Hepatoprotective Effect of Quinic Acid against Ethanol-Induced Liver Toxicity in Rats: Biochemical, Physiological, and Histological Insights

ABSTRACT

Alcohol consumption is associated with several health issues, including Alcoholic Liver Disease (ALD). Quinic acid, a cyclic polyol compound, is known for its antioxidant, anticancer, anti-inflammatory, and hepatoprotective properties. This study aims to elucidate the protective mechanisms of quinic acid against ethanol-induced liver toxicity in rats. Male rats (*n*=32) were divided into four groups (n=8 per group) and treated over 60 days. Group 1 received a standard diet with isocaloric glucose; Group 2 was treated with 30% ethanol daily; Group 3 received 30% ethanol and quinic acid (50 mg/kg) from day 31; Group 4 was given glucose and quinic acid from day 31. Biochemical, physiological, and histological evaluations were performed post-treatment. Ethanol-treated rats exhibited significant decreases in body weight, abnormal liver morphology, increased liver enzyme levels (AST, ALT, ALP, and GGT), disrupted lipid and renal profiles, and altered phase I and II enzyme activities. Quinic acid supplementation in ethanol-treated rats significantly reversed these changes by improving body weight, restoring liver morphology, normalizing liver enzyme activities, and maintaining lipid-lipoprotein balance and enzyme levels. Histopathological analysis demonstrated reduced liver damage in quinic acid-treated groups.Quinic acid exhibits hepatoprotective effects against ethanol-induced toxicity by reducing oxidative stress, normalizing liver functions, and preserving liver structure. These findings highlight its potential as a therapeutic agent for managing ALD.

Keywords: Antioxidants, detoxification enzymes, ethanol,hepatoprotective effects,liver marker enzymes, quinic acid.

1.INTRODUCTION

Alcoholic beverages, including distilled spirits, fermented wine, and mixed wine, have been consumed for thousands of years. However, ethanol is metabolized by alcohol dehydrogenase (ADH) into acetaldehyde, a toxic intermediate product of glycolysis(McGovern, 2019).

Alcohol consumption can result in liver injury and hepatocyte death through apoptotic and necroptotic pathways (Zhou et al., 2022).Alcoholic beverages have various side effects on overall health, contributing to 3.6% of global cancer cases and 20% of Alcoholic Liver Disease (ALD) cases(Zhou et al.,2022; Freudenheim et al., 2020). ALD is a form of liver damage that includes a range of conditions such as steatohepatitis, cirrhosis, progressive fibrosis, and hepatocellular carcinoma, primarily caused by excessive alcohol consumption (Addolorato et al., 2016; Orman et al., 2013). Oxidative stress and an inflammatory environment are key factors in the development of ALD. Oxidative stress results from an imbalance between oxidation and the antioxidant system, involving the overproduction of reactive oxygen species (ROS), mitochondrial dysfunction, and impaired antioxidant defences (Chen et al., 2020).Both acute and chronic ethanol exposure can lead to ROS overproduction and a reduction in antioxidants, causing liver damage through mechanisms such as attacking proteins and DNA and inducing lipid peroxidation, which disrupts cell membrane structure and alters hepatocyte permeability(Graciela et al.,2021; Wang et al., 2020).

AST (aspartate aminotransferase) and ALT (alanine aminotransferase) are liver enzymes commonly used to assess liver function. Elevated levels of these enzymes can indicate liver damage or inflammation. ALP (alkaline phosphatase) is another enzyme associated with the liver, bones, and bile ducts; increased levels may suggest bile flow problems or bone disorders. GGT (gamma-glutamyl transferase) plays a role in glutathione metabolism and is useful for evaluating liver disease, bile duct obstructions, and alcohol consumption (Jalili et al., 2022).

Urea, uric acid, creatinine, and total bilirubin are important substances that provide insights into metabolic and organ function. Urea, produced in the liver from protein breakdown and excreted by the kidneys, reflects renal function (Weiner et al., 2015). Uric acid, a byproduct of purine metabolism, can indicate conditions like gout when levels are elevated (Jin et al., 2012). Creatinine, a waste product of muscle metabolism, is used to assess kidney function and muscle mass (Canaud et al., 2020).Total bilirubin, a pigment formed from the breakdown of red blood cells, helps evaluate liver health and can indicate issues such as jaundice.Together, these biomarkers are crucial for diagnosing and monitoring various health conditions (Hansen et al., 2020).

Consumption of alcoholic beverages is linked to an increased incidence of various diseases, such as metabolic syndrome and cardiovascular disease (Clerc et al., 2010; O'Keefe et al., 2018).The relationship between alcohol consumption and cardiovascular disease risk including myocardial infarction and coronary heart disease is largely mediated by its effects on lipid profiles, particularly HDL-cholesterol and LDL-cholesterol levels (Attard et al., 2021). Hyperlipidemia, or hyperlipoproteinemia, refers to the condition where there are abnormally high levels of lipids and/or lipoproteins in the blood (Nagarthna et al., 2020). Lipids are transported to various tissues for metabolic functions, but due to their insolubility, they are carried in the plasma as macromolecular complexes with proteins, known as lipoproteins. Increased alcohol consumption is known to raise lipid levels (You et al., 2019).

The phase I detoxification system, primarily consisting of the cytochrome P450 (CYP450) superfamily of enzymes, serves as the initial enzymatic defense against foreign compounds. However, this detoxification step can produce reactive molecules that may be more toxic than the original compound. If these reactive molecules are not further metabolized through phase II conjugation, they can damage cellular proteins, RNA, and DNA (Jiang et al., 2020).

Despite significant progress in the field, developing effective drugs for the treatment of alcoholism remains a challenging goal in alcohol research. Plants, in general, contain biologically active compounds that help prevent and detoxify free radicals, protecting themselves from oxidative stress and its consequences. Thus, identifying an effective hepatoprotective agent could be a valuable approach for treating liver diseases. Quinic acid, a cyclic polyol compound, has been reported to have several beneficial pharmacological properties, including antioxidant, anticancer, anti-inflammatory, antimicrobial, and radioprotective effect (Benali et al., 2024; Anoor et al., 2022). Therefore, this study aimed to elucidate the mechanisms by which quinic acid protects against alcohol toxicity by analyzing changes in body weight, liver marker enzymes, lipid profile, lipoprotein levels, alcohol-metabolizing enzymes (phase I and phase II), and tissue histology in experimental rats.

2. MATERIALS AND METHODS

2.1. Chemicals and reagents

Quinic acid, ethanol (purity of 99.8%), biochemical analysis kits, and haematoxylin and eosin (H&E) stain were obtained from Sigma-Aldrich. All other chemicals and reagents used in the study were of analytical grade and were purchased from Himedia Laboratory Ltd., Mumbai, India.

2.2. Animals

Male albino Wistar rats, weighing approximately 150–180 g, were obtained from Biogen, Bangalore, and housed in the Central Animal House of Rajah Muthiah Medical College and Hospital, Annamalai University. The rats were cared for in accordance with the ethical guidelines of the Annamalai University Animal Care and Use Committee and the Indian National Law on Animal Care (Reg. No. 160/1999/CPCSEA/1095). All experiments followed the "Guide for the Care and Use of Laboratory Rats." The animals were kept in plastic cages with paddy husk bedding at a controlled temperature of 27±2°C, under a 12 h light/dark cycle.

2.3. Study design

The animals were divided into four groups, with each group containing 8 animals. The experiments were conducted over a period of 60 days.

Group 1: Rats were given a standard pellet diet and isocaloric glucose (40% glucose in drinking water) administered orally (p.o.) for the entire 60-day experimental period.

Group 2: Rats were administered 30% ethanol (equivalent to 50 g/kg body weight, p.o.) daily for the entire 60-day experimental period.

Group 3: Rats received 30% ethanol daily for the entire experimental period, and from the 31st day onwards, they were also administered quinic acid (50 mg/kg body weight, p.o.) until the end of the experiment.

Group 4: Rats were given a standard pellet diet with isocaloric glucose daily for the entire experimental period, and from the 31st day onwards, they were administered quinic acid (50 mg/kg body weight, p.o.) until the end of the experiment.

At the end of the experimental period, the animals were sacrificed by cervical dislocation. Blood samples were collected in heparinized tubes, and plasma was separated. The liver was excised and rinsed with ice-cold saline (0.9% sodium chloride). Tissue samples were then homogenized, and the supernatant was used for biochemical estimations.

2.4. Activities of hepatic marker enzymes in serum

The levels of serum enzymes were assessed using spectrophotometric methods and commercially available diagnostic kits from Sigma Diagnostics Pvt. Ltd, following established protocols. The activities of serum AST (E.C. 2.6.1.1), ALT (E.C. 2.6.1.2), and ALP (E.C. 3.1.3.1) were measured using standard procedures. To determine GGT (E.C. 2.3.2.2) enzyme activity, the method described by Rosalki et al. (1970)was employed, using γ-glutamyl-p-nitroanilide as the substrate.

2.5. Estimation of serum urea and uric acid

Serum urea was estimated using an enzymatic method with a diagnostic kit based on Fawcett and Scott (1960)protocol. In this assay, 10 µL of the serum sample was mixed with 1 mL of buffered enzyme solution containing phosphate buffer, urease, and sodium nitroprusside, and incubated at 37°C for 5 min. A blank was prepared by substituting the sample with 10 µL of distilled water. Following this, 1 mL of the color-developing reagent was added to each tube, mixed thoroughly, and incubated for another 5 min at 37°C. After incubation, 1 mL of distilled water was added, and the intensity of the developed green chromophore was measured at 600 nm to determine the urea concentration.

Serum uric acid estimation was performed using an enzymatic method based on Caraway (1955). In this method, uric acid is oxidized by uricase to allantoin, generating hydrogen peroxide. The hydrogen peroxide reacts with 4-aminoantipyrine and 3,5-dichloro-2-hydroxybenzene sulfonic acid to form a quinone imine dye, the intensity of which is proportional to the uric acid concentration. For the assay, 25 µL of the sample or distilled water (blank) was mixed with 1 mL of enzyme reagent containing uricase, 4-aminoantipyrine, and hydrogen peroxidase. After incubation at 37°C for 5 min, absorbance was measured at 510 nm, and results were expressed in mg/dL.

2.6. Estimation of serum creatinine and bilirubin

Serum creatinine was estimated using a diagnostic kit based on Jaffe's (1886) method.The assay relies on the reaction between creatinine and alkaline picrate, forming a colored complex. Interfering substances react more slowly, allowing for accurate detection of creatinine. For the procedure, 0.1 mL of serum was mixed with 0.5 mL of saturated picric acid and 0.5 mL of 0.75 N sodium hydroxide, then incubated for 20 min. Absorbance readings were taken at 510 nm after 20 min and again at 45 min, and creatinine concentration was calculated using a standard.

For bilirubin determination, 0.2 mL of serum was mixed with 2.5 mL of absolute methanol, 0.5 mL of 1.5% hydrochloric acid, and 0.5 mL of diazo reagent. The mixture was allowed to react at room temperature for 30 min before measuring the absorbance at 540 nm.

2.7. Estimation of Lipids and Lipoproteins

Lipids were extracted and quantified using the Folch et al. (1957) method.Total cholesterol (TC) in plasma and liver tissues was measured using the Siedel et al. (1983) kit method.Triglycerides (TG) in plasma and liver tissues were assessed according to the Foster and Dunn (1973) method.Phospholipids (PL) in plasma and liver tissues were determined using the Zilversmit and Davis (1950) technique.Free fatty acids (FFA) in plasma and liver tissues were estimated by the Falholt et al. (1973) method.High-density lipoprotein (HDL) in plasma was measured using the Burnstein et al. (1970) method.Low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) in plasma were calculated based on Friedwald et al. (1972)formulas: LDL = TC – (HDL + VLDL) and VLDL = TG/5.

2.8. Assay of phase I enzymes

Cytochrome P450 (CyP450) and cytochrome b5 (Cyb5) concentrations were determined using the method described by Omura and Sato (1964).Cytochrome P450 levels were assessed through carbon monoxide (CO) difference spectra, measuring the absorbance of CO adducts formed by the reaction of reduced cytochrome P450 with CO at 450 nm.

Cyb5 reduction was monitored by an increase in absorbance at 427 nm. The concentrations of CyP450 and Cyb5 were calculated using absorption coefficients of 91 and 185 $cm^2/M/m$, respectively.

NADPH-cytochrome P450 (NADPH-CyP450) reductase (EC 1.6.2.2) activity was assayed using the method of Mihara and Sato (1972), with absorbance measured at 450 nm. The enzyme activity was determined using an extinction coefficient of 1.02 m/M/cm, with one unit defined as the reduction of one mole of ferric cyanide per min.

NADPH-cytochrome b5 (NADPH-Cyb5) reductase (EC 1.6.2.4) activity was measured according to Omura and Takesue (1970)by tracking the rate of NADPH oxidation at 340 nm, with enzyme activity calculated using an extinction coefficient of 6.33 $cm^2/mM/cm$. One unit of enzyme activity is defined as the oxidation of one mole of NADPH per min.

2.9. Assay of phase II enzymes

Glutathione S-transferase (GST, EC.2.5.1.18) activity was determined according to the method of Habig et al. (1974).The reaction was initiated by adding the cytosolic sample, and absorbance was recorded at 340 nm. GST activity is reported as micromoles of GSH-CDNB conjugate formed per min per milligram of protein, utilizing an extinction coefficient of 9.6 $mM^{-1} cm^{-1}$.

DT-diaphorase (DTD) (EC.1.6.9.92) activity was measured using the method of Ernster et al. (1967).NADH served as the electron donor and 2,6-dichlorophenol indophenol as the electron acceptor, with reductions monitored spectrophotometrically at 600 nm using an extinction coefficient of 21 $mM^{-1} cm^{-1}$.

UDP-glucuronyl transferase (UDP-GT) activity was assessed following the method of Isselbacher et al. (1962). The incubation mixture, which included Triton X-100, $MgCl_2$, p-nitrophenol, enzyme, and UDP-glucuronic acid, was incubated and measured at 450 nm. The enzyme activity was expressed as nanomoles per min per milligram of microsomal protein.

2.10. Histopathological studies

Liver specimens from both the control and treated groups were cut into small pieces and preserved in a 10% formalin solution for 24 h. They were then dehydrated through a series of acetone baths at concentrations of 70%, 80%, and 100%, each for 1 h. Following dehydration, the specimens were infiltrated and impregnated with paraffin wax, with each treatment lasting 1 h and repeated twice. The specimens were sectioned into 3-7 µm thick slices, stained with hematoxylin and eosin, and mounted using Distrene Phthalate Xylene (DPX). Observations were made using a high-resolution microscope equipped with a camera and attachment (Axio Scope A1, Carl Zeiss, Jena, Germany).

2.11. Statistical analysis

Results are presented as means ± SD from six rats per group. Data were analyzed using a one-way analysis of variance (ANOVA), and significant differences among treatment groups were assessed with Duncan's multiple range test (DMRT). Statistical significance was set at $P < 0.05$.

3. RESULTS

3.1. Effect of quinic acid on body weight and liver morphological changes of control and experimental rats

Table 1 presents the initial and final body weights of both control and experimental rats. Ethanol-treated rats experienced a reduction in final body weight compared to the control group. However, when quinic acid was administered to ethanol-treated rats, there was a significant improvement in weight gain. Rats that received quinic acid alone did not exhibit a statistically significant difference in body weight compared to the control rats.

Fig. 1 illustrates the morphological changes in liver tissue among the different groups of rats. The livers of control rats and those treated with quinic acid alone display normal morphology. In contrast, the livers of ethanol-fed rats show significant morphological damage. Nonetheless, the livers of rats that received quinic acid along with ethanol exhibit near-normal morphology compared to the livers of rats treated with ethanol alone.

3.2. Effect of quinic acid and ethanol on the hepatic marker enzymes of the control and experimental

Table 2 presents the activities of liver marker enzymes (AST, ALT, ALP, and GGT) in both control and experimental rats. Rats treated with ethanol exhibited significantly higher levels of liver marker enzymes compared to the control group. However, when quinic acid was administered to ethanol-fed rats, there was a significant reduction in the activities of these enzymes. In contrast, rats treated with quinic acid alone did not show any statistically significant differences in liver enzyme activities compared to the control rats.

3.3. Effect of quinic acid on serum urea, uric acid, creatinine and total bilirubin of control and experimental rats

Table 3 illustrates the impact of quinic acid on renal function markers in both control and experimental rats. The levels of serum urea, uric acid, creatinine, and total bilirubin were notably higher in rats treated with ethanol alone compared to those in the control group and rats treated with quinic acid alone. In rats given both quinic acid and ethanol, these levels of serum urea, uric acid, creatinine, and total bilirubin were significantly lower compared to the ethanol-only group. Rats receiving quinic acid alone did not exhibit any statistically significant differences in the levels of serum urea, uric acid, creatinine, and total bilirubin when compared to the control group.

3.4. Effect of quinic acid on lipid profile in plasma and liver tissue of control and experimental rats

Tables 4 and 5 display the lipid profiles (TC, TG, PL, and FFA) in the plasma and liver tissue of both control and experimental rats. The study found that ethanol-only treated rats exhibited

a significant increase in lipid profile levels compared to the control group. In contrast, rats treated with quinic acid showed a marked reduction in lipid profile levels in liver tissue compared to those treated with ethanol alone.

3.5. Effect of quinic acid on plasma lipoproteins in control and experimental rats

Table 6 presents the plasma lipoprotein levels (LDL, HDL, and VLDL) in both control and experimental rats. The rats treated with control and quinic acid alone exhibited no significant changes in their plasma lipoprotein levels. Conversely, rats treated with ethanol alone displayed increased LDL and VLDL levels, along with decreased HDL levels, compared to control rats. In contrast, ethanol-induced rats treated with quinic acid showed decreased LDL and VLDL levels and increased HDL levels in their plasma.

3.6. Effect of quinic acid on phase I enzymes and phase II enzymes in the liver of control and experimental rats

Table 7 presents the levels of phase I (CyP450, Cyb5, NADPH-CyP450, and NADPH-Cyb5) and phase II detoxification (GST, UDP-GT, and DTD) enzymes in the plasma of control and experimental rats. In the rats treated with ethanol alone, phase I enzyme activities were significantly increased, while phase II enzyme activities were significantly decreased compared to the control group. However, oral administration of quinic acid significantly modified the activities of both phase I and phase II enzymes in the ethanol-treated rats compared to those treated with ethanol alone.

3.7. Histopathological changes of liver

In contrast to the normal histological appearance of the central vein, hepatocytes, and hepatic sinusoids depicted in Fig. 2 (Fig.2 A and D), ethanol exposure induced noticeable changes in the liver's tissue structure. These changes included parenchymal necrosis, lymphatic infiltration, enlarged sinusoids, cellular degeneration, intracellular vacuolation, and pyknotic nuclei (Fig.2 B). However, after treatment with ethanol combined with quinic acid, the hepatic histoarchitectural pattern was nearly restored to normal, with only minimal sinusoidal enlargement observed (Fig. 2 C).

4. DISCUSSION

Ethanol-induced tissue damage is often attributed to oxidative stress and nutritional deficiencies (Comporti et al., 2010). Alcohol is calorie-dense (7.1 kcal/g) but is devoid of

essential nutrients. Consequently, when carbohydrates are replaced with ethanol in the diet, weight gain tends to decrease. Additionally, alcohol impairs the absorption of nutrients from the intestine(Arumugam et al.,2019).Given that body weight is a potential health indicator, the increased weight gain observed in quinic acid-supplemented rats suggests that quinic acid may offer protective benefits against ethanol-related damage. Rats treated with quinic acid and ethanol showed a significant increase in body weight compared to those treated with ethanol alone. This could be due to quinic acid's role in directly eliminating ethanol from the intestines before absorption. Similarly, Arya et al. (2014)found that quinic acid supplementation led to increased body weight in streptozotocin-induced diabetic rats.

AST and ALT are well-established markers for liver function. AST is found in various tissues including the liver, cardiac and skeletal muscles, kidneys, brain, pancreas, lungs, leukocytes, and erythrocytes, while ALT is predominantly present in the liver (Lee et al., 2012). Elevated serum levels of AST and ALT indicate hepatocyte damage or necrosis, as these enzymes leak into the bloodstream due to increased membrane permeability (Zhang et al., 2009). Conversely, ALP, which is associated with bile ducts, may rise in response to bile flow obstruction. GGT is another liver function marker, often elevated in cases of chronic alcohol consumption (Poupon et al., 2015).Together, these enzymes help gauge the severity of liver damage and are crucial for diagnosing ethanol-induced liver injury. Our study found that ethanol consumption led to a significant increase in AST, ALT, ALP, and GGT activities, suggesting substantial damage to tissue membranes. However, administration of quinic acid resulted in decreased enzyme activities, indicating a hepatoprotective effect. Additionally, Pistacia lentiscus extract, which is rich in quinic acid and other phytocompounds, was shown to reduce liver marker enzyme levels in DMBA-induced carcinogenesis in C57Bl/6 mice (Abidi et al., 2024).

Ethanol can significantly impact various organs, leading to disruptions in important biochemical markers such as serum urea, uric acid, creatinine, and total bilirubin. These markers are vital for evaluating kidney and liver function as well as overall metabolic health. Ethanol consumption can result in increased urea levels primarily due to its effects on the liver and kidneys (Brzoska et al., 2003). Chronic alcohol intake can damage the liver, impairing its ability to convert ammonia a byproduct of protein metabolism into urea. Normally, ammonia is converted to urea in the liver and then excreted by the kidneys. When liver function is compromised, this process is disrupted, leading to ammonia accumulation and elevated urea levels (Walker et al., 2014). Additionally, ethanol can cause dehydration

and reduce blood flow to the kidneys, further impairing their ability to excrete urea effectively. Ethanol can also impact uric acid levels, often resulting in hyperuricemia (elevated uric acid in the blood). Ethanol metabolism increases the production of purines, which are then broken down into uric acid. Moreover, alcohol-induced dehydration and decreased renal excretion of uric acid can exacerbate this issue. Hyperuricemia is linked to conditions like gout and can contribute to kidney damage over time (Oh et al., 2021).

Creatinine levels serve as a crucial marker of kidney function. Ethanol toxicity can lead to elevated serum creatinine levels, indicating impaired renal function. Chronic alcohol use can damage the kidneys through mechanisms such as oxidative stress, inflammation, and direct nephrotoxicity. Ethanol can disrupt renal blood flow and glomerular filtration rate (GFR), leading to increased creatinine levels. Acute alcohol intoxication can also cause acute kidney injury (AKI), further raising creatinine levels as the kidneys struggle to filter waste products. Elevated total bilirubin levels can be indicative of ethanol-induced liver damage (Quraishi et al., 2021). Bilirubin, a breakdown product of hemoglobin, is processed by the liver. Ethanol toxicity can impair this processing, leading to an accumulation of bilirubin in the blood. This can result from hepatocellular injury (damage to liver cells) or cholestasis (obstruction of bile flow). Elevated total bilirubin levels are a marker of liver dysfunction and can manifest as jaundice, which causes yellowing of the skin and sclera (the white part of the eyes) (Jie et al., 2013; Di et al., 1982).

In our study, ethanol exposure in rats led to increased levels of serum urea, uric acid, creatinine, and bilirubin. However, rats treated with quinic acid showed reduced levels of these markers. *Ficus sprague*ana Mildbr. & Burret, which is rich in 3,5-O-dicaffeoylquinic acid, was effective in lowering serum urea, uric acid, creatinine, and bilirubin levels in a model of gentamicin-induced nephrotoxicity in rats (Taher et al., 2021).

Ethanol-induced toxicity disrupts various lipid profile components, including TC, TG, PL, and FFA (Arulmozhi et al., 2010). Chronic ethanol consumption disrupts liver lipid metabolism, resulting in elevated TG and FFA levels. This is due to ethanol's inhibition of fatty acid oxidation and its promotion of lipogenesis, leading to fatty liver disease (steatosis)(Wang et al., 2022).Ethanol also impacts cholesterol homeostasis, often increasing TC levels and potentially contributing to cardiovascular problems (Vasdev et al., 2006).Additionally, ethanol can affect PL levels by impairing their synthesis and altering cell membrane integrity, which may result in cell dysfunction and death(Pamplona et al.,

2008).These lipid imbalances contribute to liver injury, oxidative stress, and inflammation, which can progress to more severe conditions such as steatohepatitis, fibrosis, and cirrhosis(Masarone et al.,2018).In the present study, lipid profiles were elevated in both plasma and liver tissue of rats exposed to ethanol alone. However, supplementation with quinic acid reduced the lipid profile. Similarly, Xu et al. (2019)found that chlorogenic acid, a conjugate of caffeic acid and quinic acid, also reduced lipid profiles in high-fat diet-induced obese mice.

Plasma lipoproteins are crucial for supplying the fatty acids necessary for triacylglycerol synthesis. A diet high in fats can lead to elevated TG levels, contributing to arterial hardening(Kostov et al., 2018).TGs are transported to peripheral tissues via VLDL. Excessive ethanol consumption impairs VLDL secretion, thereby reducing TG transport and the release of FFAs from lipoproteins. HDL is essential for removing cholesterol from extrahepatic tissues (You et al., 2019). In rats with ethanol-induced hepatotoxicity, HDL levels were notably lower compared to normal rats, while VLDL and LDL levels were significantly higher. However, administration of quinic acid to ethanol-fed rats improved HDL levels and reduced LDL and VLDL levels compared to those in ethanol-treated rats. Generally, antihyperlipidemic drugs are known to significantly lower TC and increase HDL levels (Rauf et al., 2022).

Most hepatotoxic drugs are not inherently toxic but become harmful due to the production of intermediate metabolites by phase I xenobiotic-metabolizing enzymes (Gomez-Lechon et al., 2010). While the majority of CYP450 enzymes are predominantly expressed in the liver, several CYPs also play a role in drug metabolism in extrahepatic tissues such as the small intestine, colon, respiratory tract, and skin organs that come into direct contact with xenobiotics (Gundert-Remy et al., 2014).Excessive alcohol consumption is linked to the induction of the CYP2E1 pathway for alcohol metabolism. This pathway can indirectly contribute to ALD by generating high levels of superoxide radicals. This occurs through the interaction of CYP2E1 with cytochrome reductase, causing electron leaks in the respiratory chain and increased ROS production (Albano et al., 2015). In our study, we observed elevated activities of phase I enzymes, including CyP450, Cyb5, NADPH-CyP450, and NADPH-Cyb5, in ethanol-fed rats. This increase likely impacts the production of toxic metabolites and contributes to ethanol-induced liver injury. Additionally, the rise in free radicals and acetaldehyde production due to ethanol metabolism by CYP2E1 can impair the liver's defense mechanisms against oxidative stress. Furthermore, the liver is crucial for enhancing

the solubility and excretion of lipophilic compounds through phase II xenobiotic-metabolizing enzymes (Kurianet al., 2023). Ethanol-fed rats showed reduced activities of phase II enzymes, such as GST, UDP-GT, and DTD. Conversely, quinic acid supplementation inhibited phase I enzyme activities while stimulating phase II enzymes, potentially offering protection against certain liver diseases.

Alcohol administration leads to various histological abnormalities in the liver (MacSween et al., 1986). In ethanol-treated rats, liver histology revealed pathomorphological alterations primarily in the centrilobular region, which experiences reduced oxygen perfusion. Hepatic damage may be partially due to the activity of cytochrome P450 enzymes, which are most concentrated near the central vein and least near the peripheral areas (Xu et al., 2013). Supplementation with quinic acid significantly mitigated the liver changes induced by alcohol.

5. CONCLUSION

Quinic acid demonstrates a protective effect against ethanol-induced damage in rats, as evidenced by improvements in body weight, liver morphology, and biochemical markers. Ethanol-treated rats showed decreased body weight, liver morphological disruptions, elevated liver enzyme activities, altered lipid profiles, and histopathological changes, indicating hepatic damage. However, supplementation with quinic acid significantly restored body weight, liver morphology, and normalized liver marker enzyme activities (AST, ALT, ALP, and GGT). Quinic acid also reduced serum urea, uric acid, creatinine, and total bilirubin levels and improved lipid profiles by decreasing TC, TG, PL, and FFA levels, along with lowering LDL and VLDL while increasing HDL levels. Moreover, quinic acid modulated phase I and phase II detoxification enzyme activities and mitigated ethanol-induced histopathological changes. These findings suggest that quinic acid has a protective role in counteracting ethanol-induced hepatotoxicity and oxidative stress in rats.

ANIMAL ETHICS

This work carried out after getting ethical approval from the Institutional Animal Ethics Committee for the Control and Supervision of Experimental Animals (Reg. No. 160/1999/CPCSEA/1095).

DISCLAIMER (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

CONFLICT OF INTEREST

All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report

ABBREVIATIONS

AKI: Acute kidney injury; **ALT:**Alanine aminotransferase; **ADH:** Alcohol dehydrogenase; **ALD:** Alcoholic liver disease; **ALP:** Alkaline phosphatase; **ANOVA:** Analysis of variance;**AST:**Aspartate aminotransferase; **CO:** Carbon monoxide; **Cyb5:** Cytochrome b5; **CyP450:**Cytochrome P450; **DTD:** DT-diaphorase; **DMRT:**Duncan's multiple range test; **FFA:**Free fatty acids; **GGT:** Gamma-glutamyl transferase; **GFR:** Glomerular filtration rate; **GST:** Glutathione S-transferase; **H&E:** Haematoxylin and eosin; **HDL:**High-density lipoprotein; **LDL:** Low-density lipoprotein; **NADH:** Nicotinamide-adenine dinucleotide; **NADPH:** Nicotinamide adenine dinucleotide phosphate; **PL:** Phospholipids; **ROS:** Reactive oxygen species; **TC:** Total cholesterol; **TG:** Triglycerides; **UDP-GT:**UDP-glucuronyl transferase; **VLDL:** Very low-density lipoprotein.

REFERENCES

1. Abidi, O., Hammami, I., Jebali, J., Srairi-Abid, N., Alqahtani, AS., Gressier, B., Eto, B. & SOUILEM, O. (2024) Dietary Supplementation of Pistacia lentiscus: Hepato□Protective Potential Against 7, 12□dimethylbenz (a) anthracene Carcinogen in C57Bl/6 Mice, Alongside In Vitro Anti□Cancer Efficacy.https://doi.org/10.20944/preprints202404.0726.v1
2. Addolorato, G., Mirijello, A., Barrio, P., & Gual, A. (2016). Treatment of alcohol use disorders in patients with alcoholic liver disease. *Journal of hepatology*, *65*(3), 618-630.
3. Albano, E. (2015). Oxidative stress in alcoholic liver disease. In *Studies on hepatic disorders* (pp. 215-239). Cham: Springer International Publishing.

4. Anoor, P. K., Yadav, A. N., Rajkumar, K., Kande, R., Tripura, C., Naik, K. S., &Burgula, S. (2022). Methanol extraction revealed anticancer compounds Quinic Acid, 2 (5H)-Furanone and Phytol in Andrographis paniculata. *Molecular and Clinical Oncology*, *17*(5), 1-13.
5. Arulmozhi, V., Krishnaveni, M., Karthishwaran, K., Dhamodharan, G., & Mirunalini, S. (2010). Antioxidant and antihyperlipidemic effect of Solanum nigrum fruit extract on the experimental model against chronic ethanol toxicity. *Pharmacognosy magazine*, *6*(21), 42.
6. Arumugam, S. (2019). Thiamine deficiency in alcoholics with normal body mass index. *Journal of Dr. NTR University of Health Sciences*, *8*(3), 175-182.
7. Arya, A., Al-Obaidi, M. M. J., Shahid, N., Noordin, M. I. B., Looi, C. Y., Wong, W. F., ... & Mustafa, M. R. (2014). Synergistic effect of quercetin and quinic acid by alleviating structural degeneration in the liver, kidney and pancreas tissues of STZ-induced diabetic rats: a mechanistic study. *Food and Chemical Toxicology*, *71*, 183-196.
8. Attard, R., Dingli, P., Doggen, C. J., Cassar, K., Farrugia, R., & Bezzina Wettinger, S. (2021). The impact of frequency, pattern, intensity, and type of alcohol consumption, and its combined effect with smoking on inflammation, lipid profile, and the risk of myocardial infarction. *Journal of Public Health*, *29*, 611-624.
9. Benali, T., Bakrim, S., Ghchime, R., Benkhaira, N., El Omari, N., Balahbib, A., ... &Bouyahya, A. (2024). Pharmacological insights into the multifaceted biological properties of quinic acid. *Biotechnology and Genetic Engineering Reviews*, *40*(4), 3408-3437.
10. Brzoska, M. M., Moniuszko-Jakoniuk, J., Piłat-Marcinkiewicz, B., & Sawicki, B. (2003). Liver and kidney function and histology in rats exposed to cadmium and ethanol. *Alcohol and Alcoholism*, *38*(1), 2-10.
11. Burstein, M. S. H. R., Scholnick, H. R., & Morfin, R. (1970). Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. *Journal of lipid research*, *11*(6), 583-595.
12. Canaud, B., Ye, X., Usvyat, L., Kooman, J., van Der Sande, F., Raimann, J., ... &Kotanko, P. (2020). Clinical and predictive value of simplified creatinine index used as muscle mass surrogate in end-stage kidney disease haemodialysis patients—results from the international MONitoring Dialysis Outcome initiative. *Nephrology Dialysis Transplantation*, *35*(12), 2161-2171.
13. Caraway, W. T. (1955). Determination of uric acid in serum by a carbonate method. *American journal of clinical pathology*, *25*(7_ts), 840-845.

14. Chen, Z., Tian, R., She, Z., Cai, J., & Li, H. (2020). Role of oxidative stress in the pathogenesis of nonalcoholic fatty liver disease. *Free Radical Biology and Medicine*, *152*, 116-141.

15. Clerc, O., Nanchen, D., Cornuz, J., Marques□Vidal, P., Gmel, G., Daeppen, J. B., ... &Rodondi, N. (2010). Alcohol drinking, the metabolic syndrome and diabetes in a population with high mean alcohol consumption. *Diabetic Medicine*, *27*(11), 1241-1249.

16. Comporti, M., Signorini, C., Leoncini, S., Gardi, C., Ciccoli, L., Giardini, A., ... &Arezzini, B. (2010). Ethanol-induced oxidative stress: basic knowledge. *Genes & nutrition*, *5*, 101-109.

17. Di Padova, C., Tritapepe, R., Rovagnati, P., Bessone, E., & Di Padova, F. (1982). Effect of ethanol on biliary unconjugated bilirubin and its implication in pigment gallstone pathogenesis in humans. *Digestion*, *24*(2), 112-117.

18. Ernster, L. (1967). [56] DT diaphorase. In *Methods in enzymology* (Vol. 10, pp. 309-317). Academic Press.

19. Falholt, K., Lund, B., & Falholt, W. (1973). An easy colorimetric micromethod for routine determination of free fatty acids in plasma. *Clinica chimica acta*, *46*(2), 105-111.

20. Fawcett, J., & Scott, J. (1960). A rapid and precise method for the determination of urea. *Journal of clinical pathology*, *13*(2), 156-159.

21. Folch, J., Lees, M., & Stanley, G. S. (1957). A simple method for the isolation and purification of total lipides from animal tissues. *Journal of biological chemistry*, *226*(1), 497-509.

22. Foster, L. B., & Dunn, R. T. (1973). Stable reagents for determination of serum triglycerides by a colorimetric Hantzsch condensation method. *Clinical chemistry*, *19*(3), 338-340.

23. Freudenheim, J. L. (2020). Alcohol's effects on breast cancer in women. *Alcohol research: current reviews*, *40*(2).https://doi.org/10.35946/arcr.v40.2.11

24. Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical chemistry*, *18*(6), 499-502.

25. Gomez-Lechon, M. J., Lahoz, A., Gombau, L., Castell, J. V., & Donato, M. T. (2010). In vitro evaluation of potential hepatotoxicity induced by drugs. *Current pharmaceutical design*, *16*(17), 1963-1977.

26. Graciela, K. A., Juanita, B., & Silvia, L. A. (2021). Alcohol toxicity: the role of oxidative stress. In *Toxicology* (pp. 225-232). Academic Press.

27. Gundert-Remy, U., Bernauer, U., Blömeke, B., Döring, B., Fabian, E., Goebel, C., ... &Roos, P. H. (2014). Extrahepatic metabolism at the body's internal–external interfaces. *Drug metabolism reviews*, *46*(3), 291-324.

28. Habig, W. H., Pabst, M. J., & Jakoby, W. B. (1974). Glutathione S-transferases: the first enzymatic step in mercapturic acid formation. *Journal of biological Chemistry*, *249*(22), 7130-7139.

29. Hansen, T. W., Wong, R. J., & Stevenson, D. K. (2020). Molecular physiology and pathophysiology of bilirubin handling by the blood, liver, intestine, and brain in the newborn. *Physiological reviews*, *100*(3), 1291-1346.

30. Isselbacher, K. J., Chrabas, M. F., & Quinn, R. C. (1962). The solubilization and partial purification of a glucuronyl transferase from rabbit liver microsomes. *Journal of Biological Chemistry*, *237*(10), 3033-3036.

31. Jaffe, M. Z. (1886). Method for measurement of creatinine in serum. *Physiol Chem*, *10*(391), 31.

32. Jalili, V., Poorahmadi, Z., HasanpourArdekanizadeh, N., Gholamalizadeh, M., Ajami, M., Houshiarrad, A., ... &Doaei, S. (2022). The association between obesity with serum levels of liver enzymes, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and gamma□glutamyl transferase in adult women. *Endocrinology, diabetes & metabolism*, *5*(6), e367.

33. Jiang, Y., Zhang, T., Kusumanchi, P., Han, S., Yang, Z., &Liangpunsakul, S. (2020). Alcohol metabolizing enzymes, microsomal ethanol oxidizing system, cytochrome P450 2E1, catalase, and aldehyde dehydrogenase in alcohol-associated liver disease. *Biomedicines*, *8*(3), 50.

34. Jie, Q., Tang, Y., Deng, Y., Li, Y., Shi, Y., Gao, C., ... & Yao, P. (2013). Bilirubin participates in protecting of heme oxygenase-1 induction by quercetin against ethanol hepatotoxicity in cultured rat hepatocytes. *Alcohol*, *47*(2), 141-148.

35. Jin, M., Yang, F., Yang, I., Yin, Y., Luo, J. J., Wang, H., & Yang, X. F. (2012). Uric acid, hyperuricemia and vascular diseases. *Frontiers in bioscience: a journal and virtual library*, *17*, 656.

36. Kostov, K., &Halacheva, L. (2018). Role of magnesium deficiency in promoting atherosclerosis, endothelial dysfunction, and arterial stiffening as risk factors for hypertension. *International journal of molecular sciences*, *19*(6), 1724.

37. Kurian, R., Steen, L. T., & Wang, H. (2023). Liver Drug Metabolism. *Oral Bioavailability and Drug Delivery: From Basics to Advanced Concepts and Applications*, 189-212.

38. Lee, T. H., Kim, W. R., &Poterucha, J. J. (2012). Evaluation of elevated liver enzymes. *Clinics in liver disease*, *16*(2), 183-198.

39. MacSween, R. N. M., & Burt, A. D. (1986, August). Histologic spectrum of alcoholic liver disease. In *Seminars in liver disease* (Vol. 6, No. 03, pp. 221-232). © 1986 by Thieme Medical Publishers, Inc.

40. Malloy, H. T., & Evelyn, K. A. (1937). The determination of bilirubin with the photoelectric colorimeter. *Journal of biological Chemistry*, *119*(2), 481-490.

41. Masarone, M., Rosato, V., Dallio, M., Gravina, A. G., Aglitti, A., Loguercio, C., ... & Persico, M. (2018). Role of oxidative stress in pathophysiology of nonalcoholic fatty liver disease. *Oxidative medicine and cellular longevity*, *2018*(1), 9547613.

42. Masarone, M., Rosato, V., Dallio, M., Gravina, A. G., Aglitti, A., Loguercio, C., ... & Persico, M. (2018). Role of oxidative stress in pathophysiology of nonalcoholic fatty liver disease. *Oxidative medicine and cellular longevity*, *2018*(1), 9547613.

43. Mihara, K., & SATO, R. (1972). Partial purification of NADH-cytochrome b5 reductase from rabbit liver microsomes with detergents and its properties. *The Journal of Biochemistry*, *71*(4), 725-735.

44. Nagarthna, P. K. M., HarshaVardhini, N., Bashir, B., & Sridhar, K. M. (2020). Hyperlipidemia and its treatment: A review. *Journal of Advanced Scientific Research*, *11*(01), 1-6.

45. Oh, M. S., Briefel, G., & Pincus, M. R. (2021). 15 Evaluation of renal function, water, electrolytes, and acid-base balance. *Henry's Clinical Diagnosis and Management by Laboratory Methods E-Book*, 182.

46. O'Keefe, E. L., DiNicolantonio, J. J., O'Keefe, J. H., & Lavie, C. J. (2018). Alcohol and CV health: Jekyll and Hyde J-curves. *Progress in cardiovascular diseases*, *61*(1), 68-75.

47. Omura, T., & Sato, R. (1964). The carbon monoxide-binding pigment of liver microsomes. I. Evidence for its hemoprotein nature. *J biol Chem*, *239*(7), 2370-2378.

48. Omura, T., & TAKESUE, S. (1970). A new method for simultaneous purification of cytochrome b 5 and NADPH-cytochrome c reductase from rat liver microsomes. *The Journal of Biochemistry*, *67*(2), 249-257.

49. Orman, E. S., Odena, G., & Bataller, R. (2013). Alcoholic liver disease: pathogenesis, management, and novel targets for therapy. *Journal of gastroenterology and hepatology*, *28*, 77-84.

50. Pamplona, R. (2008). Membrane phospholipids, lipoxidative damage and molecular integrity: a causal role in aging and longevity. *Biochimica et Biophysica Acta (BBA)-Bioenergetics*, *1777*(10), 1249-1262.

51. Poupon, R. (2015). Liver alkaline phosphatase: a missing link between choleresis and biliary inflammation. *Hepatology*, *61*(6), 2080-2090.

52. Quraishi, R., Sarkar, S., & Jain, R. (2021). Impact of chronic alcohol and opioid dependence on biochemical parameters: A retrospective case control study from a tertiary care treatment center in north India. *Addiction & Health*, *13*(3), 148.

53. Rauf, A., Akram, M., Anwar, H., Daniyal, M., Munir, N., Bawazeer, S..& Khan, H. (2022). Therapeutic potential of herbal medicine for the management of hyperlipidemia: latest updates. *Environmental Science and Pollution Research*, *29*(27), 40281-40301.

54. Rosalki, S. B., Rau, D., Lehmann, D., & Prentice, M. (1970). Determination of serum γ-glutamyl transpeptidase activity and its clinical applications. *Annals of Clinical Biochemistry*, *7*(6), 143-147.

55. Siedel, J., Hägele, E. O., Ziegenhorn, J., &Wahlefeld, A. W. (1983). Reagent for the enzymatic determination of serum total cholesterol with improved lipolytic efficiency. *Clinical chemistry*, *29*(6), 1075-1080.

56. Vasdev, S., Gill, V., & Singal, P. K. (2006). Beneficial effect of low ethanol intake on the cardiovascular system: possible biochemical mechanisms. *Vascular Health and Risk Management*, *2*(3), 263-276.

57. Walker, V. (2014). Ammonia metabolism and hyperammonemic disorders. *Advances in clinical chemistry*, *67*, 73-150.

58. Wang, X., Chang, X., Zhan, H., Zhang, Q., Li, C., Gao, Q., & Sun, Y. (2020). Curcumin and Baicalin ameliorate ethanol□induced liver oxidative damage via the Nrf2/HO□1 pathway. *Journal of Food Biochemistry*, *44*(10), e13425.

59. Wang, X., Wang, Y., Liu, Y., Cong, P., Xu, J., & Xue, C. (2022). Hepatoprotective effects of sea cucumber ether-phospholipids against alcohol-induced lipid metabolic dysregulation and oxidative stress in mice. *Food & function*, *13*(5), 2791-2804.

60. Weiner, I. D., Mitch, W. E., & Sands, J. M. (2015). Urea and ammonia metabolism and the control of renal nitrogen excretion. *Clinical Journal of the American Society of Nephrology*, *10*(8), 1444-1458.

61. Xu, M., Ju, W., Hao, H., Wang, G., & Li, P. (2013). Cytochrome P450 2J2: distribution, function, regulation, genetic polymorphisms and clinical significance. Drug metabolism reviews, 45(3), 311-352.

62. You, M., &Arteel, G. E. (2019). Effect of ethanol on lipid metabolism. *Journal of hepatology*, *70*(2), 237-248.

63. Zhang, R., Hu, Y., Yuan, J., & Wu, D. (2009). Effects of Puerariae radix extract on the increasing intestinal permeability in rat with alcohol-induced liver injury. *Journal of Ethnopharmacology*, *126*(2), 207-214.

64. Zhou, Y., Wu, R., Wang, X., Bao, X., & Lu, C. (2022). Roles of necroptosis in alcoholic liver disease and hepatic pathogenesis. *Cell Proliferation*, *55*(3), e13193.

65. Zilversmit, D. B., & Davis, A. K. (1950). Microdetermination of plasma phospholipids by trichloroacetic acid precipitation. *The Journal of Laboratory and Clinical Medicine*, *35*(1), 155-160.

66. McGovern, P. E. (2019). Alcoholic beverages as the universal medicine before synthetics. In *Chemistry's Role in Food Production and Sustainability: Past and Present* (pp. 111-127). American Chemical Society.\

67. Taher, R. F., Raslan, M. A., Masoud, M. A., Nassar, M. I., &Aboutabl, M. E. (2021). HPLC–ESI/MS profiling, phytoconstituent isolation and evaluation of renal function, oxidative stress and inflammation in gentamicin□induced nephrotoxicity in rats of Ficus spragueanaMildbr. &Burret. *Biomedical Chromatography*, *35*(9), e5135.

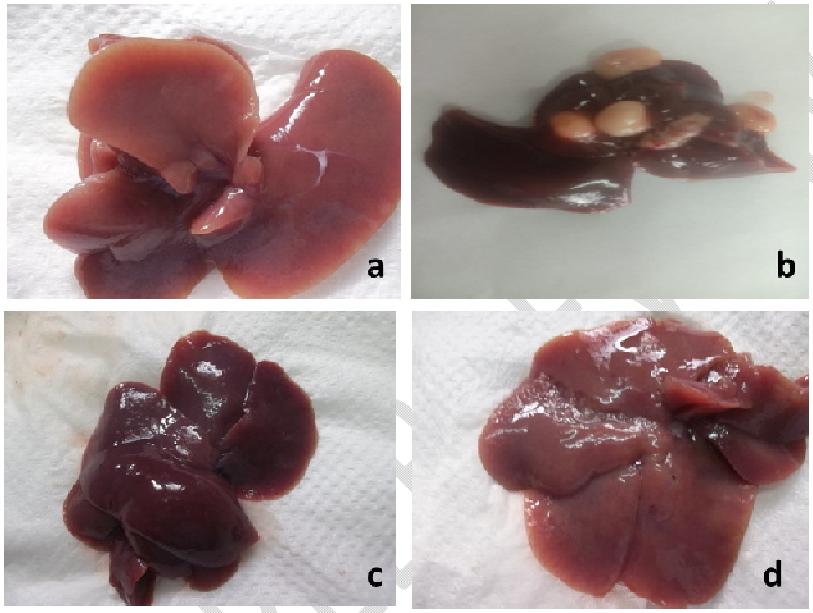

Fig. 1:Effect of quinic acid on body weight changes of control and experimental rats. (a) control and (d) quinic acid alone-rat liver tissue showed normal appearance, (b) Ethanol treated rat liver tissue showed injured (c) Ethanol + quinic acid treated rat liver tissue showed regression of the liver.

Table 1: Effectofquinic acid onbodyweightofcontrolandexperimentalrats.

	Control	30% Ethanol alone	30% Ethanol+quinic acid (50mg/kg b.w)	Quinic acid (50mg/kg b.w) alone
Initial body weight (g)	170.56 ± 2.51[a]	172.42 ± 2.49[a]	169.12 ± 1.99[a]	176.85 ± 2.18[a]
Final body weight (g)	200.47 ± 4.24[a]	184.76 ± 3.96[b]	194.34 ± 3.82[c]	204.19 ± 3.21[a]

Valuesaremeans ±SDof6 rats fromeachgroup. Values notsharingcommonalphabetsassuperscriptaresignificantlydifferentfromeach otheratthelevelof$P$<0.05(ANOVAfollowed byDMRT).

Table2: Effectofquinic acid onliver markers enzyme in serum ofcontrolandexperimentalrats.

	Control	30% Ethanol alone	30% Ethanol+quinic acid (50mg/kg b.w)	Quinic acid (50mg/kg b.w) alone
AST (IU/L)	72.62 ± 4.21[a]	110.32 ± 5.55[b]	80.32 ± 5.45[c]	71.95 ± 3.28[a]
ALT (IU/L)	29.64 ± 1.68[a]	49.57 ± 2.34[b]	34.78 ± 2.34[c]	30.16 ± 3.01[a]
ALP (IU/L)	89.46 ± 3.83[a]	126.98 ± 5.33[b]	100.03 ± 3.26[c]	88.89 ± 3.19[a]
GGT (IU/L)	9.64 ± 1.36[a]	25.63 ± 1.95[b]	14.36 ± 2.50[c]	10.04 ±1.51[a]

Valuesaremeans ±SDof6 rats fromeachgroup. Values notsharingcommonalphabetsassuperscriptaresignificantlydifferentfromeach otheratthelevelof$P$<0.05(ANOVAfollowed byDMRT).

Table3: Effect of quinic acid on serum urea, uric acid, creatinine and total bilirubinof controlandexperimentalrats.

	Control	30% Ethanol alone	30% Ethanol+quinic acid (50mg/kg b.w)	Quinic acid (50mg/kg b.w) alone
Serum urea (mg/dL)	2.76 ± 0.21^{a}	7.20 ± 0.55^{b}	5.86 ± 0.45^{c}	2.40 ± 0.18^{a}
Uric acid (mg/dL)	3.12 ± 0.24^{a}	11.46 ± 0.87^{b}	8.87 ± 0.68^{c}	4.09 ± 0.31^{a}
Creatinine (mg/dL)	39.17 ± 2.98^{a}	92.34 ± 7.03^{b}	70.76 ± 5.42^{c}	42.85 ± 3.28^{a}
Total bilirubin (mg/dL)	16.42 ± 1.25^{a}	28.23 ± 2.15^{b}	20.05 ± 1.53^{c}	16.68 ± 1.28^{a}

Valuesaremeans ±SDof6 rats fromeachgroup. Values notsharingcommonalphabetsassuperscriptaresignificantlydifferentfromeach otheratthelevelof$P<0.05$(ANOVAfollowed byDMRT).

Table4: Effect of quinic acid on lipidsprofile inplasma of controlandexperimentalrats.

	Control	30% Ethanol alone	30% Ethanol+quinic acid (50mg/kg b.w)	Quinic acid (50mg/kg b.w) alone
TC (mg/dL)	51.63 ± 4.96[a]	109.56 ± 3.63[b]	59.54 ± 3.96[c]	50.67 ±5.12[a]
TG (mg/dL)	85.96 ± 3.89[a]	120.95 ± 3.47[b]	91.36 ± 2.63[c]	84.93 ± 4.85[a]
PL (mg/dL)	82.33. ± 5.31[a]	118.37 ± 5.08[b]	89.52 ± 4.31[c]	83.69 ± 4.04[a]
FFA (mg/dL)	11.91 ± 1.63[a]	25.39 ± 1.47[b]	16.62 ± 2.13[c]	11.49 ± 1.64[a]

Valuesaremeans ±SDof6 rats fromeachgroup. Values notsharingcommonalphabetsassuperscriptaresignificantlydifferentfromeach otheratthelevelof$P$<0.05(ANOVAfollowed byDMRT).

Table5: Effect of quinic acid on lipidsprofile inliver tissue of controlandexperimentalrats.

	Control	30% Ethanol alone	30% Ethanol+quinic acid (50mg/kg b.w)	Quinic acid (50mg/kg b.w) alone
TC (mg/g)	6.93 ± 1.43^{a}	16.69 ± 0.93^{b}	7.34 ± 0.98^{c}	6.43 ± 0.83^{a}
TG (mg/g)	4.93 ± 0.92^{a}	9.25 ± 1.47^{b}	5.68 ± 0.46^{c}	5.02 ± 1.02^{a}
PL (mg/g)	17.94 ± 1.06^{a}	21.99 ± 2.63^{b}	19.01 ± 1.07^{c}	17.12 ± 2.08^{a}
FFA (mg/g)	13.56 ± 1.09^{a}	18.63 ± 1.06^{b}	14.69 ± 1.14^{c}	13.34 ± 0.94^{a}

Valuesaremeans ±SDof6 rats fromeachgroup. Values notsharingcommonalphabetsassuperscriptaresignificantlydifferentfromeach otheratthelevelof$P<0.05$(ANOVAfollowed byDMRT).

Table6: Effect of quinic acid on plasma lipoproteinof controlandexperimentalrats.

	Control	30% Ethanol alone	30% Ethanol+quinic acid (50mg/kg b.w)	Quinic acid (50mg/kg b.w) alone
LDL (mg/dL)	32.69 ± 2.63^{a}	89.05 ± 3.78^{b}	40.89 ± 3.97^{c}	33.64 ± 1.89^{a}
HDL (mg/dL)	31.09 ± 1.62^{a}	23.64 ± 1.21^{b}	28.96 ± 1.08^{c}	31.98 ± 1.64^{a}
VLDL (mg/dL)	16.76 ± 2.78^{a}	27.68 ± 2.67^{b}	21.64 ± 3.17^{c}	15.98 ± 1.68^{a}

Valuesaremeans ±SDof6 rats fromeachgroup. Values notsharingcommonalphabetsassuperscriptaresignificantlydifferentfromeach otheratthelevelof$P<0.05$(ANOVAfollowed byDMRT).

Table7: Effect of quinic acid on phase I and phase II enzymes inliver tissue of controlandexperimentalrats.

	Control	30% Ethanol alone	30% Ethanol+quinic acid (50mg/kg b.w)	Quinic acid (50mg/kg b.w) alone
Cytochrome P450 (µmol/mg protein)	0.94 ± 0.13^{a}	1.58 ± 0.15^{b}	1.05 ± 0.15^{c}	0.93 ± 0.18^{a}
Cytochrome b5 (µmols/mg protein)	0.75 ± 0.16^{a}	1.84 ± 0.21^{b}	0.98 ± 0.18^{c}	0.77 ± 0.11^{a}
NADPH-cytochrome P450 reductase*	4.62 ± 1.18^{a}	8.96 ± 1.34^{b}	5.74 ± 1.31^{c}	4.55 ± 1.65^{a}
NADPH-cytochrome b5 reductase^{+}	9.85 ± 1.95^{a}	16.98 ± 1.48^{b}	11.06 ± 1.44^{c}	9.47 ± 1.10^{a}
GST (µmol of CDNB-GSH conjugate formed/min/mg protein)	1.66 ± 0.23^{a}	0.71 ± 0.31^{b}	1.44 ± 0.13^{c}	1.68 ± 0.19^{a}
DTD (µmols of 2,6-dichlorophenolindophenol reduced/min/mg protein))	5.96 ± 1.28^{a}	1.88 ± 0.99^{b}	5.53 ± 1.34^{c}	5.89 ± 1.56^{a}
UDP-GT (UDP-glucuronyl transferase: units/min/mg protein)	11.36 ± 2.47^{a}	5.68 ± 1.69^{b}	10.65 ± 1.95^{c}	11.47 ± 2.13^{a}

One unit of enzyme activity is defined as that causing the oxidation of 1 mole of NADPH/min/mg protein. $^{+}$ One unit of enzyme activity is defined as that causing the reduction of 1 mole of ferriccyanide/min/mg/protein. Valuesaremeans ±SDof6 rats fromeachgroup. Values notsharingcommonalphabetsassuperscriptaresignificantlydifferentfromeach otheratthelevelof$P$<0.05(ANOVAfollowed byDMRT).

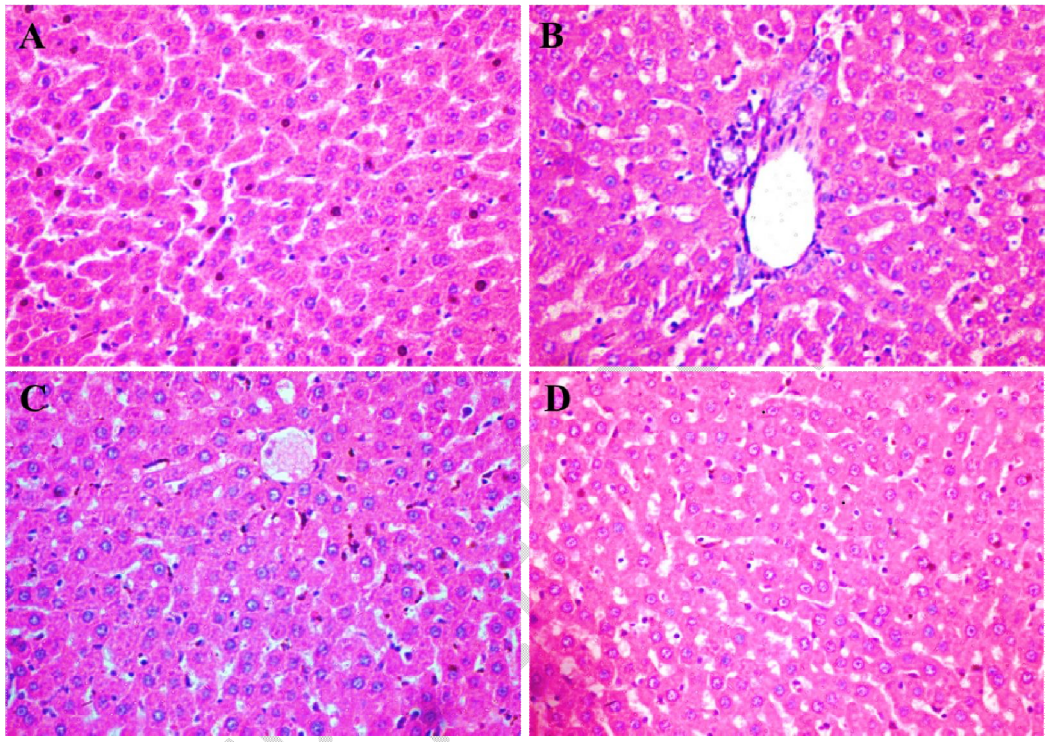

Fig.2: Histopathological changes of liver tissue of control and experimental rats. A) Control, B) 30% Ethanol, C) 30% Ethanol+quinic acid (50mg/kg b.w) D) Quinic acid (50mg/kg b.w) alone.