International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
ReAvailable online on: https://ijmpr.in/

Original Research Article

Hepatoprotective and antioxidant effect of Nigella sativa seed extract on Ethanol induced Liver damage in Rats

Afroz Abidi [1], Fardan Qadeer[2], Fariha Fatima[2], Ghizal Fatima[3]

[1]Prof. and head, Department of Pharmacology, Era's Lucknow Medical college, Lucknow
[2]Associate Professor, Department of Pharmacology, Era's Lucknow Medical college, Lucknow
[3]Associate Professor, Department of Biotechnology-Chronobiology Unit, Era University, Lucknow

OPEN ACCESS

Corresponding Author:

Dr. Afroz Abidi
Professor & HOD, Department of Pharmacology,
Era's Lucknow Medical College, Lucknow
Email: afrozabidi@gmail.com

Received: 16-01-2026
Accepted: 10-02-2026
Available online: 28-02-2026

ABSTRACT

Background: Alcohol-associated liver disease is a major cause of chronic liver morbidity and is primarily mediated through oxidative stress, inflammation, and depletion of endogenous antioxidant defenses. Nigella sativa has been traditionally used for various liver disorders and is reported to possess antioxidant and hepatoprotective properties. This study was done to assess the hepatoprotective and antioxidant potential of Nigella sativa seed extract (NSE) alone and in combination with silymarin in ethanol-induced alcoholic liver injury in rats.

Materials and Methods: Hepatotoxicity was induced by chronic oral administration of alcohol in male Wistar rats 30% v/v ethanol (2 ml/100 g body weight) for eight weeks. The animals were divided into six groups: normal control, ethanol control, silymarin (100 mg/kg), NSE 500 mg/kg, NSE 800 mg/kg, and NSE (500 mg/kg) plus silymarin. Serum liver enzymes (AST, ALT, ALP), hepatic lipid peroxidation (MDA), and antioxidant enzymes (SOD, GSH, CAT) were estimated. Histopathological analysis was performed from the hepatic tissue at the end of the study. Data were analyzed using one-way ANOVA and post-hoc multiple comparison test.

Results: Ethanol treatment resulted in a significant increase in serum AST, ALT, and ALP levels and raised hepatic malondialdehyde levels along with significant depletion of antioxidant enzymes ($p < 0.001$). Nigella sativa treatment resulted in a dose-dependent decrease in liver enzymes and lipid peroxidation and in restoration of antioxidant defenses. Nigella sativa and silymarin as a combination was optimal in hepatoprotection, with near normalization of biochemical and antioxidant parameters.

Conclusion: Nigella sativa seed extract demonstrates dose-dependent hepatoprotective and antioxidant activity against ethanol-induced liver damage. Combination therapy with silymarin provides increased protection and might be a potentially selective multi-targeted therapeutic strategy for alcoholic liver diseas.

Keywords: Nigella sativa; Alcoholic liver disease; Silymarin; Oxidative stress; Antioxidants.

INTRODUCTION

Alcohol-associated liver disease (ALD) is a major global public health crisis. It is the leading cause of chronic liver-related morbidity and mortality [1]. Chronic ethanol consumption is a major cause of chronic liver diseases because it is easily absorbed and sustained in the bloodstream, generating a wide range of liver diseases from steatosis, alcoholic hepatitis through fibrosis to cirrhosis [2] . Notwithstanding significant progress in knowledge of disease mechanisms, effective pharmacological therapy for ethanol-induced liver injury remains limited and requires further investigation on safer and multi-targeted hepatoprotective agents.[3]

Ethanol metabolism in hepatocytes is predominantly performed by alcohol dehydrogenase and the cytochrome P450 2E1 (CYP2E1) microsomal ethanol-oxidizing system [4]. CYP2E1 shows increased accumulation after repeated exposure to ethanol, generating reactive oxygen species (ROS), mediating lipid peroxidation, protein oxidation, and mitochondrial dysfunction [5]. The toxic metabolite acetaldehyde produced by ethanol exacerbates hepatocellular injury by forming protein adducts and impairing cellular repair pathways [6]. Recent evidence underlines mitochondrial oxidative stress, impaired β-oxidation, and ATP depletion as key events in ethanol-induced hepatotoxicity[7].

Beyond inducing oxidative stress, ethanol triggers inflammatory pathways through gut-derived endotoxins. Lipopolysaccharide-mediated activation of Kupffer cells triggers toll-like receptor-4 signaling and NF-κB activation, leading to increased production of pro-inflammatory cytokines such as tumor necrosis factor-α and interleukins [8]. Recent studies include NLRP3 inflammasome activation in increasing hepatic inflammation and progression of alcoholic hepatitis [9]. Ethanol-induced depletion of endogenous antioxidants such as glutathione, superoxide dismutase, and catalase further exacerbates liver injury [10].

Nigella sativa L. (black cumin) has been traditionally used in Ayurvedic and Unani medicine for liver dysfunction, gastrointestinal issues, and inflammation [11]. Its pharmacological activity is attributed to bioactive constituents such as thymoquinone, flavonoids, and phenolic compounds [12]. Experimentally, it has been observed that Nigella sativa is highly effective as an antioxidant, anti-inflammatory, and hepatoprotective agent [13]. Such effects are mediated by scavenging free radicals and enhancement of endogenous antioxidant defenses via activation of nuclear factor erythroid 2-related factor-2 (Nrf2), as well as inhibition of NF-κB-mediated inflammatory signaling [14]. Nigella sativa has also inhibited ethanol-induced elevation of hepatic transaminases and ameliorated histopathological changes in experimental models [15].

Silymarin, a standardized extract from Silybum marianum, is a well-known hepatoprotective agent and has antioxidant, membrane-stabilizing, and anti-fibrotic properties [16]. It increases hepatic glutathione content, diminishes lipid peroxidation, and aids healing of hepatocytes [17]. Due to the multifactorial nature of ethanol-induced liver injury, combination therapy addressing oxidative stress and inflammation may provide better hepatoprotection [18]. Hence, the study was designed to determine the hepatoprotective and antioxidant effects of Nigella sativa seed extract in ethanol-induced liver damage alone and in combination with silymarin.

MATERIALS AND METHODS

Experimental Animals

The study was conducted using healthy adult male Wistar rats weighing 150–200 g, procured from a CPCSEA-certified animal house. Animals were housed in standard polypropylene cages under controlled laboratory conditions with a temperature of 22 ± 2 °C, relative humidity of 50–60%, and a 12 h light/dark cycle. Rats were provided with standard pellet diet and water ad libitum during the period of study. The study was conducted after the approval from the institutional animal ethics committee (No: IAEC/ELMCH/2/19/2)

Drugs and Chemicals:

- **Silymarin**, used as the standard hepatoprotective drug, was procured from the hospital pharmacy. The dose was freshly prepared using distilled water prior to administration.
- ***Nigella sativa*** seeds were procured from a certified local supplier. The seeds were cleaned thoroughly to remove extraneous matter and authenticated by a qualified botanist from the Department of Botany.

Preparation of *Nigella sativa* Seed Extract

Nigella sativa seeds were shade-dried and coarsely powdered using a mechanical grinder. The powdered material was subjected to extraction using aqueous methanol (70% v/v) as solvent. Powdered seeds were macerated with aqueous methanol for **72 hours** at room temperature with intermittent shaking. The extract was then filtered through muslin and filter paper. The extract was stored in airtight containers in refrigerator at 4 °C until further use.

Induction of Alcoholic Hepatitis

The induction of alcoholic hepatitis was done by method devised by *Charles S. Lieber et al (1982)* by oral administration of 30% v/v ethanol at a dose of 2 ml/100 g animal body weight, once daily, for a period of 8 weeks. [19]

Experimental Design

After acclimatization, animals were randomly divided into six groups of six rats each (n = 6):

Group	Intervention
Group I (Normal Control):	Received normal saline
Group II (Ethanol Control):	Received ethanol only (2ml/100 gm animal body weight) [19]
Group III (Standard):	Received ethanol + silymarin (100 mg/kg, p.o.)
Group IV (NS1)	Received ethanol + Nigella sativa extract (500 mg/kg, p.o.)
Group V (NS2)	Received ethanol + Nigella sativa extract (800 mg/kg, p.o.)

Group VI: (Combination)	Received ethanol + Nigella sativa extract (500 mg/kg) + silymarin (100 mg/kg, p.o.)

Collection of Blood and Tissue Samples

At the end of the study animals were fasted overnight and euthanized under short acting thiopentone sodium anaesthesia. Blood samples were collected by cardiac puncture to obtain serum for biochemical estimations. The liver was excised immediately, washed with ice-cold normal saline, blotted dry, and processed for antioxidant assays and histopathological analysis. Tissue was fixed in 10% neutral buffered formalin for 24–48 hours to preserve tissue architecture.

Following fixation, the tissues were processed routinely using graded concentrations of ethanol for dehydration, cleared in xylene, and embedded in paraffin wax. Paraffin-embedded tissue blocks were sectioned at a thickness of 4–5 µm using a rotary microtome. The sections were mounted on clean glass slides and subsequently stained with haematoxylin and eosin (H&E) for histological evaluation. Stained sections were examined under a light microscope at different magnifications.

Serum liver function parameters including aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) were estimated using standard diagnostic kits following the manufacturer's instructions.

Hepatic tissue homogenate (10% w/v) was prepared in ice-cold phosphate buffer (0.1 M, pH 7.4) and centrifuged at 10,000 rpm for 15 min at 4 °C. The supernatant was used for biochemical estimations. Lipid peroxidation was assessed by measuring malondialdehyde (MDA) levels using the Thio barbituric acid reactive substances (TBARS) method. Reduced glutathione (GSH) was estimated using Ellman's reagent (DTNB). Superoxide dismutase (SOD) activity was determined based on inhibition of epinephrine auto-oxidation, and catalase (CAT) activity was measured by monitoring the decomposition of hydrogen peroxide.[20]

Statistical Analysis

Data were expressed as Mean ± SEM. Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by appropriate post-hoc multiple comparison tests. A p value of < 0.05 was considered statistically significant.

RESULTS

Effect on liver parameter:

Chronic ethanol administration for eight weeks produced a significant elevation in serum AST, ALT, and ALP levels, confirming successful induction of alcoholic liver injury ($p < 0.001$). Serum AST increased from 101.45 ± 6.02 IU/L in the control group to 209.50 ± 6.09 IU/L in ethanol-treated rats. Treatment with silymarin and Nigella sativa extract significantly reduced AST levels in a dose-dependent manner, with the combination therapy showing near normalization (109.21 ± 8.83 IU/L) (Table 1A). Similarly, ethanol exposure caused a marked increase in ALT levels (122.76 ± 8.31 IU/L) compared to controls (28.31 ± 5.94 IU/L). Silymarin and Nigella sativa significantly attenuated this elevation, with maximal reduction observed in the combination group (33.48 ± 9.21 IU/L) (Table 1B). Serum ALP levels were also significantly elevated following ethanol administration (174.47 ± 2.73 IU/L) and were effectively reduced by treatment, with the greatest improvement seen in the combination group (89.02 ± 4.71 IU/L) (Table 1C)

Table 1: Liver Function Parameter

Table 1A: Aspartate Aminotransferase (AST, IU/L)

Parameter	Group I	Group II	Group III	Group IV	Group V	Group VI	ANOVA
Week 0	101.45 ±6.02	101.36±6.11	102.04±5.97	101.89±6.25	100.73±5.69	101.11±6.03	F(5,30)=0.12 p=0.98 (NS)
Week 8	101.45 ±6.02#	209.50±6.09*	120.66±9.54#	173.01±10.22*#	157.56±7.90#	109.21±8.83#	F(5,30)=42.18 p<0.0001
p value	NS	<0.0001	NS	<0.05	NS	NS	

Table 1B: Alanine Aminotransferase (ALT, IU/L)

Parameter	Group I	Group II	Group III	Group IV	Group V	Group VI	
Week 0	28.31±5.94	28.17±5.71	28.59±5.88	27.93±5.66	28.22±5.79	27.68±5.53	F(5,30)=0.09 p=0.99 (NS)
Week 8	28.31±5.94 #	122.76±8.31 *	47.45±9.34 #	78.59±12.41* #	52.39±11.58 #	33.48±9.21 #	F(5,30)=56.74 p<0.0001
p value	NS	<0.0001	NS	<0.05	NS	NS	

Table 1C: Alkaline Phosphatase (ALP, IU/L)

Parameter	Group I	Group II	Group III	Group IV	Group V	Group VI	
Week 0	81.49±2.82	81.22±2.68	81.07±2.79	80.88±2.83	81.15±2.71	80.91±2.77	(5,30)=0.15 p=0.97 (NS)
Week 8	81.49±2.82 #	174.47±2.73 *	96.46±5.67 #	119.39±5.86* #	100.35±3.32 #	89.02±4.71 #	F(5,30)=63.09 p<0.0001 (HS)
p value	NS	<0.0001	NS	<0.05	NS	NS	

*Table 1A, 1B and 1 C Data expressed as Mean ± SEM. * Significant difference when compared to Week 0 # standard difference when compared to Group II (Ethanol control). P value <0.001 (highly significant) and P value <0.05 (significant)*

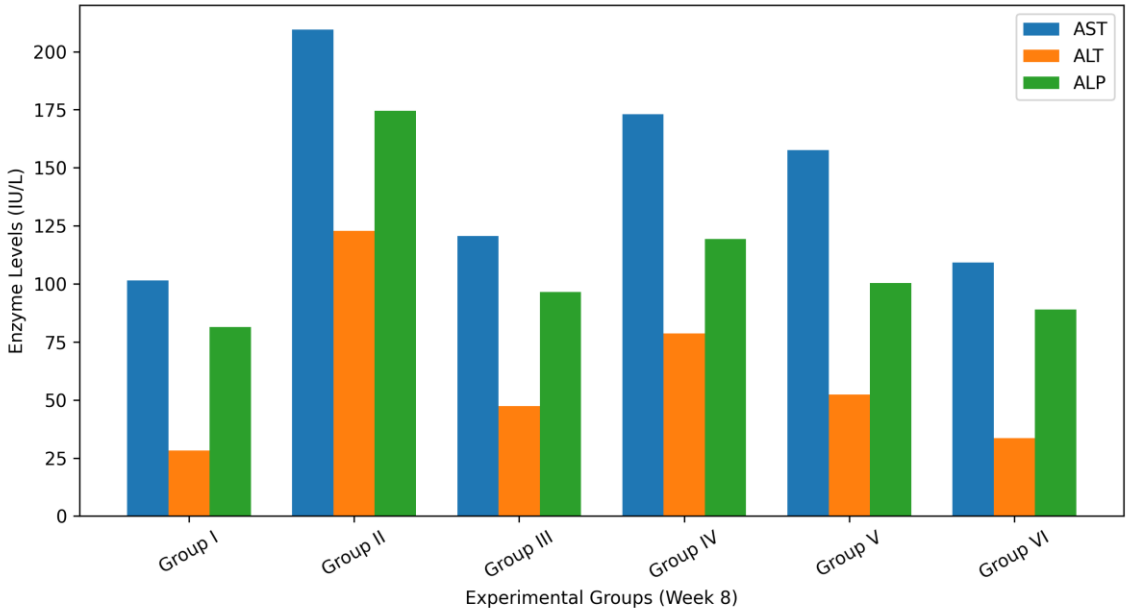


Figure 1: Effect of Nigella sativa seed extract and silymarin on serum liver enzymes (AST, ALT, and ALP) at Week 8 in ethanol-induced liver injury in rats.
Values are expressed as Mean ± SEM (n = 6). Statistical analysis was performed using one-way ANOVA followed by post-hoc multiple comparison test. p < 0.001 indicates highly significant difference and p < 0.005 indicates significant difference

Effect on Lipid Peroxidation and Antioxidant Enzymes

Ethanol administration significantly increased hepatic malondialdehyde (MDA) levels, indicating enhanced lipid peroxidation (78.39 ± 5.70 nmol/g tissue) compared to controls (26.93 ± 2.59 nmol/g tissue, $p < 0.05$). Treatment with silymarin and Nigella sativa extract significantly reduced MDA levels in a dose-dependent manner, with the combination therapy producing near-normal values (30.43 ± 2.57 nmol/g tissue).
Chronic ethanol exposure markedly depleted endogenous antioxidant defenses, evidenced by significant reductions in hepatic superoxide dismutase (SOD), reduced glutathione (GSH), and catalase (CAT) levels. SOD levels decreased to 56.32 ± 5.19 µg/g tissue in ethanol-treated rats and were significantly restored by silymarin and Nigella sativa, with maximal recovery observed in the combination group (99.92 ± 1.25 µg/g tissue). Similarly, ethanol-induced depletion of GSH (0.25 ± 0.002 U/g tissue) and CAT (39.27 ± 5.46 U/g tissue) was significantly reversed following treatment, with the combination therapy restoring values close to normal(Table 2).

Table 2: Antioxidant and Oxidative Stress Parameters

Parameter	Group I	Group II	Group III	Group IV	Group V	Group VI
Hepatic malondialdehyde (MDA)	26.93±2.59	78.39±5.70*	36.45±1.38#	61.99±3.27*	44.03±2.82#	30.43±2.57#

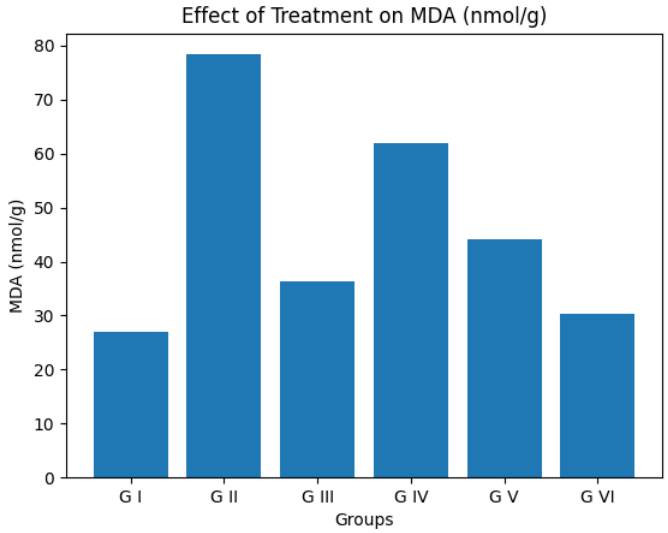
ANOVA F(5,30) = 71.62 p < 0.0001 (HS)

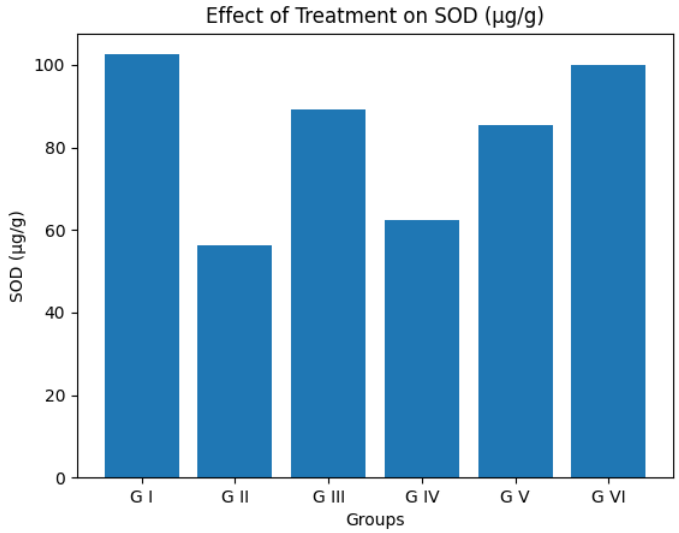
Parameter	Group I	Group II	Group III	Group IV	Group V	Group VI
Glutathione(GSH)	0.69±0.011	0.25±0.002*	0.51±0.034#	0.46±0.025*	0.58±0.122#	0.65±0.009#
F(5,30) = 88.91 p < 0.0001 (HS)						

Parameter	Group I	Group II	Group III	Group IV	Group V	Group VI
Catalase (CAT)	72.43±6.71	39.27±5.46*	61.98±8.30#	52.39±6.66*	60.02±6.47#	68.11±5.92#
F(5,30) = 27.66 p < 0.0001						

Parameter	Group I	Group II	Group III	Group IV	Group V	Group VI
Superoxide Dismutase (SOD)	102.56 ± 3.38	56.32 ± 5.19*	89.11 ± 2.86#	| 62.51 ± 4.58*	85.46 ± 2.99#	99.92 ± 1.25#
F(5,30) = 39.84 p < 0.0001						

*Data are expressed as Mean ± SEM. *p < 0.05 vs Control group: #p < 0.05 vs Alcohol control group (ANOVA followed by post-hoc test)*





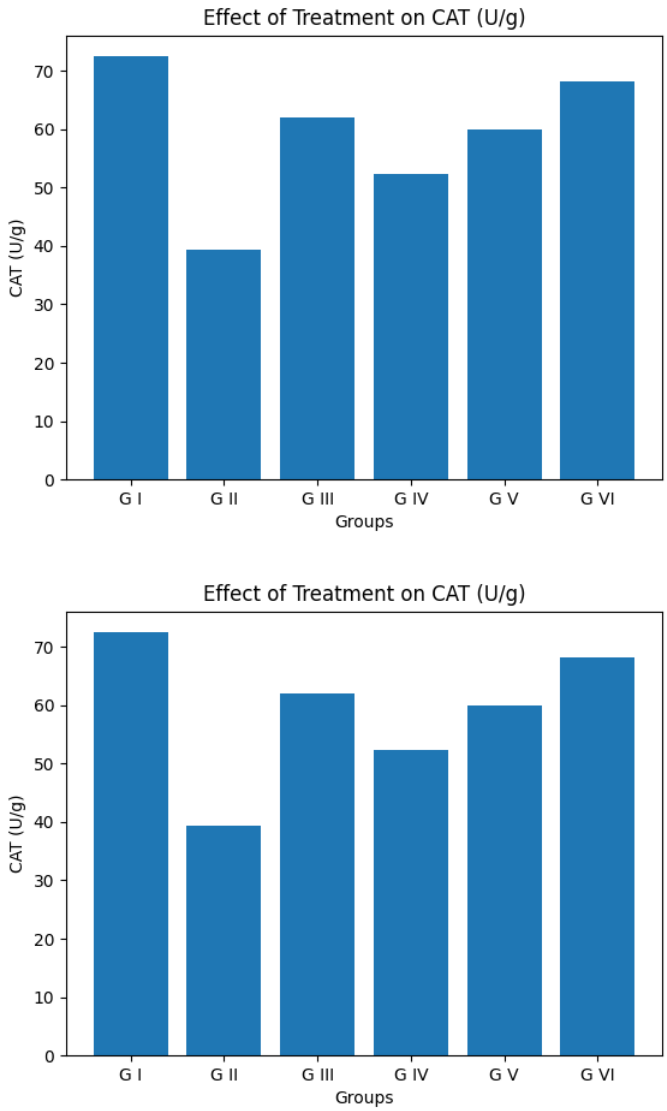


Figure 2: Effect of Nigella sativa seed extract and silymarin on Antioxidant and Oxidative Stress Parameters at Week 8 in ethanol-induced liver injury in rats.

Statistical analysis was performed using one-way ANOVA followed by post-hoc multiple comparison test. $p < 0.001$ indicates highly significant difference and $p < 0.005$ indicates significant difference

Histopathological Evaluation of Liver Tissue

Histopathological examination of liver sections stained with hematoxylin and eosin (H&E) was performed to assess structural alterations induced by experimental intervention and to correlate morphological changes with biochemical findings.

Liver sections from the control group demonstrated normal hepatic architecture, characterized by well-defined hepatic lobules with a clearly visible central vein. Hepatocytes were arranged in regular cords radiating from the central vein, displaying eosinophilic cytoplasm and centrally placed round nuclei. Hepatic sinusoids were intact and free of congestion or inflammatory cell infiltration, indicating normal liver histology. (Fig. 3A)

Liver sections from the ethanol control group (II) showed marked histopathological alterations. Prominent ballooning degeneration of hepatocytes was observed, characterized by swollen hepatocytes with pale, vacuolated cytoplasm and loss of normal cellular boundaries. These changes indicate reversible hepatocellular injury likely due to metabolic or oxidative stress. ((Fig. 3B)

In several areas, apoptotic bodies were evident as small, round, intensely eosinophilic structures with condensed nuclear material, suggestive of programmed cell death. Additionally, mild to moderate inflammatory cell infiltration,

predominantly mononuclear cells, was observed within the hepatic lobules and around affected hepatocytes, reflecting an inflammatory response to hepatocellular injury. (Fig. 3C)

Mild disruption of hepatic cord arrangement and focal sinusoidal dilatation were also noted, further supporting the presence of hepatocellular damage.

Liver sections from animals treated with Nigella sativa demonstrated a marked improvement in hepatic architecture compared with the toxicant-exposed group. Most hepatocytes retained their normal polygonal shape with well-preserved cytoplasm and centrally located nuclei. Well preserved liver architecture was observed in the combination group (VI) which exhibited near-normal hepatic histology, closely resembling that of the control group.

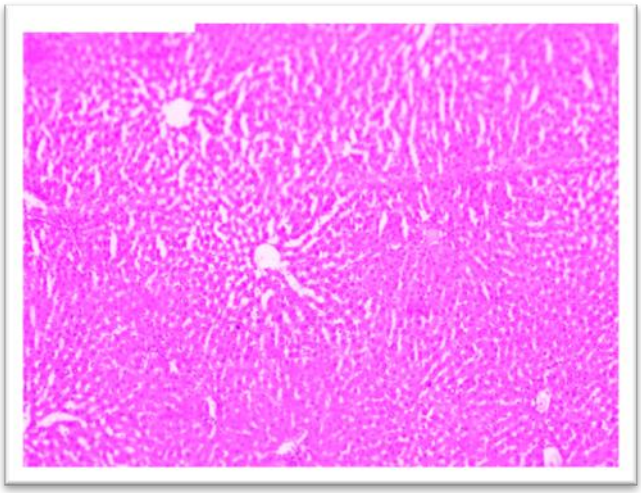


Figure 3A: Normal control liver showing intact hepatic architecture with preserved hepatic cords and central vein (10×)..

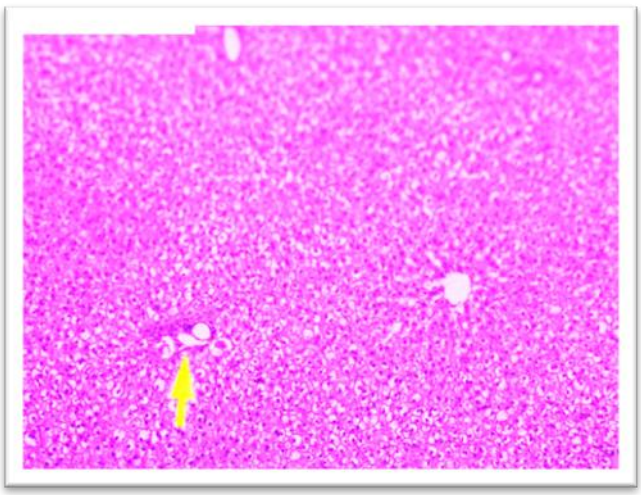


Figure 3B: Ballooning degeneration associated with inflammatory cell infiltration (arrow) (10×).

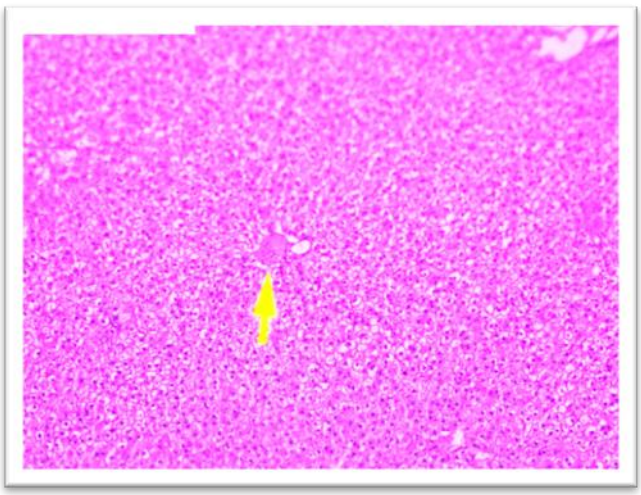


Figure 3C: Apoptotic body (arrow) indicating hepatocyte apoptosis (H&E).

DISCUSSION

The current study shows that long-term ethanol use could induce severe hepatocellular injury based on impaired hepatic activity enzymes, increase in oxidative stress and decrease of endogenous antioxidant defenses. Dose-dependent hepatoprotection of Nigella sativa seed extract was generated with treatment, and such a dose sensitivity was subsequently increased by use with silymarin, with synergistic healing effects. Serum AST, ALT and ALP were significantly increased in ethanol rats indicating hepatocyte membrane damage and higher permeability. The biochemical changes are characteristic of ethanol-induced liver injury and are mainly mediated by ethanol metabolism via cytochrome P450 2E1, leading to overproduction of reactive oxygen species and accumulation of acetaldehyde [1–4].

Further, the markedly elevated ALP suggests cholestasis and dysfunction in the biliary system that are also noted in alcoholic hepatitis [5]. A consistent profile of hepatic injury was obtained with the combined AST–ALT–ALP analysis to show the ethanol treatment group was severely affected, which made consistent with the experimental model applied. Focusing on Nigella sativa seed extract, it was observed a dose-dependent inhibition of liver enzymes increasing at this dose. Higher dosage (800 mg/kg) was associated with more normalization of AST, ALT and ALP relative to lower dose also indicative of an enhanced hepatoprotective activity. These results are in line with previous literature that explains the hepatoprotective effects of Nigella sativa through its bioactive compounds, especially thymoquinone, which is reported to present high antioxidant and membrane-stabilizing properties [11–13].

Nigella sativa scavenges free radicals and inhibits lipid peroxidation of hepatocyte membranes with the result that enzymes enter circulation more sparingly. Oxidative stress is the primary mode of pathogenesis in ethanol-induced liver damage, as hepatic malondialdehyde was significantly elevated in ethanol-treated rats. Increased MDA reflects enhanced lipid peroxidation after ethanol exposure due to the overuse of reactive oxygen species generation during ethanol metabolism [3, 10]. MDA levels were analyzed and were significantly lower in Nigella sativa treatment and MDA levels were nearly normal in combination therapy. This lipid peroxidation reduction is strongly supportive of the antioxidant activity of Nigella sativa, consistent with prior experimental results [13–15]. During chronic ethanol exposure the endogenous antioxidant enzymes superoxide dismutase, reduced glutathione and catalase also markedly decreased. These enzymes constitute the primary cellular defender against oxidative injury, and their depletion exacerbates hepatocellular injury [10]. The restoration of SOD, GSH, and CAT levels after Nigella sativa treatment further confirms the strengthening of intracellular antioxidant defenses. Nigella sativa activated the nuclear factor erythroid 2-related factor-2 signaling pathway by recent studies, which also has a positive effect on upregulation of antioxidant gene expression and enhanced redox homeostasis [14].

This method of action is likely to account for the biochemical benefits noted. Silymarin, employed as the conventional hepatoprotective agent, resulted in a notable improvement of liver function parameters and antioxidant enzyme contents. It has well-established hepatoprotective activities, specifically suppression of peroxidation, increase in glutathione availability and hepatocyte regeneration [16,17]. It is particularly notable that in comparison to one of the two, the anti-epithelial cell protection of Nigella sativa plus silymarin consistently was better in the case of Nigella sativa with and without silymarin. This synergistic action might be mediated by the simultaneous effect due to synergistic mechanisms in which silymarin supports the stabilization of hepatocyte membranes and enhances protein synthesis and the production by its activator, with Nigella sativa having antioxidant and anti-inflammatory activity [18]. Inflammation is another key contributor for ethanol induced liver damage from ethanol-induced injury. Activation of Kupffer cells and hence their subsequent release of pro-inflammatory cytokines through nuclear factor-κB signaling has been previously reported by ethanol to cause hepatic damage [8,9]. Although inflammatory markers were not directly measured here, the dramatic improvement in biochemical and antioxidant parameters reflects reduction of inflammatory processes. Nigella sativa has been shown to inhibit nuclear factor-κB activation and cytokine production in previous studies, thereby preventing inflammatory liver injury [14].

The hepatoprotective effects observed in the present study are consistent with previous experimental evidence demonstrating the protective role of Nigella sativa against alcohol- and toxin-induced liver injury. Study done by **Hosseinzadeh H et al** has shown that Nigella sativa and its major bioactive constituent, thymoquinone, significantly reduce oxidative stress and lipid peroxidation while restoring endogenous antioxidant defenses, including superoxide dismutase, catalase, and reduced glutathione [19]

More recent studies have further highlighted the role of thymoquinone in preserving mitochondrial function and attenuating oxidative and inflammatory damage in hepatic tissue [20,21]

In conclusion, the current study found that Nigella sativa seed extract has potential hepatoprotective effects on alcoholic liver injury by antioxidant defenses against ethanol-induced liver damage through decreasing oxidative stress and redrawing antioxidant defenses. The improved effectiveness observed with combination therapy supports the therapeutic value of the dual use of multiple-targeted antioxidant strategies in the treatment of alcoholic liver disease.

CONCLUSION

Nigella sativa seed extract has considerable hepatoprotective and antioxidant activities against ethanol-induced liver injury. The use of silymarin in combination can provide improved protection and could be used as a therapeutic strategy.

REFERENCES

1. Osna NA, Donohue TM Jr, Kharbanda KK. Alcoholic liver disease: pathogenesis and current management. Alcohol Res. 2020;40(1):01.
2. Ceni E, Mello T, Galli A. Pathogenesis of alcoholic liver disease: role of oxidative metabolism. World J Gastroenterol. 2021;27(30):4751–4763.
3. DOI: 10.3748/wjg.v27.i30.4751
4. Wu D, Cederbaum AI. Oxidative stress and alcoholic liver disease. Semin Liver Dis. 2021;41(1):35–47. DOI: 10.1055/s-0040-1719200
5. Zakhari S, Li TK. Determinants of alcohol metabolism. Alcohol Res Health. 2019;40(2):02.
6. Gao B, Tsukamoto H. Inflammation in alcoholic and non-alcoholic fatty liver disease. J Hepatol. 2020;72(4):716–729. DOI: 10.1016/j.jhep.2019.10.037
7. Setshedi M, Wands JR, de la Monte SM. Acetaldehyde adducts in liver injury. Alcohol Clin Exp Res. 2020;44(1):66–75. DOI: 10.1111/acer.14235
8. Mansouri A, Gattolliat CH, Asselah T. Mitochondrial dysfunction and liver disease. J Hepatol. 2019;71(4):811–825. DOI: 10.1016/j.jhep.2019.05.033
9. Szabo G, Saha B. Alcohol's effect on host defense. Alcohol Res. 2020;40(2):02.
10. Wang S, Pacher P, De Lisle RC. NLRP3 inflammasome in alcoholic liver disease. Hepatology. 2022;75(1):291–304. DOI: 10.1002/hep.32154
11. Lu Y, Cederbaum AI. Antioxidant depletion in alcoholic liver disease. Free Radic Biol Med. 2021;163:214–226. DOI: 10.1016/j.freeradbiomed.2020.11.011
12. Ali BH, Blunden G. Pharmacological and toxicological properties of Nigella sativa. Phytother Res. 2003;17(4):299–305. DOI: 10.1002/ptr.1309
13. Tavakkoli A, Mahdian V, Razavi BM, Hosseinzadeh H. Review on Nigella sativa and thymoquinone. J Pharmacopuncture. 2019;22(2):65–79. DOI: 10.3831/KPI.2019.22.010
14. Mahmoud AM, Hussein OE, Abd El-Twab SM. Protective role of Nigella sativa in liver injury. Biomed Pharmacother. 2020;131:110769. DOI: 10.1016/j.biopha.2020.110769
15. Gholamnezhad Z, Keyhanmanesh R, Boskabady MH. Anti-inflammatory effects of Nigella sativa. J Ethnopharmacol. 2020;258:112844. DOI: 10.1016/j.jep.2020.112844
16. Khader M, Bresgen N, Eckl PM. Hepatoprotective mechanisms of thymoquinone. Food Chem Toxicol. 2021;148:111896. DOI: 10.1016/j.fct.2020.111896
17. Gillessen A, Schmidt HHJ. Silymarin as supportive treatment in liver diseases. Clin Phytosci. 2020;6:19. DOI: 10.1186/s40816-020-00185-y
18. Polyak SJ, Morishima C, Lohmann V. Mechanisms of silymarin hepatoprotection. Hepatology. 2021;74(1):308–321. DOI: 10.1002/hep.31667
19. Agarwal S, Singh R, Sinha N. Herbal antioxidants in alcohol-induced liver injury. Indian J Pharmacol. 2022;54(5):321–329. DOI: 10.4103/ijp.ijp_898_21
20. Lieber CS, DeCarli LM. The feeding of alcohol in liquid diets: two decades of applications and 1982 update. Alcohol Clin Exp Res. 1982;6(4):523–531. DOI: 10.1111/j.1530-0277.1982.tb04981.x
21. Rotto D, Maria LS, Valentini J, et al. Importance of the lipid peroxidation biomarkers and methodological aspects for malondialdehyde quantification. Quim Nova. 2009;32(1):169–174. DOI: 10.1590/S0100-40422009000100032
22. Hosseinzadeh H, Behravan E, Soleimani MM. Protective effects of thymoquinone against oxidative liver injury: recent advances. Phytother Res. 2021;35(9):4935–4947. DOI: 10.1002/ptr.7204