EXPERIMENTAL STUDY

The role of geraniol on hepatic ischemia-reperfusion injury model in rats

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ABSTRACT

BACKGROUND: Hepatic ischemia/reperfusion (I/R) injury is a significant clinical condition that can arise during liver resections, trauma, and shock. Geraniol, an isoterpene molecule commonly found in nature, possesses antioxidant and hepatoprotective properties. This study investigates the impact of geraniol on hepatic damage by inducing experimental liver I/R injury in rats.

METHODS: Twenty-eight male Wistar Albino rats weighing 350-400 g were utilized for this study. The rats were divided into four groups: control group, I/R group, 50 mg/kg geraniol+I/R group, and 100 mg/kg geraniol+I/R group. Ischemia times were set at 15 minutes with reperfusion times at 20 minutes. Ischemia commenced 15 minutes after geraniol administration. Serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactic acid were measured, along with superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activity levels in liver tissues. Liver tissues were also examined histopathologically.

RESULTS: It was observed that intraperitoneal administration of 50 mg/kg and 100 mg/kg geraniol significantly reduced AST, lactic acid, and tumor necrosis factor-alpha (TNF-α) levels. The serum ALT level decreased significantly in the 50 mg/kg group, whereas no significant decrease was found in the 100 mg/kg group. SOD and GPx enzyme activities were shown to increase significantly in the 100 mg/kg group. Although there was an increase in these enzyme levels in the 50 mg/kg group, it was not statistically significant. Similarly, CAT enzyme activity increased in both the 50 mg/kg and 100 mg/kg groups, but the increase was not significant. The Suzuki score significantly decreased in both the 50 mg/kg and 100 mg/kg groups.

CONCLUSION: The study demonstrates that geraniol reduced hepatic damage both biochemically and histopathologically and increased antioxidant defense enzymes. These findings suggest that geraniol could be used to prevent hepatic I/R injury, provided it is corroborated by large-scale and comprehensive studies.

Keywords: Geraniol; liver; ischemia/reperfusion injury; oxidative stress.

INTRODUCTION

Ischemia, the most common cellular injury mechanism, results from the complete or partial interruption of blood flow to a tissue or organ due to various factors.[1] The medical or mechanical restoration of blood flow to ischemic tissues is called reperfusion. Oxygen free radicals (OFRs), produced during reperfusion, can paradoxically induce reperfusion injury by activating immunological, vascular, and metabolic events. Vascular incidents such as myocardial infarction, ischemic cerebrovas-

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cular events, mesenteric ischemia, and conditions characterized by impaired tissue perfusion due to hypovolemia, such as shock, burns, ileus, and their respective treatments, may lead to ischemia-reperfusion (IR) injury. Several pharmacological agents and surgical techniques are employed in clinical practice to mitigate this damage.[2,3]

Hepatic IR injury was first identified in the medical literature through an experimental liver transplantation study by Toledo et al. in 1975.[4] Beyond liver transplantations, hepatic IR injury can also arise during elective liver surgeries using the Pringle maneuver, and from traumatic liver injuries.

The body maintains oxidative balance through intricate processes, including neutralization steps to mitigate damage from superoxide radicals continuously produced by metabolic activities. This balance involves both enzymatic and non-enzymatic antioxidants. Enzymatic defenders against oxidative stress include superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), and thioredoxin reductase (TrxR). Non-enzymatic antioxidants comprise vitamins (A, C, and E), minerals (selenium and zinc), uric acid, β-carotene, bilirubin, melatonin, glutathione, flavonoids, and terpenes.[5,6]

Geraniol (GR), derived from plants and herbivorous insects, is an isoprene alkaloid categorized among non-enzymatic antioxidants, noted for its hepatoprotective, cardioprotective, neuroprotective, antitumoral, and antimicrobial effects.[1]

This study aimed to evaluate the efficacy of two different doses of intraperitoneal geraniol administered prior to inducing experimental hepatic IR injury in rats, assessing both biochemical and histological parameters.

MATERIALS AND METHODS

The study was conducted following approval from Istanbul University, Cerrahpaşa Faculty of Medicine (No: 2020/30), and was funded by the Istanbul University Scientific Research Projects unit (Project Code: 2021-35581). A total of 28 Wistar-Albino male rats, aged 8-10 weeks, were procured from the Cerrahpaşa Faculty of Medicine. The experiments were performed in the operating room and utilized the hosting facilities of the same center.

Experimental Groups and Surgical Procedure

The subjects, 28 Wistar-Albino male rats weighing 350-400 grams, were confirmed suitable after preliminary research. They were housed in standard cages, four per cage, in rooms maintained at a standard temperature of 24±2°C with a 12-hour light/dark cycle. Conditions also included standard humidity levels. The rats had unrestricted access to standard rat chow and water prior to the treatment. The animals were randomly divided into four groups (Fig. 1).

Control Group: Following anesthesia administration, a laparotomy was performed on these subjects without any medical intervention or induction of IR injury. Subsequently, blood and liver tissue samples were collected before the rats were euthanized.

IR Group: After administering anesthesia, laparotomy was performed without medical intervention, and the hepatic pedicle was encircled and clamped with an atraumatic clamp for 15 minutes. Following this, the clamp was removed to induce reperfusion for 20 minutes. Subsequently, blood and liver tissue samples were collected before the subjects were euthanized.

50-GR Group: Following anesthesia, 50 mg/kg of geraniol was administered intraperitoneally. A laparotomy was then performed. Fifteen minutes after geraniol administration, the hepatic pedicle was encircled and clamped for 15 minutes to induce hepatic ischemia. After removing the clamp, reperfusion was allowed for 20 minutes, after which blood and liver tissue samples were collected, and the subjects were euthanized.

100-GR Group: After administering anesthesia, 100 mg/kg of geraniol was given intraperitoneally, followed by a laparotomy. Fifteen minutes post-administration, the hepatic pedicle was encircled and clamped for 15 minutes to induce hepatic ischemia. Upon removal of the clamp, reperfusion was facilitated for 20 minutes. Blood and liver tissue samples were then collected, and the subjects were euthanized.

All surgical procedures were performed in a sterile environment using sterile surgical instruments under operating room conditions. To account for the effects of diurnal hormonal changes in rats, all procedures were conducted between 08:00 and 11:00 A.M. The animals were anesthetized by intramuscular (i.m.) administration of 10 mg/kg xylazine (Alfazyne, 2%, Alfasan, Woerden, Holland) and 80 mg/kg ketamine (Ketalar, Pfizer Pharma, GMBH, Germany).

The animals were positioned supine on a warm, stable dissection table. The surgical site was cleaned with a 10% polyvinylpyrrolidone-iodine complex (Batticon, Adeka), and a 3-4 cm midline incision was made in the abdomen to perform laparotomy. An atraumatic vascular clamp was applied to the iso-

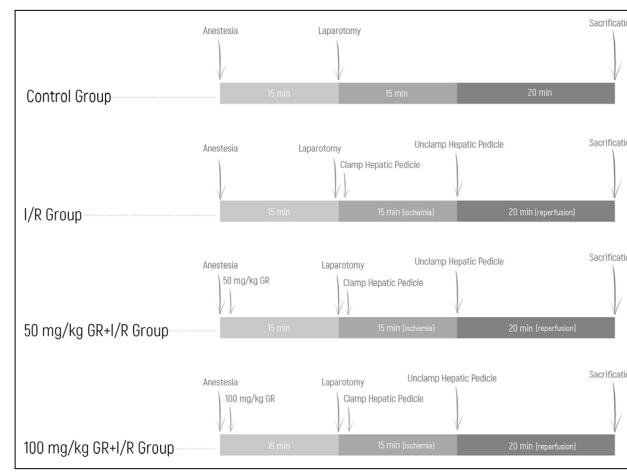

Figure 1. Experimental groups.

Table 1. Mean and standard deviations of ALT, AST, lactic acid, TNF-α, SOD, GPx, and catalase values of the groups

	Control[1]	IR[2]	50-GR[3]	100-GR[4]	p
ALT (U/L)	11.80±4.91	172.25±64.96	21.95±6.78	26.84±7.37	$p<0.05^{ab}$
AST (ng/ml)	7.01±2.16	87.36±59.18	9.09±1.42	8.86±2.49	$p<0.05^{abc}$
Lactic Acid (micromol/ml)	0.66±0.08	7.36±2.82	0.58±0.21	0.69±0.06	$p<0.05^{abc}$
TNF-α (pg/ml)	20.36±7.90	221.70±98.65	18.39±6.44	19.74±4.66	$p<0.05^{abc}$
SOD (pg/mg protein)	5.56±0.76	2.02±0.61	4.85±1.29	5.74±1.52	$p<0.05^{ac}$
GPx (pg/mg protein)	697.70±157.44	288.96±57.86	549.31±97.03	708.54±176.86	$p<0.05^{ac}$
CAT (pg/mg protein)	33.77±9.00	23.62±2.40	30.71±6.32	31.77±7.44	$p<0.05^{a}$

Post-hoc significance indicators: a: 1 compared to 2; b: 2 compared to 3; c: 2 compared to 4.

lated hepatic pedicle, inducing ischemia for 15 minutes. After 15 minutes of ischemia, the clamp was removed and reperfusion was induced for 20 minutes. Liver tissue samples were collected for biochemical and pathological examinations, blood was drawn via the intracardiac route, and then all subjects were euthanized. The blood samples were centrifuged for 10 minutes at 4000 rpm at 4°C. The serum samples were immediately stored at -80°C until analysis. The liver samples (500 mg) were homogenized in 100 mmol/L phosphate buffer (pH: 7.4), for 1 minute on ice, then centrifuged at 20,000 g at +4°C for 15 minutes, and supernatants were collected.

Biochemical and Histopathological Assessment

Serum levels of aspartate aminotransferase (AST) (E-BC-K236-M, Elabscience, USA), alanine aminotransferase (ALT) (E-BC-K235-M, Elabscience, USA), and lactic acid (E-BC-K044-M, Elabscience, USA) were determined using a spectrophotometric method. Tumor Necrosis Factor-alpha (TNF-α) levels were analyzed by enzyme-linked immunoassay (ELISA) (E-CL-R0019, Elabscience, USA).

In liver supernatants, the levels of oxidative stress indicators—SOD (E-EL-R1424, Elabscience, USA), CAT (E-BC-K031-S, Elabscience, USA), and GPx (E-EL-R2491, Elabscience, USA)—were determined by ELISA.

From the formalin-fixed and paraffin-embedded liver samples collected for histopathological examination, 5 µm sections were taken and stained with hematoxylin-eosin. A single pathologist assessed changes in cell histology, including congestion, necrosis, cytoplasmic vacuolization, eosinophilia, nuclear pyknosis, and inflammatory cell density. These measures were assessed according to the pathological scoring system defined by Suzuki et al. in 1993.[7]

Hepatocyte injury was graded as follows: 0: no injury, 1: minimal injury, 2: mild injury, 3: moderate injury, and 4: severe injury.

Statistical Analysis

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago, IL, USA). Histogram analysis and the Kolmogorov-Smirnov test were employed to assess the normality of the variables. Descriptive statistics included means, standard deviations, medians, and min-max values. The Kruskal-Wallis test was utilized to evaluate non-parametric variables between groups. Spearman's Correlation test was applied to analyze numerical data. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The distribution of serum ALT, AST, lactic acid, and TNF-α levels, along with liver tissue levels of SOD, GPx, and CAT enzyme activities for the experimental groups, is presented in Table 1.

A comparison of serum ALT levels across the groups showed that the IR group had significantly higher serum ALT levels compared to the control group (p=0.001). The 50-GR group exhibited a significant reduction in serum ALT levels compared to those who received only IR (p=0.031). Although serum ALT levels were lower in the 100-GR group compared to the IR group, the difference was not statistically significant (p=0.177). Similarly, serum AST levels were significantly higher in the IR group compared to the control group (p=0.001). Both the 50-GR and 100-GR groups showed significant

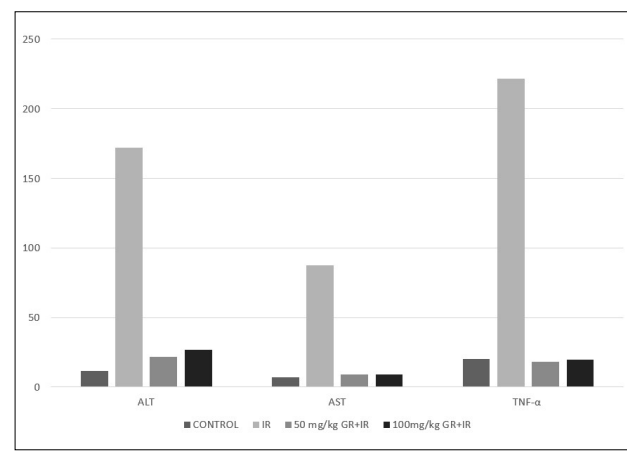

Figure 2. Comparison of serum ALT, AST, and TNF-α levels among the groups.

decreases in serum AST levels compared to the IR group (p=0.02, p=0.046), with no significant difference between the 50-GR and 100-GR groups (p=1.00). Serum TNF-α levels were also compared between the groups. These levels were significantly elevated in the IR group compared to the control group (p=0.011). There was a significant reduction in serum TNF-α levels in both the 50-GR and 100-GR groups compared to the IR group (p=0.004, p=0.015). No significant difference was observed between the 50-GR and 100-GR groups (p=1.00) (Fig. 2).

Serum lactic acid levels were significantly higher in the IR group subjects than in the control group subjects (p=0.07). The levels were significantly lower in both the 50-GR and 100-GR group subjects compared to the IR group subjects (p=0.04, p=0.015). There was no significant difference between the 50-GR and 100-GR groups (p=1.00). The analysis of liver tissue levels of SOD activity revealed significantly decreased SOD enzyme activity in the IR group compared to the control group (p=0.003). SOD enzyme activity was significantly increased in the 100-GR group subjects compared to the IR group (p=0.003). There was an increase in SOD enzyme activity in the 50-GR group compared to the IR group, though this difference was not statistically significant (p=0.059) (Fig. 3).

The comparison of liver tissue levels of CAT enzyme activity showed decreased activity in the IR group compared to the control group (p=0.22). CAT enzyme activity levels were increased in both the 50-GR and 100-GR groups compared to the IR group; however, these differences were not statistically significant (p=0.097, p=0.077). The comparison of liver tissue GPx levels revealed significantly decreased enzyme activity in the IR group compared to the control group (p=0.002). GPx enzyme activity was significantly increased in the 100-GR group compared to the IR group (p=0.001). There was an increase in GPx enzyme activity in the 50-GR group compared to the IR group; however, the difference was not statistically significant (p=0.15).

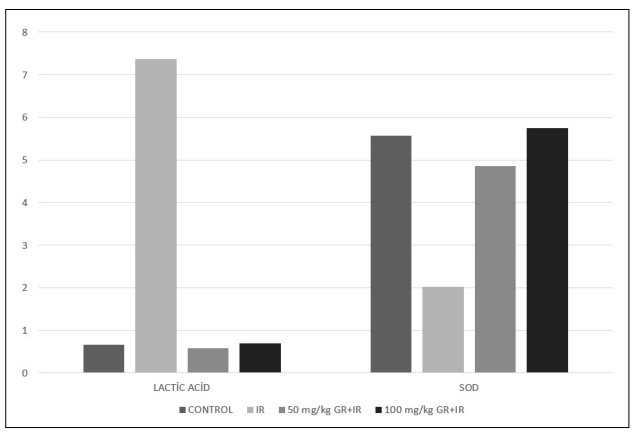

Figure 3. Comparison of SOD and lactic acid levels among the groups.

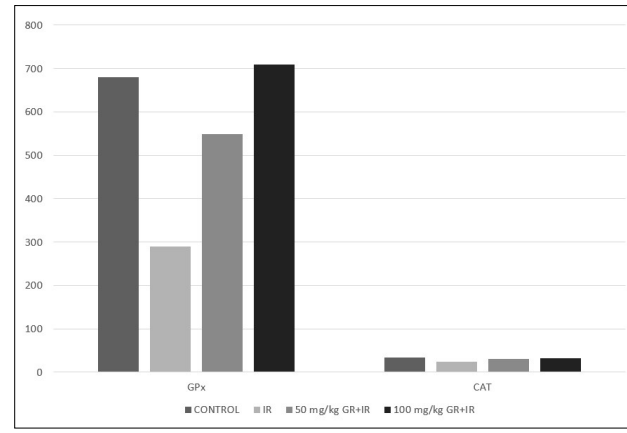

Figure 4. Vacuolization of pericentral hepatocytes in the IR group (hematoxylin and eosin stain, 200x magnification).

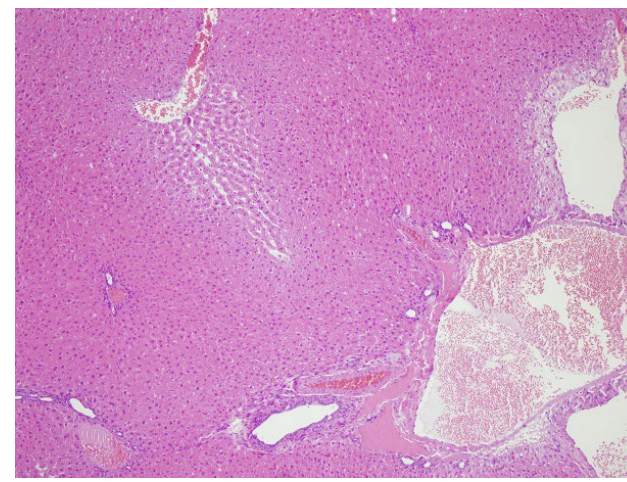

Figure 5. Congestion of the portal and central veins in the 50-GR group (hematoxylin and eosin stain, 40x magnification).

Histopathological Assessment Results

Upon examining the control group, one subject exhibited minimal vacuolization (Suzuki score: 1), and another showed minimal congestion (Suzuki score: 1), but the remaining subjects were normal (Suzuki score: 0). In the IR group, all subjects showed minimal congestion, with slight vacuolization in two subjects and minimal vacuolization in others (Fig. 4). Moderate liver injury was detected in two subjects (Suzuki score: 3) and mild liver injury in five other subjects (Suzuki score: 2) within the IR group. Examination of the 50-GR group revealed minimal congestion (Suzuki score: 1) in two subjects, while the remaining subjects were normal (Suzuki score: 0) (Fig. 5). In the 100-GR group, one subject exhibited minimal congestion (Suzuki score: 1), and the others were normal (Suzuki score: 0). Histological assessments indicated no necrosis in any subjects. The histopathological examinations showed significantly higher Suzuki scores in the IR group compared to the control group (p=0.004). Suzuki scores were significantly lower in the 50-GR and 100-GR group subjects than in the IR group subjects (p=0.04, p=0.01). There was no significant difference between the 50-GR and 100-GR group subjects (p=1.00).

DISCUSSION

The concept of hepatic IR injury was first introduced to the medical literature through an experimental liver transplantation study, and since then, many different clinical scenarios have been identified as causes of hepatic IR injury.[4] The process of organ removal and storage during liver transplants is referred to as cold IR injury. Conversely, warm IR injury occurs under hypovolemic shock due to the Pringle maneuver, which is used to reduce bleeding during liver resections and in cases of liver trauma, among various other clinical scenarios.[8]

Hepatic IR injury is a significant cause of early graft failure in liver transplantations and contributes to increased mortality and morbidity in other liver surgeries. This has spurred a rise in research aimed at understanding the mechanisms of this injury, particularly over the last decade.[9] With an understanding of injury mechanisms, several pharmacological agents and surgical techniques have been tested to prevent this injury in experimental studies.[2,3]

Geraniol, a monoterpene alkaloid, has demonstrated antioxidant and anti-inflammatory properties through multiple mechanisms, including increasing glutathione levels, reducing lipid peroxidation, inhibiting Nuclear Factor Kappa B (NF-κB) and Cyclooxygenase-2 (COX-2), and enhancing Interleukin-10 (IL-10) activity. Studies have examined the antioxidant, hepatoprotective, cardioprotective, neuroprotective, antitumoral, and antimicrobial efficacy of this molecule across various administration routes and doses.[10] Research has demonstrated that 200 mg/kg enteral administration reduces liver injury in the steatohepatitis model induced by methionine-choline deficiency, 100 mg/kg intraperitoneal administration enhances liver regeneration, and 50 mg/kg intraperitoneal administration prevents H2O2-induced oxidative stress-related liver injury.[11-13]

Our study found a significant increase in ALT and AST levels in the IR group, indicators of hepatic injury. In contrast, these levels were significantly decreased in the 50-GR group compared to the IR group. While a significant reduction in AST was observed in the 100-GR group compared to the IR group, ALT levels did not decrease, aligning with the literature. Similarly, Andrade et al. reported higher ALT levels in geraniol-inhaled rats compared to other groups, a finding not mirrored in AST levels.[14] The authors attributed the increase in ALT to the hepatotoxic effects of geraniol inhalation over 30 days. Although our study's design, administration route, and duration of geraniol exposure differed significantly from theirs, we observed a decrease in ALT levels, albeit not statistically significant, suggesting the experiment involved a limited number of subjects rather than hepatotoxic effects. In vivo studies on mice identified the hepatotoxic dose of geraniol as 120 mg/kg.[15] Upon reviewing the literature, we noted that an experimental hepatic IR study utilizing genistein, a flavonoid with established antioxidant properties, reported increased ALT and AST levels in the IR group compared to controls. These levels decreased in the genistein group, similar to our study's findings.[16] Similarly, Uylaş et al. conducted an experimental hepatic IR study administered quercetin, another flavonoid, to rats intraperitoneally and observed decreased ALT and AST levels in the treated group compared to the untreated IR group, aligning with our results.[17]

TNF-α is an important cytokine involved in the early response to IR injury and can be released from all liver cells, although it is predominantly released from Kupffer cells during hepatic IR.[18] Hepatic IR injury plays a key role in the transition from the early to the late response by increasing the expression of adhesion molecules and releasing cytokines that activate neutrophils.[19] Upon assessing the serum levels of TNF-α, a key cytokine in hepatic IR injury, we noted a significant increase in the IR group compared to the control group. Conversely, in the 50-GR and 100-GR groups, serum TNF-α levels were significantly reduced compared to the IR group, indicating that the geraniol-treated groups were less affected by IR injury, consistent with our hypothesis.

Lactic acid, directly related to tissue perfusion, rises in conditions such as myocardial infarction, shock, and necrotizing tissue infections, serving as a critical indicator of ischemia and liver failure. Our findings indicate a significant elevation in serum lactic acid levels in the IR group compared to other groups. While the lactic acid levels in the 50-GR and 100-GR groups were lower than those in the IR group, no significant differences were observed between the groups receiving different doses. The experimental hepatic IR study by Peralta et al. on rats showed that ischemic preconditioning reduced hepatic injury and, correspondingly, lactic acid levels, aligning with our findings, through the activation of adenosine monophosphate-activated protein kinase.[20] SOD activity serves as the primary defense against OFRs, and a decrease in this activity is linked to increased severity of oxidative damage.[21] Our study indicated significantly lower SOD activity in the liver tissue of the IR group compared to other groups. In the 100-GR group, however, the liver tissue SOD level was significantly higher than in the IR group, and there was also an increase in the 50-GR group, though it was not statistically significant in comparison to the IR group. Similar to our study, an experimental hepatic IR study involving rats and the dioscin molecule—a saponin with antioxidant properties derived from plants—reported increased SOD activity and reduced hepatic injury.[22] In contrast, a study on the pharmacological properties of the geraniol molecule found no significant increase in SOD enzyme activity in rats given high-dose oral geraniol for four weeks, unlike the results of our study and other literature.[15] Our study revealed that the liver tissue GPx level was significantly lower in the IR group than in the control group, while this activity was significantly higher in the 100-GR group compared to the IR group. Although the 50-GR group showed increased enzyme activity levels relative to the IR group, the difference was not statistically

significant. GPx activity in liver tissue, crucial for protecting membrane lipids and hemoglobin against oxidative stress by reducing organic hydroperoxides, was enhanced in the geraniol-treated groups, demonstrating the molecule's protective effect against hepatic IR injury.[23]

Reviewing the literature, experimental hepatic IR studies on CAT activity have shown that CAT activity increases significantly with substances like crocin and tocopherol, antioxidant molecules with proven effects on hepatic IR injury.[24,25] In our study, CAT activity in liver tissue was the lowest in the IR group, consistent with the literature. Although CAT activity was higher in the 50-GR and 100-GR groups compared to the IR group, no statistically significant elevation was detected. There was a tendency for an increase in liver tissue levels of CAT enzyme activity in the subjects administered the geraniol molecule, but the increase was not statistically significant, which was attributed to the limited number of study subjects.

Lai et al.'s study on rats found that acetyl-3-aminoethyl salicylate, which is used as an antioxidant, prevents liver injury by inhibiting the High Mobility Group Box 1/Toll-Like Receptor 4 (HMGB-1/TLR4) pathway and reducing the Suzuki score. [26] Another investigation explored hepatic IR injury in rats undergoing liver transplantation using the Kamada method. It was observed that the levels of AST, ALT, lactate dehydrogenase (LDH), and gamma-glutamyl transferase (GGT), as well as Suzuki scores, were lower in zoledronate liposome-treated rats than in non-treated rats.[27] A study demonstrated that the geraniol molecule reduced IR injury by decreasing oxidative stress through the nuclear factor erythroid 2-related factor 2 heme oxygenase-1 (Nrf-2/HO-1) pathway, significantly reducing congestion in liver tissue in rats.[28] In our study, histological assessments revealed that the Suzuki score, an indicator of hepatic injury, was significantly higher in the IR group compared to other groups, aligning with other parameters and literature. There was no significant difference in Suzuki scores between the 50-GR and the 100-GR groups. Additionally, necrosis did not develop in any subjects, likely due to the short ischemia period.

CONCLUSION

Our study demonstrated that the geraniol molecule could biochemically and histopathologically reduce experimental liver IR injury in rats. The relevance of these findings to clinical practice will depend on further validation through comprehensive, multicenter studies involving geraniol.

Ethics Committee Approval: This study was approved by the Istanbul University Ethics Committee (Date: 22.10.2020, Decision No: 57885).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: E.T., V.D., O.A.; Design: E.T., V.D., O.A., S.E.; Supervision: V.D., O.Ş., O.A., S.E.; Resource: E.T., O.Ş., O.A., S.E.; Materials: E.T., İ.M.B., N.K.; Data collection and/or processing: E.T., İ.M.B., N.K.; Analysis and/or interpretation: E.T., V.D., O.Ş.; Literature search: E.T., O.A., S.E.; Writing: E.T., O.A., O.Ş.; Critical review: V.D., İ.M.B., NK., O.Ş.

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DENEYSEL ÇALIŞMA - *ÖZ*

Sıçanlarda oluşturulan hepatik iskemi reperfüzyon hasarı modelinde geraniolün etkisi

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AMAÇ: Hepatik iskemi/reperfüzyon (I/R) hasarı; karaciğer rezeksiyonları, travma, şok gibi durumlarda gelişebilen önemli bir klinik durumdur. Geraniol; doğada yaygın bulunan ve antioksidan, hepatoprotektif özellikleri gösterilmiş izoterpen grubu bir moleküldür.Çalışmamızda sıçanlarda deneysel karaciğer I/R hasarı oluşturarak, geraniolün hasara etkisini araştırmayı amaçladık.

GEREÇ VE YÖNTEM: 350-400 gr ağırlığında, 28 adet Wistar Albino türü erkek sıçan kullanıldı. Sıçanlar kontrol grubu, I/R grubu, 50 mg/kg geraniol+ I/R grubu ve 100 mg/kg geraniol+ I/R grubu olarak 4'e ayrıldı. İskemi süreleri 15 dk, reperfüzyon süreleri 20 dk olarak belirlendi. İskemiye geraniol uygulamasının 15. dk'sında başlandı. Serumlardan ALT, AST, laktik asit düzeyleri ölçüldü. Karaciğer dokularından SOD, CAT ve GPx aktivite düzeyleri ölçüldü. Karaciğer dokuları histopatolojik olarak incelendi.

BULGULAR: Geraniol molekülünün intraperitoneal olarak 50 mg/kg ve 100 mg/kg uygulanmasının, AST, laktik asit ve TNF-α düzeylerini anlamlı şekilde azalttığı görülmüştür. Serum ALT düzeyinin ise 50 mg/kg uygulanan grupta anlamlı şekilde azaldığı gösterilmesine rağmen, 100 mg/kg uygulanan grupta olan azalmada anlamlılık saptanmamıştır. SOD ve GPx enzim aktivitelerinin 100 mg/kg grubunda anlamlı şekilde arttığı gösterilmiş, ancak 50 mg/kg grubunda enzim düzeylerinde artış olmasına rağmen anlamlılık saptanmamıştır. Yine CAT enzim aktivitesinin 50 mg/kg ve 100 mg/kg gruplarında artmış olduğu gösterilmesine rağmen, artış anlamlı bulunmamıştır. Suzuki skorunun, 50 mg/kg ve 100 mg/kg grubunda anlamlı şekilde azaldığı saptanmıştır.

SONUÇ: Çalışmada geraniol molekülünün, hepatik hasarı biyokimyasal ve histopatolojik olarak azalttığı ve antioksidan savunma enzimlerini arttırdığı gösterilmiş, böylece yapılacak geniş merkezli, kapsamlı çalışmalarla desteklenirse hepatik I/R hasarını engellemede kullanılabileceği sonucuna varılmıştır.

Anahtar sözcükler: Geraniol; iskemi-reperfüzyon hasarı; karaciğer; oksidatif stres.

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