EXPERIMENTAL STUDY

Impact of the 1,2,3-triazole compound derived from salicylaldehyde on localized and systemic organ injury in an experimental superior mesenteric artery ischemia/reperfusion model

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ABSTRACT

BACKGROUND: Despite several studies indicating the efficacy of different molecules in preventing ischemia/reperfusion (I/R) damage, the most effective treatment remains unknown.

METHODS: This study included 28 male Sprague rats, which were randomly assigned to four equal groups, with seven rats in each group: Group S (Sham), Group C (Control), Group E (Ethanol), and Group T (Triazole). The superior mesenteric arteries of rats in all groups except Group S were exposed and closed with a vascular clamp, and ischemia was induced for one hour. Oxidative stress parameters, ischemia markers, and biochemical tests indicating organ function were examined.

RESULTS: The mean total antioxidant status (TAS) value of Group T was significantly higher than those of Groups C and E, while being significantly lower than that of Group S ($p=0.001$). The mean total oxidant status (TOS) value of Group T was significantly lower than those of Groups C and E and significantly higher than that of Group S ($p<0.001$). Although the mean oxidative stress index (OSI) value of Group T was markedly lower than those of Groups C and E, no statistically significant difference was observed compared to Group S ($p=0.002$, $p<0.001$, and $p=0.721$, respectively). The mean ischemia-modified albumin (IMA) value of Group T was significantly lower than those of Groups C and E and significantly higher than that of Group S ($p<0.001$). The mean malondialdehyde (MDA) value of Group T was significantly lower than those of Groups C and E and significantly higher than that of Group S ($p<0.001$).

CONCLUSION: This study represents the first investigation into the effect of a 1,2,3-triazole compound derived from salicylaldehyde on ischemia/reperfusion injury. The findings provide strong evidence that the 1,2,3-triazole compound significantly enhances the prevention or treatment of experimental I/R injury. We conclude that this triazole derivative may represent a viable therapeutic option for the treatment and prevention of I/R injury, supported by further experimental and clinical research. The triazole is expected to exhibit enhanced protective properties, particularly when solubilized using alternative methods.

Keywords: Ischemia/reperfusion; triazole; liver; small intestine; superior mesenteric artery.

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INTRODUCTION

Ischemia/reperfusion (I/R) injury frequently presents as a clinical condition associated with increased mortality following acute mesenteric ischemia, shock, laparoscopic procedures, and major surgical interventions. The incidence and mortality rates are gradually increasing.[1,2] I/R injury arises from oxidative stress, lipid peroxidation, and oxygen-derived free radicals.[3] Reactive oxygen species (ROS) are primarily responsible for the damage induced by ischemia/reperfusion. ROS are generated by four interrelated biochemical mechanisms: xanthine oxidase-mediated processes, the mitochondrial electron transport chain (ETC), nitric oxide synthase, and phagocytic cells.[4,5] The extent of tissue damage resulting from ischemia/reperfusion depends on variations in ischemia duration and the distinct structural and biochemical metabolic characteristics of tissues and organs.[4-6] Tissue injury resulting from ischemia/reperfusion may extend beyond the ischemic area, potentially inflicting varying degrees of damage on remote organ systems. Damage to remote organs is believed to result from circulating leukocytes, inflammatory cytokines, and systemic oxidants that induce the migration of polymorphonuclear leukocytes to distant sites, along with reactive oxygen species.[6-10] This study examined regional damage by analyzing terminal ileum tissue and distant organ damage using liver tissue samples.

Although multiple studies have reported the efficacy of different molecules in mitigating I/R injury, the most effective therapeutic intervention remains unclear.[3,11] Consequently, further studies are required to improve the prevention of ischemia/reperfusion injury. The primary hypothesis of this study is that ischemia/reperfusion damage can be prevented by inhibiting xanthine oxidase activity during ischemia/reperfusion. The objective was to examine the efficacy of a 1,2,3-triazole derivative as a xanthine oxidase inhibitor in preventing I/R damage.

1,2,3-triazole derivatives are novel compounds identified as inhibitors of xanthine oxidase. The primary xanthine oxidase inhibitor used in the clinical treatment of gout is allopurinol, which is associated with significant side effects due to its involvement in purine metabolism. Consequently, triazole compounds have been identified as xanthine oxidase inhibitors lacking purine analog structures in in vitro experiments arising from novel drug research.[12] Numerous studies have demonstrated that 1,2,3-triazole compounds exhibit antiallergic, antibacterial, and antituberculous activity in vitro.[13-15] Nonetheless, in vivo studies demonstrating the effects of these newly identified triazole compounds on xanthine oxidase inhibition and ischemia/reperfusion damage are lacking. This study represents the first in vivo investigation demonstrating the effect of a 1,2,3-triazole derivative on xanthine oxidase inhibition and ischemia/reperfusion injury.

The primary hypothesis of this study is that ischemia/reperfusion damage can be prevented by inhibiting xanthine oxidase activity using a 1,2,3-triazole compound. The primary outcome of the investigation was the oxidative stress index (OSI).

MATERIALS AND METHODS

This study was carried out at the University of Health Sciences Hamidiye Animal Experiments Laboratory after approval by the Hamidiye Animal Experiments Local Ethics Committee (Date: 24.07.2024, Approval Number: 02/03). The study included 28 male Sprague rats with an average weight of 200±20 grams and aged 16-20 weeks. Throughout the investigation, all rats were maintained at a standard room temperature of 21±2°C and humidity levels of 40-60%, under a 12-hour light/12-hour dark cycle. Each cage housed four rats, which were kept in metal cages and provided with standard rat feed and tap water. Cage maintenance was performed routinely with daily inspections. During the study, all rats were treated humanely in accordance with the Guide for the Care and Use of Laboratory Animals. All surgical interventions were performed under anesthesia. For anesthetic induction, ketamine hydrochloride (Ketalar® vial, 50 mg/mL, Eczacıbasi, Istanbul, Türkiye) was administered intraperitoneally (ip) at a dose of 80 mg/kg, and xylazine hydrochloride (ROMPUN® vial, 23.32 mg/mL, Bayer) was administered intraperitoneally at a dose of 10 mg/kg.

Rats were divided into four equal groups, with seven rats in each group:

Group S (Sham) (n=7): Laparotomy

Group C (Control) (n=7): 1 mL intraperitoneal saline + laparotomy + ischemia/reperfusion

Group E (Ethanol) (n=7): 1 mL intraperitoneal saline/ethanol + laparotomy + ischemia/reperfusion

Group T (Triazole) (n=7): 1 mL intraperitoneal 20 mg/kg triazole/ethanol/saline + laparotomy + ischemia/reperfusion.

After eight hours of fasting, the weights of all rats were recorded under anesthesia. All rats were anesthetized, and vascular access was subsequently obtained using a 26G angiocath inserted into the tail vein. Following shaving of the abdominal regions of all rats and disinfection of the surgical field with povidone-iodine under operating room conditions, 1 mL of saline was administered to the rats in Group C, 1 mL of ethanol/saline (1/9) to the rats in Group E, and 20 mg/kg of triazole/ethanol/saline in 1 mL was administered intraperitoneally to the rats in Group T. After 30 minutes, a 3-cm full-thickness midline abdominal incision was performed in all rats. Immediately after laparotomy, the superior mesenteric arteries of rats in all groups except Group S were exposed and closed with a vascular clamp, and ischemia was induced for one hour. Reperfusion was subsequently performed for one hour (1). At the end of this period, approximately 4-6 mL of blood samples for biochemical analysis were obtained via intracardiac puncture. All rats were sacrificed to obtain liver and terminal ileum tissue samples for histological analysis. The inclusion of the ethanol group in our investigation was due to the use of the 1,2,3-triazole compound as a solvent for intraperitoneal administration. Ethanol was used in Groups E and T at a concentration of 10%.

Biochemical Method (Blood)

The individual performing the blood sample analyses was blinded to group assignments. Blood samples were analyzed for glucose (GLU), aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), and serum creatinine (CR) using an Abbott Architect c16000 analyzer (Abbott, Abbott Park, IL, USA). Total antioxidant status (TAS) and total oxidant status (TOS) were assessed using the Real Assay Total Antioxidant Status Assay Kit (Mega Medikal, Ankara, Türkiye). TAS values were expressed as mmol ascorbic acid equivalent per liter, while TOS values were expressed as μmol H_2O_2 equivalent per liter. The oxidative stress index was calculated using the formula:

OSI (AU) = (TOS [μmol/L]) / (TAS [mmol Trolox equivalent/L] × 100) (19).

Ischemia-modified albumin (IMA) and malondialdehyde (MDA) concentrations were measured using the method described by Ertürk et al.[1,16]

Histopathological Examination

All assessments were conducted by the same pathologist, who was unaware of the group assignments.

Liver: One-hour post-reperfusion, tissue samples were obtained from the right lobe of the liver. Liver tissue samples were immersed in a 10% formaldehyde solution, embedded in paraffin blocks, sectioned at 5 μm thickness, and stained with hematoxylin-eosin. Biopsy specimens were evaluated at 200 magnification using a sequential scale to determine the severity of liver injury:

• Grade 0: No evidence of mild injury or any injury present.

• Grade 1: Minor damage characterized by cytoplasmic vacuolation and localized nuclear pyknosis.

• Grade 2: Widespread nuclear pyknosis, cytoplasmic hypereosinophilia, intercellular loss, and mild neutrophilic infiltration.

• Grade 3: Significant injury characterized by disintegration of hepatic cords, hemorrhage, and pronounced polymorphonuclear neutrophil infiltration.

Each sample was evaluated using an average of 100 adjacent points on a 1 mm² grid.[17]

Small Intestine: Tissue samples designated for histopathological analysis were stained with hematoxylin and eosin, examined under light microscopy at 10× and 40× magnification, and scored according to the modified Chiu scoring system.[18] The scoring criteria were as follows:

• Grade 0: Normal,

• Grade 1: Desquamation and necrosis involving one-third of the villi,

• Grade 2: Progressive desquamation in the center of the villi,

• Grade 3: Necrosis with desquamation and involvement of crypt cells beneath one-third of the villi,

• Grade 4: Necrosis of one-third of the crypt cells,

• Grade 5: Total loss of the basal lamina.

Preparation of 1,2,3-Triazole

The target compound, a 1,2,3-triazole derivative derived from salicylaldehyde and previously synthesized by a member of our group member,[19] was re-synthesized as reported in the literature and re-characterized using various spectroscopic techniques for this study.[19] Initially, 4-chloroaniline was treated with chloroacetyl chloride in the presence of $NaHCO_3$ in MeCN at 0°C to obtain 2-chloro-N-(4-chlorophenyl)acetamide. Subsequently, 2-chloro-N-(4-chlorophenyl)acetamide was reacted with NaN3 in dimethyl sulfoxide (DMSO) at room temperature to obtain 2-azido-N-(p-tolyl)acetamide. On the other hand, salicylaldehyde was reacted with propargyl bromide in the presence of K_2CO_3 in MeCN, yielding the 2-(prop-2-yn-1-yloxy)benzaldehyde compound at the end of the reaction. Finally, to synthesize the target 1,2,3-triazole compound, the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) method was utilized.[20-23] In this step, 2-azido-N-(p-tolyl)acetamide (azide) and 2-(prop-2-yn-1-yloxy)benzaldehyde compound (alkyne) were reacted in the presence of sodium L-ascorbate and $CuSO_4 \cdot 5H_2O$ in a MeOH/H_2O (1:1) solvent system at room temperature, resulting in the synthesis of the target compound.[19]

Sample Calculation

MedCalc® Statistical Software version 19.7.2 (MedCalc Software Ltd., Ostend, Belgium; https://www.medcalc.org; 2021) was used. According to Kartal et al.,[3] the analysis indicated a type I error rate of α=0.05 and a statistical power of 1-β=80%. The sample size was determined to be five rats per group. Due to the absence of experimental studies involving the combination of ethanol and triazole, and because the anticipated difference was expected to be comparable to that between the control and triazole groups, the sample size for the other groups was also set at five. Considering possible losses, seven rats were ultimately included in each group.

Statistical Analysis

SPSS version 15.0 software for Windows was used for statistical analysis. Descriptive statistics included numbers and percentages for categorical variables and mean, standard deviation, minimum, and maximum values for numerical variables. The Kruskal-Wallis test was applied when numerical variables did not show a normal distribution, whereas one-way analysis of variance (ANOVA) was used when the normality assumption was met across groups. Subgroup analyses in nonparametric tests were performed using the Mann-Whitney U test and interpreted with Bonferroni adjustment. Differences in rates among groups were analyzed using the chi-square test. The level of statistical significance was set at $p<0.05$.

RESULTS

During the study, rats no. 2 and 6 from the Sham group and rat no. 3 from the Ethanol group were excluded due to death following anesthesia induction.

No statistically significant difference was observed in the mean body weight of the rats among the groups (p=1.000). Statistically significant differences were observed among the groups in oxidative stress parameters (mean TAS, TOS, and OSI) and ischemia markers (mean IMA and MDA) (p<0.001). Table 1 presents the mean body weights of the rats in each group, along with oxidative stress parameters and ischemia markers.

Significant differences were also detected in the biochemical parameters (GLU, AST, ALT, BUN, and CR) among the groups (p<0.001). The biochemical parameters of the rats are presented in Table 2.

Table 1. Body weight, oxidative stress parameters, and ischemia markers of rats in the study groups

Parameter	Sham	Ethanol	Triazole	Control	p*
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
Weight	193.9±7.2	193.8±4.1	193.9±14.0	194.0±10.5	
	(181.9-204)	(188-199)	(180-215.7)	(182.3-212)	1.000
TAS	0.69±0.10	0.18±0.06	0.39±0.05	0.22±0.06	
	(0.60-0.85)	(0.11-0.27)	(0.32-0.48)	(0.12-0.29)	<0.001
TOS	2.85±0.42	16.25±1.17	9.57±1.27	13.88±1.79	
	(2.39-3.25)	(15.46-18.53)	(8.27-11.78)	(12.06-16.89)	<0.001
OSI	4.22±0.91	99.98±33.66	24.92±4.56	68.98±26.46	
	(2.85-5.31)	(61.37-142.11)	(17.86-30.16)	(52.49-124.14)	<0.001**
IMA	0.32±0.04	1.79±0.07	1.19±0.09	1.64±0.03	
	(0.28-0.38)	(1.71-1.88)	(1.10-1.34)	(1.61-1.69)	<0.001
MDA	0.74±0.09	3.01±0.28	1.67±0.16	2.70±0.29	
	(0.65-0.86)	(2.70-3.34)	(1.44-1.97)	(2.36-3.06)	<0.001

**Mann-Whitney U test; p<0.017. SD: Standard deviation; Min: Minimum; Max: Maximum; TAS: Total antioxidant status; TOS: Total oxidant status; OSI: Oxidative stress index; IMA: Ischemia-modified albumin; MDA: Malondialdehyde.

Table 2. Biochemical parameters of rats in the study groups

Parameter	Sham	Ethanol	Triazole	Control	
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	p*
GLU	83.0±8.2	142.7±30	110.7±4.1	127.6±13.1	
	(73-92)	(139-147)	(105-116)	(108-148)	<0.001
AST	69.0±4.9	104.5±7.0	85.0±6.2	94.9±6.3	
	(65-77)	(92-112)	(73-91)	(86-105)	<0.001
ALT	54.6±5.7	93.3±3.8	79.7±5.0	86.3±8.1	
	(45-60)	(88-98)	(75-90)	(76-99)	<0.001**
BUN	31.0±5.5	75.0±7.1	56.7±6.2	66.1±8.4	
	(25-38)	(66-87)	(50-68)	(53-77)	<0.001
CR	0.51±0.06	0.85±0.07	0.74±0.07	0.82±0.10	
	(0.44-0.57)	(0.74-0.93)	(0.62-0.85)	(0.69-0.99)	<0.001

**Mann-Whitney U test; p<0.017. SD: Standard deviation; Min: Minimum; Max: Maximum; GLU: Glucose; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BUN: Blood urea nitrogen; CR: Creatinine.

Analysis of the biochemical parameters revealed that the mean GLU value in Group T was significantly lower than those in Groups C and E and significantly higher than that in Group S (p=0.006, p<0.001, and p<0.001, respectively). The mean AST value in Group T was significantly lower than those in Groups C and E and significantly higher than that in Group S (p=0.043, p<0.001, and p=0.001, respectively). The mean ALT value in Group T was lower than that in Group C without reaching statistical significance, showed a statistically significant decrease compared to Group E, and a statistically significant increase compared to Group S (p=0.061, p=0.005, and p=0.004, respectively). The mean BUN value in Group T was lower than that in Group C without statistical significance, significantly lower than that in Group E, and significantly higher than that in Group S (p=0.119, p=0.001, and p<0.001, respectively). The mean CR value in Group T was lower than those of Groups C and E without reaching statistical significance and significantly higher than that of Group S (p=0.424, p=0.140, and p<0.001, respectively). Subgroup analyses are summarized in Table 3.

Upon examination of oxidative stress parameters, the mean TAS value of Group T was significantly higher than those of Groups C and E, while being significantly lower than that of Group S (p=0.001). The mean TOS value of Group T was significantly lower than those of Groups C and E and significantly higher than that of Group S (p<0.001). Although the mean OSI value of Group T was markedly lower than those of Groups C and E, no statistically significant difference was observed compared to Group S (p=0.002, p<0.001, and p=0.721, respectively).

Evaluation of the ischemia markers demonstrated that the mean IMA value of Group T was significantly lower than those of Groups C and E and significantly higher than that of Group S (p<0.001). The mean MDA value of Group T was also significantly lower than those of Groups C and E and significantly higher than that of Group S (p<0.001). Subgroup analyses of oxidative stress parameters and ischemia markers are presented in Table 4.

Histological evaluation revealed no liver damage in any of the rats across the groups, precluding statistical comparison of the mean liver histopathological scores (LHS). No statistically significant difference was observed among the intestinal histopathological scores (IHSs) of the groups (p=0.345). The mean histopathological scores of the groups are summarized in Table 5.

DISCUSSION

In this study, the mean TAS values of Group T were statistically significantly higher than those of Groups C and E. The mean TOS, OSI, IMA, MDA, GLU, and AST values of Group T were statistically significantly lower than those of Groups C and E. The mean ALT and BUN values of Group T were statistically significantly lower than those of Group E.

Despite being a critical clinical condition associated with significant mortality, an effective treatment strategy for I/R

Table 3. Subgroup analyses of biochemical parameters among the groups

	Group	Sham	Ethanol	Triazole
		p	p	p
GLU	Ethanol	<0.001		
	Triazole	<0.001	<0.001	
	Control	<0.001	0.022	0.006
AST	Ethanol	<0.001		
	Triazole	0.001	<0.001	
	Control	<0.001	0.065	0.043
ALT	Ethanol	<0.001		
	Triazole	0.004**	0.005**	
	Control	<0.001	0.270	0.061**
BUN	Ethanol	<0.001		
	Triazole	<0.001	0.001	
	Control	<0.001	0.201	0.119
CR	Ethanol	<0.001		
	Triazole	<0.001	0.140	
	Control	<0.001	1.000	0.424

**Mann-Whitney U test; p<0.017. GLU: Glucose; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BUN: Blood urea nitrogen; CR: Creatinine.

Table 4. Subgroup analyses of oxidative stress parameters and ischemia markers among the groups

	Group	Sham	Ethanol	Triazole
		p	p	p
TAS	Ethanol	<0.001		
	Triazole	<0.001	<0.001	
	Control	<0.001	1.000	0.001
TOS	Ethanol	<0.001		
	Triazole	<0.001	<0.001	
	Control	<0.001	0.024	<0.001
OSI	Ethanol	<0.001		
	Triazole	0.721	<0.001	
	Control	0.004**	0.032**	0.002**
IMA	Ethanol	<0.001		
	Triazole	<0.001	<0.001	
	Control	<0.001	0.002	<0.001
MDA	Ethanol	<0.001		
	Triazole	<0.001	<0.001	
	Control	<0.001	0.143	<0.001

**Mann-Whitney U test; p<0.017. TAS: Total antioxidant status; TOS: Total oxidant status; OSI: Oxidative stress index; IMA: Ischemia-modified albumin; MDA: Malondialdehyde.

Table 5. Histopathological findings of rats in the study groups

	Sham	Ethanol	Triazole	Control	p
LHS, n (%)					
No damage	5 (100)	6 (100)	7 (100)	7 (100)	-
IHS					
No damage	5 (100)	4 (66.7)	7 (100)	6 (85.7)	0.345
Damage	0 (0.0)	2 (33.3)	0 (0.0)	1 (14.3)	

LHS: Liver histopathological score; IHS: Intestinal histopathological score.

damage has yet to be established.[3] The incidence and mortality rates are increasing.[1,2] Consequently, the prevention and/or treatment of I/R injury is of paramount therapeutic importance. Although the literature suggests that I/R damage can be reduced using various medications, the underlying mechanisms remain inadequately elucidated in these studies.[1,2] Therefore, inhibiting ROS production, which contributes to I/R damage through multiple formation pathways, is considered crucial for the development of effective treatment strategies. Xanthine oxidase, an enzyme involved in ROS production, is implicated in organ damage through endothelial dysfunction.[8] Accordingly, compounds that inhibit xanthine oxidase are anticipated to effectively reduce I/R damage.

Ethanol has a narrow therapeutic window, and both low and high doses can produce opposing effects. Studies in the literature report that acute ethanol exposure causes ischemia.[24, 25] Our investigation revealed that acute ethanol exposure negatively affected all oxidative stress parameters, ischemia markers, and biochemical indicators, with statistically significant changes observed in TOS, IMA, and GLU values. These results indicate that acute ethanol exposure exacerbates I/R damage, which is consistent with existing research.[24,25]

This study demonstrated no statistically significant difference in mean IHSs among the groups. Due to the absence of liver injury in any rat with respect to LHS, statistical comparison was not possible. These findings were attributed to the short I/R duration and insufficient time for damage to manifest in regional and distant organs.

Triazole derivatives have recently been investigated as alter-

native therapeutic agents due to the side effects of allopurinol (e.g., hepatotoxicity and hypersensitivity reactions), which is commonly used in the treatment of gout.[12] The present study aimed to examine the efficacy of the triazole derivative outside its original development context, suggesting its potential to alleviate I/R damage through xanthine oxidase inhibition. No in vivo studies were identified in the literature concerning the impact of the 1,2,3-triazole derivative on I/R injury. Consequently, this research is considered the first study of its kind in the literature.

Due to the absence of studies evaluating the effects of triazole derivatives on I/R damage, the findings were compared with those from investigations involving other compounds and analyzed accordingly. Dexmedetomidine (Dex) is one of the most commonly investigated compounds for this purpose in research studies. Some studies examining the effects of Dex on I/R damage indicate that it generally exerts favorable effects on oxidative stress parameters, although these effects are not always statistically significant. Nevertheless, despite numerous investigations on Dex, evidence supporting its use in the treatment of I/R damage remains limited.[1,3] Our investigation demonstrated that all oxidative stress markers were significantly improved in the triazole group compared to Groups C and E. Given that ethanol administration in Group E adversely affected the mean oxidative stress parameters relative to Group C, it is noteworthy that triazole treatment substantially reduced oxidative stress compared to Group C, despite the presence of ethanol. This finding indicates that triazole may serve as an effective agent in reducing I/R damage. The reported effects of Dex on IMA and MDA levels are controversial.[1,26,27] In contrast, our study showed that triazole significantly decreased mean IMA and MDA values, suggesting a potential protective effect. The effects of Dex on biochemical indicators of organ function remain unclear in the existing literature.[1,26] In our study, triazole significantly reduced GLU and AST levels compared to Groups C and E, and ALT and BUN levels compared to Group E. These findings indicate that triazole may have a significant organoprotective effect. Dexamethasone is another compound commonly used to reduce I/R damage.[2,28] These investigations primarily assessed cellular immune suppression, and sufficient data regarding oxidative stress indicators, ischemia markers, and biochemical parameters were not presented. Sun et al.[2] reported that dexamethasone resulted in reductions in BUN and CR levels.

Although experimental studies in the literature report that allopurinol may be effective in preventing I/R injury through inhibition of the xanthine oxidase enzyme, sufficient clinical evidence has not yet been presented.[29-32] Given the significant adverse effects associated with allopurinol, a purine analog, the use of newly synthesized non-purine analog triazole derivatives for this indication may be promising. In this study, the 1,2,3-triazole compound significantly improved all oxidative stress parameters, ischemia markers, and some biochemical indicators of organ function in an experimental superior mesenteric artery (SMA) I/R model. These results strongly suggest that the 1,2,3-triazole compound may be useful in the prevention and/or treatment of I/R injury. This study represents the first investigation in the literature examining the impact of a 1,2,3-triazole compound on I/R injury. Since 1,2,3-triazole compounds are already used in humans for other therapeutic indications, these findings suggest promising potential for accelerated clinical application in I/R injury. Moreover, because ethanol was used as the solvent for the triazole compound in our study, it is noteworthy that, despite the immediate adverse effects of ethanol, I/R damage was significantly reduced compared to the control group. Consequently, these findings indicate that triazole may exhibit even greater protective effects when dissolved in alternative solvents other than ethanol that do not exacerbate tissue injury.

Limitations of the Study

1. Experimental study design

2. As this is the first study, comparison with other results was not possible

3. The mechanism could not be fully elucidated due to a focus on clinical outcomes

4. Use of ethanol as a solvent.

CONCLUSION

In conclusion, I/R injury is a critical clinical condition following major surgical and laparoscopic procedures, with its incidence increasing. Despite numerous compounds being tested for its treatment and prevention, I/R injury remains a significant health problem due to the lack of an effective therapy. In response to the substantial adverse effects of allopurinol, novel 1,2,3-triazole derivatives have recently been developed as alternative therapeutic agents for gout management. However, there is a lack of research in the literature regarding the effects of 1,2,3-triazole derivatives on I/R injury. This study represents the first investigation into the effects of a 1,2,3-triazole derivative on ischemia/reperfusion injury. The findings of this study provide strong evidence that the 1,2,3-triazole compound significantly enhances the prevention or treatment of experimental I/R injury. We support the notion that 1,2,3-triazole derivatives may offer a viable therapeutic option for the treatment and prevention of I/R injury, supported by further experimental and clinical research. Triazole is anticipated to exhibit enhanced protective properties, particularly when dissolved using alternative methods.

Ethics Committee Approval: This study was approved by the Hamidiye Animal Experiments Local Ethics Committee (Date: 24.07.2024, Decision No: 02/03).

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DENEYSEL ÇALIŞMA - *ÖZ*

Deneysel superior mezenterik arter iskemi/reperfüzyon modelinde salisilaldehitten türetilmiş 1,2,3 triazol bileşiğinin lokalize ve sistemik organ hasarı üzerindeki etkisi

AMAÇ: Farklı moleküllerin iskemi/reperfüzyon (I/R) hasarını önlemede etkili olduğunu gösteren birçok çalışmaya rağmen, en etkili tedavi yöntemi henüz bilinmemektedir.

GEREÇ VE YÖNTEM: Bu çalışmada 28 erkek Sprague sıçanı kullanılmıştır. Sıçanlar, her grupta yedi sıçan olacak şekilde dört eşit gruba ayrılmıştır. Gruplar; Grup S (Sham), Grup C (Kontrol), Grup E (Etanol), Grup T (Triazol). Grup S hariç tüm gruplardaki sıçanların superior mezenterik arterleri açığa çıkarılıp vasküler klemp ile kapatılmış ve 1 saat boyunca iskemi oluşturulmuştur. Oksidatif stres parametreleri, iskemi belirteçleri ve organ fonksiyonlarını gösteren biyokimyasal testler incelenmiştir.

BULGULAR: Grup T ortalama Total antioksidan seviye (TAS) değeri Grup C ve E'ye göre istatiksel olarak anlamlı düzeyde yüksek, Grup S'ye göre anlamlı düzeyde düşük tespit edildi ($p=0.001$). Grup T ortalama Total oksidan seviye (TOS) değeri Grup C ve E'ye göre istatiksel olarak anlamlı düzeyde düşük, Grup S'ye göre anlamlı düzeyde yüksek tespit edildi ($p<0.001$). Grup T ortalama Oksidatif stres indeksi (OSI) değeri Grup C ve E'ye göre istatiksel olarak anlamlı düzeyde düşük, Grup S'ye göre yüksek olmasına rağmen istatiksel olarak anlamlı fark tespit edilmedi (Sırasıyla; $p=0.002$, $p<0.001$, $p=0.721$). Grup T ortalama skemi modifiye albümin (İMA) değeri Grup C ve E'ye göre istatiksel olarak anlamlı düzeyde düşük, Grup S'ye göre anlamlı düzeyde yüksek tespit edildi ($p<0.001$). Grup T ortalama Malendialdehit (MDA) değeri Grup C ve E'ye göre istatiksel olarak anlamlı düzeyde düşük, Grup S'ye göre anlamlı düzeyde yüksek tespit edildi ($p<0.001$).

SONUÇ: Bu çalışma, salisilaldehitten türetilmiş 1,2,3-triazol bileşiğinin iskemi/reperfüzyon hasarı üzerindeki etkisine ilişkin ilk araştırmayı temsil etmektedir. Bu çalışmanın bulguları, 1,2,3-triazol bileşiğinin deneysel İ/R hasarının önlenmesini veya tedavisini önemli ölçüde artırdığına dair güçlü kanıtlar sunmaktadır. Kapsamlı deneysel ve klinik araştırmalarla desteklenen triazol türevinin İ/R hasarının tedavisi ve önlenmesi için uygulanabilir bir tedavi seçeneği sunabileceğini savunuyoruz. Triazolün, özellikle alternatif yöntemlerle çözündürüldüğünde gelişmiş koruyucu özelliklere sahip olması beklenmektedir.

Anahtar sözcükler: İskemi/reperfüzyon, triazol, karaciğer, ince bağırsak, süperior mezenterik arter.

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