğini göstermektedir. Daha geniş kapsamlı ve farklı dozların değerlendirileceği ileri çalışmalar gereklidir.

Anahtar sözcükler: Esansiyel yağ; karaciğer; obstrüktif sarılık; rosa damascena; sıçan; türk gül yağı.

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