HepatoprotectiveEffect ofQuinicAcidagainstEthanol-InducedLiverToxicityinRats: Biochemical, Physiological, and Histological Insights

ABSTRACT

AlcoholconsumptionisassociatedwithseveralhealthissuesincludingAlcoholicLiver Disease(ALD).Quinicacid,acyclicpolyolcompound,isknownforitsantioxidant,anticancer, anti-inflammatory,andhepatoprotectiveproperties.Thisstudyaimstoelucidatetheprotective mechanismsofquinicacidagainstethanol-inducedlivertoxicityinrats.Malerats(*n*=32)were dividedintofourgroups(n=8pergroup)andtreatedover60days.Group1receivedastandard 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 andrenalprofiles,andalteredphaseIandIIenzymeactivities.Quinicacidsupplementationin 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-inducedtoxicitybyreducingoxidativestress,normalizingliverfunctions,andpreservingliver structure. These findings highlight its potential as a therapeutic agent for managing ALD.

Keywords: Antioxidants,detoxificationenzymes,ethanol,livermarkerhnzymes,quinicacid.

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1. INTRODUCTION

Alcoholic beverages, including distilled spirits, fermented wine, and mixed wine, have been consumed for thousands of years. However, ethanol is metabolized byalcoholdehydrogenase (ADH)intoacetaldehyde,atoxicintermediateproductofglycolysis.Alcoholconsumptioncan 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

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3.6%ofglobalcancercasesand20%ofAlcoholicLiverDisease(ALD)casesZhouetal.,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). Oxidativestress and an inflammatoryenvironment are keyfactors in the developmentofALD. Oxidative stress results from an imbalance between oxidation and the antioxidant system, involving the overproduction of reactive oxygen species (ROS), mitochondrial dysfunction,andimpairedantioxidantdefences(Chenetal.,2020).Bothacuteandchronicethanolexposure can lead to ROSoverproduction and a reduction in antioxidants, causing liver damagethrough mechanisms such as attacking proteins and DNA and inducing lipid peroxidation, which disrupts cell membrane structure and alters hepatocyte permeability (Graciela et al.,2021; Wangetal..2020).

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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,andbileducts;increasedlevelsmaysuggestbileflowproblemsorbonedisorders. 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 excretedbythekidneys, reflectsrenalfunction(Weineretal.,2015).Uricacid,abyproductof purinemetabolism,canindicateconditionslikegoutwhenlevelsareelevated(Jinetal.,2012). Creatinine,awasteproductofmusclemetabolism,isusedtoassesskidneyfunctionandmuscle mass(Canaudetal.,2020).Totalbilirubin,apigmentformedfromthebreakdownofredblood cells, helps evaluate liver health and can indicate issues such as jaundice. Together, these biomarkersarecrucialfordiagnosingand monitoringvarioushealthconditions (Hansenetal., 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).Therelationshipbetweenalcoholconsumptionandcardiovasculardiseaseriskincluding myocardial infarction and coronary heart disease is largely mediated by its effects on lipid profiles,particularlyHDL-cholesterolandLDL-cholesterollevels(Attardetal.,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, thisdetoxification step canproducereactive molecules that maybemore 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 avaluable 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. MATERIALSANDMETHODS

Chemicalsandreagents

Quinic acid,ethanol (purityof99.8%),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.

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,AnnamalaiUniversity.Theratswerecaredforinaccordancewiththeethical

guidelines of the Annamalai University Animal Care and Use Committee and the Indian National LawonAnimal Care(Reg. No.160/1999/CPCSEA/1095).Allexperiments followed the "Guide for the Care and Use of Laboratory Rats." The animals were kept in plastic cages withpaddyhuskbeddingatacontrolledtemperatureof27±2°C,under a12hlight/darkcycle.

Studydesign

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.

Group2: Rats wereadministered30%ethanol(equivalentto50g/kgbodyweight,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 dayonwards, they were also administered quinic acid (50 mg/kgbody 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.

ActivitiesofhepaticmarkerenzymesinserumThe

levels of serum enzymes were assessed using spectrophotometric methods and commerciallyavailablediagnostickitsfromSigmaDiagnosticsPvt.Ltd,followingestablished 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)weremeasuredusingstandardprocedures.TodetermineGGT(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.

Estimationofserumureaand uricacid

Serum urea was estimated using an enzymatic method with a diagnostic kit based on Fawcett and Scott (1960)protocol. In this assay, 10 µLof the serum sample was mixed with 1 mLof buffered enzyme solution containing phosphate buffer, urease, and sodium nitroprusside, and incubated at 37°C for 5 min.Ablank was prepared by substituting the sample with 10 µLof distilled water. Following this, 1 mLof the color-developing reagent was added to each tube, mixedthoroughly,andincubatedforanother5minat37°C.Afterincubation,1mLofdistilled water was added, and the intensityof 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 proportionaltotheuricacidconcentration.Fortheassay,25µLofthesampleordistilledwater (blank) was mixed with 1 mL of enzyme reagent containing uricase, 4-aminoantipyrine, and hydrogenperoxidase.Afterincubationat37°Cfor5min,absorbancewasmeasuredat510nm, and results were expressed in mg/dL.

Estimationofserumcreatinineand bilirubin

Serum creatinine was estimated using a diagnostic kit based on Jaffe's (1886) method.The assayreliesonthereactionbetweencreatinineandalkalinepicrate,formingacoloredcomplex. Interferingsubstancesreact moreslowly,allowingforaccuratedetectionofcreatinine.Forthe procedure,0.1mLofserumwasmixedwith0.5mLofsaturated picricacidand0.5mLof0.75 N sodium hydroxide, then incubated for 20 min. Absorbance readings were taken at 510 nm after20minandagainat45min,andcreatinineconcentrationwascalculatedusingastandard.

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Forbilirubindetermination,0.2mLofserumwasmixedwith2.5mLofabsolutemethanol,0.5 mLof1.5%hydrochloricacid, and0.5mLofdiazoreagent.The mixturewasallowed toreact at room temperature for 30 min before measuring the absorbance at 540 nm.

Estimationof Lipidsand 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) inplasmaandlivertissueswereassessedaccordingtotheFosterandDunn (1973) method. Phospholipids (PL) in plasma and liver tissues were determined using the ZilversmitandDavis(1950)technique.Freefattyacids(FFA)inplasmaandlivertissueswere 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.

AssayofphaseI enzymes

CytochromeP450(CyP450)andcytochromeb5(Cyb5)concentrationsweredeterminedusing 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 byan increasein absorbance at 427 nm. Theconcentrationsof 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 enzymeactivitywasdeterminedusinganextinctioncoefficientof1.02m/M/cm,withoneunit 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 andTakesue (1970)by tracking therate of NADPH oxidation at 340 nm, with enzyme activity calculated using an extinction coefficient of6.33 $cm^2/mM/cm$. One unit of enzyme activity is defined as the oxidation of one mole of NADPH per min.

AssayofphaseIIenzymes

GlutathioneS-transferase(GST,EC.2.5.1.18)activitywasdeterminedaccordingtothemethod 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).NADHservedastheelectrondonorand2,6-dichlorophenolindophenolastheelectron 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.

Histopathologicalstudies

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 acetonebaths atconcentrationsof70%,80%, and100%, each for 1 h.Followingdehydration, thespecimens wereinfiltrated andimpregnated withparaffin wax, with eachtreatmentlasting 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).

Statisticalanalysis

Results arepresented asmeans ± SD fromsixrats pergroup.Datawere analyzed using aone-wayanalysisofvariance(ANOVA), andsignificant differences among treatmentgroupswere assessed with Duncan's multiple range test (DMRT). Statistical significance was set at $P < 0.05$.

3. RESULTS

Effect of quinic acidon body weight andlivermorphological 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 liversofcontrolratsand those treated withquinic acid alonedisplaynormal morphology. Incontrast,theliversofethanol-fedratsshowsignificantmorphologicaldamage.Nonetheless, thelivers of rats that received quinic acid along with ethanol exhibitnear-normal morphology compared to the livers of rats treated with ethanol alone.

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 controlandexperimentalrats.Ratstreatedwithethanolexhibitedsignificantlyhigherlevelsof AST, ALT, ALP, and GGT 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.

Effectofquinicacidonserumurea,uricacid,creatinineandtotalbilirubinofcontrol and experimental rats

Table 3 illustrates the impact of quinic acid on renal function markers in both control and experimentalrats.Theserumlevelsofserumurea,uricacid,creatinine,andtotalbilirubinwere notably higher in rats treated with ethanol alone compared to those in the control group and ratstreatedwithquinicacidalone.Inratsgivenbothquinicacidandethanol,theseserumlevels 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 significantdifferencesinthelevelsofserumurea,uricacid,creatinine,andtotalbilirubinwhen compared to the control group.

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

Tables 4 and 5 displaythe lipid profiles(TC, TG, PL, and FFA) in theplasma and liver tissue ofboth controland experimental rats.The studyfound that ethanol-onlytreated rats exhibited

asignificantincreaseinTC,TG,PL,andFFAlevelscomparedtothecontrolgroup.Incontrast, ratstreatedwithquinicacidshowedamarkedreductioninTC,TG,PL,andFFAlevelsinliver tissue compared to those treated with ethanol alone.

Effectofquinicacidonplasma lipoproteinsincontrolandexperimentalrats

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 changesintheirplasmalipoproteinlevels.Conversely,ratstreatedwithethanolalonedisplayed increased LDLandVLDLlevels, along with decreased HDLlevels, 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.

Effect of quinicacidonphaseI enzymes and phase IIenzymes in theliverof 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.

Histopathologicalchangesofliver

In contrast to the normal histological appearance of the central vein, hepatocytes, and hepatic sinusoids depicted in Fig. 2 (Fig.2Aand 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.2B).However,aftertreatmentwithethanolcombinedwithquinicacid,thehepatic histoarchitectural pattern was nearly restored to normal, with only minimal sinusoidal enlargement observed (Fig. 2 C).

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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 lacks essentialnutrients.Consequently,whencarbohydratesarereplacedwithethanolinthediet,weightgai n

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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. Thiscouldbeduetoquinicacid'sroleindirectlyeliminatingethanolfromtheintestinesbefore absorption.Similarly,Aryaetal.(2014)foundthatquinicacidsupplementationledtoincreased body weight in streptozotocin-induced diabetic rats.

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ASTandALTare well-established markers for liver function.ASTis found in various tissues including the liver, cardiac and skeletal muscles, kidneys, brain, pancreas, lungs, leukocytes, and erythrocytes, whileALTis predominantlypresent in the liver (Lee et al., 2012). Elevated serum levels ofAST andALT indicate hepatocyte damage or necrosis, as these enzymes leak intothebloodstreamduetoincreasedmembranepermeability(Zhangetal.,2009).Conversely, ALP,whichisassociatedwithbileducts,mayriseinresponsetobileflowobstruction.GGTis anotherliverfunctionmarker,oftenelevatedincasesofchronicalcoholconsumption(Poupon et al., 2015).Together, these enzymes help gauge the severity of liver damage and are crucial fordiagnosingethanol-inducedliverinjury.Ourstudyfoundthatethanolconsumptionledtoa significant increase inAST,ALT,ALP, and GGT activities, suggesting substantial damage to tissue membranes. However, administration of quinic acid resulted in decreased enzyme activities,indicatingahepatoprotectiveeffect.Additionally,Pistacialentiscusextract,whichis richinquinicacidandotherphytocompounds,wasshowntoreducelivermarkerenzymelevels 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. Ethanolconsumptioncanresultinincreaseduralevelsprimarilyduetoitseffectsontheliver and kidneys (Brzoska et al., 2003). Chronicalcohol intake can damagetheliver, 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(Walkeretal.,2014).Additionally,ethanolcancausedehydrationandreducebloodflow to the kidneys, further impairing their ability to excrete urea effectively. Ethanol can also impacturicacidlevels,oftenresultinginhyperuricemia(elevateduricacidintheblood).

Ethanolmetabolismincreasestheproductionofpurines, whicharethenbrokendownintouric 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 ofbile 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).

Inourstudy, ethanolexposureinratsledtoincreasedlevelsofserumurea,uricacid, creatinine, and bilirubin. However, rats treated with quinic acid showed reduced levels of these markers. FicusspragueanaMildbr. &Burret, which is rich in 3,5-O-dicaffeoylquinicacid, was effective in lowering serum urea, uric acid, creatinine, and bilirubin levels in a model of gentamicin-inducednephrotoxicityinrats.

Ethanol-inducedtoxicityaffectsvariouscomponentsofthelipidprofile,includingTC,TG,PL, and FFA (Arulmozhi et al., 2010). Chronic ethanol consumption disrupts liver lipid metabolism,resultinginelevatedTGandFFAlevels.Thisisduetoethanol'sinhibitionoffatty acidoxidationanditspromotionoflipogenesis,leadingtofattyliverdisease(steatosis)(Wang et al., 2022) .Ethanol also impacts cholesterol homeostasis, often increasing TC levels and potentiallycontributingtocardiovascularproblems(Vasdevetal.,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 contributetoliverinjury,oxidativestress,andinflammation,whichcanprogresstomoresevere conditionssuchassteatohepatitis,fibrosis,andcirrhosis(Masaroneetal.,2018).Inthepresent

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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)foundthatchlorogenicacid,aconjugateofcaffeicacidandquinicacid,alsoreduced lipid profiles in high-fat diet-induced obese mice.

Plasma lipoproteins are crucial for supplying the fatty acids necessary for triacylglycerol synthesis.Adiet 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 impairsVLDLsecretion, thereby reducingTGtransport and therelease ofFFAs fromlipoproteins.HDLisessentialforremovingcholesterolfromextrahepatictissues(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,respiratorytract,andskinorgansthatcomeintodirectcontactwithxenobiotics (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 toALD by generating high levels of superoxide radicals. This occurs through the interaction of CYP2E1 with cytochromereductase,causing electron leaks intherespiratorychainand increased ROS production (Albano et al., 2015). In our study, we observed elevated activities of phase I enzymes, includingCyP450, 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, therise 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 iscrucial for enhancingthe solubility and excretionof 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, quinicacidsupplementation inhibited phaseIenzyme activitieswhilestimulating phase II enzymes, potentially offering protection against certain liver diseases.

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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). Supplementationwithquinicacidsignificantlymitigatedtheliverchangesinducedbyalcohol.

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 liverenzymeactivities,alteredlipidprofiles,andhistopathologicalchanges,indicatinghepatic damage. However, supplementation with quinic acid significantlyrestored 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 FFAlevels, along with lowering LDL and VLDL while increasing HDLlevels. 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.

ANIMALETHICS

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).

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-densitylipoprotein;**NADH:**Nicotinamide-adeninedinucleotide;**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.

REFERENCE

1. ABIDI,O.,Hammami,I.,Jebali,J.,Srairi-Abid,N.,Alqahtani,AS.,Gressier,B.,Eto,B.&SOUILEM,O.(2024)DietarySupplementationof Pistacialentiscus:Hepato- Protective PotentialAgainst7,12- dimethylbenz(a)anthraceneCarcinogeninC57Bl/6Mice,Alongside In Vitro Anti- Cancer Efficacy.
2. Addolorato,G.,Mirijello,A.,Barrio,P.,&Gual,A.(2016).Treatmentofalcoholuse disorders in patients with alcoholic liver disease. *Journal of hepatology*, *65*(3), 618-630.
3. Albano,E.(2015).Oxidativestressinalcoholicliverdisease.In *Studiesonhepatic 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).Methanolextractionrevealedanticancercompoundsquinic Acid,2 (5H)-FuranoneandPhytolinAndrographispaniculata. *MolecularandClinical 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).Thiaminedeficiencyinalcoholicswithnormalbodymass 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 itscombinedeffectwithsmokingoninflammation,lipidprofile,andtheriskofmyocardial infarction. *Journal of Public Health*, *29*, 611-624.

Commented[h21]: Plural(References)

Commented[h22]: Abidi,O.,Hammami,I.,Jebali,J.,Srairi-Abid,N.,Alqahtani,A.S., Gressier,B.,Eto,B., &Souilem,O.(2024).DietarySupplementationof*Pistaciale ntiscus*: Hepato-Protective Potential Against 7,12-dimethylbenz(a)anthraceneCarcinogeninC57Bl/6Mice,A longside In Vitro Anti-Cancer Efficacy. Preprints.https://doi.org/10.20944/preprints202404.0726.v1

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).Liverandkidneyfunctionandhistologyinratsexposedtocadmiumand 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 musclemasssurrogateinend-stagekidneydiseasehaemodialysispatients—resultsfromthe international MONitoring Dialysis Outcome initiative. *Nephrology Dialysis Transplantation*, *35*(12), 2161-2171.
13. Caraway,W.T.(1955).Determinationofuricacidinserumbyacarbonate 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).Alcoholdrinking,themetabolicsyndromeanddiabetesinapopulation 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. DiPadova,C.,Tritapepe,R.,Rovagnati,P.,Bessone,E.,&DiPadova,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]DTdiaphorase.In*Methodsinenzymology* (Vol.10,pp.309-317).Academic Press.
19. Falholt, K., Lund, B., & Falholt, W. (1973). An easy colorimetric micromethod forroutine 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 ofurea. *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).

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).Extrahepaticmetabolismatthebody'sinternal–external interfaces. *Drug metabolism reviews*, *46*(3), 291-324.

28. Habig, W. H., Pabst, M. J., & Jakoby, W. B. (1974). Glutathione S-transferases: the firstenzymaticstepinmercapturicacidformation. *Journalofbiological 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).Thesolubilizationandpartial purificationofaglucuronyltransferasefromrabbitlivermicrosomes. *JournalofBiological Chemistry*, *237*(10), 3033-3036.

31. Jaffe,M.Z.(1886).Methodformeasurementofcreatinineinserum. *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 levelsofliverenzymes,alanineaminotransferase,aspartateaminotransferase,alkaline

Commented[h23]: Aftervolume&number**add**doi"40(2):11.https://doi.org/10.35946/arcr.v40.2.11"

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,andaldehydedehydrogenaseinalcohol-associatedliver 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 liverdisease.In *Seminarsinliverdisease* (Vol.6,No.03,pp.221-232).©1986byThieme 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). Hyperlipidemiaanditstreatment:Areview. *JournalofAdvancedScientific Research*, *11*(01), 1-6.

45. Oh, M. S., Briefel, G., & Pincus, M. R. (2021). 15 EVALUATION OF RENAL FUNCTION,WATER,ELECTROLYTES,ANDACID-BASEBALANCE.*Henry's ClinicalDiagnosisand Management by Laboratory MethodsE-Book*, 182.

46. O'Keefe,E.L.,DiNicolantonio,J.J.,O'Keefe,J.H.,&Lavie,C.J.(2018).Alcoholand 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,andnoveltargetsfortherapy. *Journalofgastroenterologyand 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 enzymaticdeterminationofserumtotalcholesterolwithimprovedlipolytic efficiency. *Clinical chemistry*, *29*(6), 1075-1080.

Commented[h24]: Maintainuniformityasotherwrotereferences

56. Vasdev, S., Gill, V., & Singal, P. K. (2006). Beneficial effect oflow 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).Ureaandammoniametabolismand 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).CytochromeP4502J2: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).EffectsofPuerariaeradixextractonthe 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).Rolesofnecroptosisinalcoholic liver disease and hepatic pathogenesis. *Cell Proliferation*, *55*(3), e13193.

65. Zilversmit,D.B.,&Davis,A.K.(1950).Microdeterminationofplasmaphospholipids bytrichloroaceticacidprecipitation. *TheJournalofLaboratoryandClinicalMedicine*, *35*(1), 155-160.

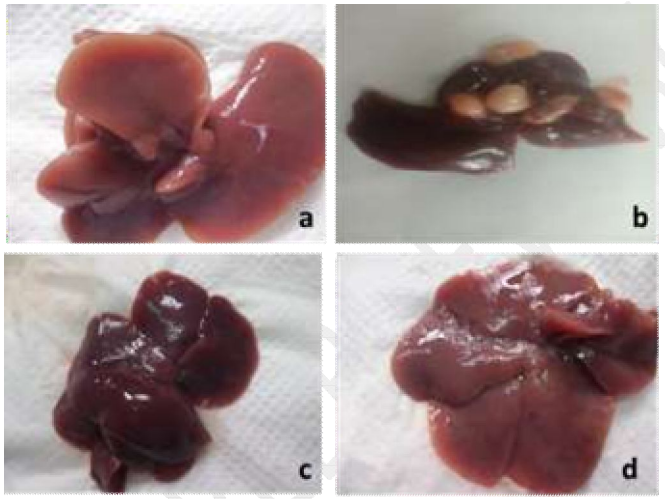

Fig. 1:Effect of quinic acid on body weight changes of control and experimental rats. (a) control and (d) quinic acid alone-rat liver tissue showed normal appearance, (b) Ethanol treated rat liver tissue showed injured (c) Ethanol + quinic acid treated rat liver tissue showed regression of the liver.

Table1:Effectofquinicacidonbodyweightofcontrolandexperimentalrats.

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

Valuesaremeans±SDof 6ratsfrom eachgroup. Valuesnotsharingcommonalphabetsassuperscriptaresignificantly differentfromeachother at the level of $P<0.05$ (ANOVA followed by DMRT).

Table2:Effectofquinicacidonlivermarkersenzymeinserumofcontrolandexperimentalrats.

	Control	30%Ethanolalone	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±SDof 6ratsfrom eachgroup. Valuesnotsharingcommonalphabetsassuperscriptaresignificantly differentfromeachother at the level of $P<0.05$ (ANOVA followed by DMRT).

Table3:Effectofquinicacidonserumurea,uricacid,creatinineandtotalbilirubinofcontrolandexperimentalrats.

	Control	30%Ethanolalone	30% Ethanol+quinic acid (50mg/kg b.w)	Quinic acid (50mg/kg b.w) alone
Serumurea(mg/dL)	2.76±0.21[a]	7.20±0.55[b]	5.86±0.45[c]	2.40±0.18[a]
Uricacid(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]
Totalbilirubin(mg/dL)	16.42±1.25[a]	28.23±2.15[b]	20.05±1.53[c]	16.68±1.28[a]

Valuesaremeans±SDof 6ratsfrom eachgroup. Valuesnotsharingcommonalphabetsassuperscriptaresignificantly differentfromeachother at the level of $P<0.05$ (ANOVA followed by DMRT).

Table4:Effectofquinicacidonlipidsprofileinplasmaofcontrolandexperimentalrats.

	Control	30%Ethanolalone	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±SDof 6ratsfrom eachgroup. Valuesnotsharingcommonalphabetsassuperscriptaresignificantly differentfromeachother at the level of $P<0.05$ (ANOVA followed by DMRT).

Table5:Effectofquinicacidonlipidsprofileinlivertissueofcontrolandexperimentalrats.

	Control	30%Ethanolalone	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±SDof 6ratsfrom eachgroup. Valuesnotsharingcommonalphabetsassuperscriptaresignificantly differentfromeachother at the level of $P<0.05$ (ANOVA followed by DMRT).

Table6:Effectofquinicacidonplasmalipoproteinofcontrolandexperimentalrats.

	Control	30%Ethanolalone	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±SDof 6ratsfrom eachgroup. Valuesnotsharingcommonalphabetsassuperscriptaresignificantly differentfromeachother at the level of $P<0.05$ (ANOVA followed by DMRT).

Table7:EffectofquinicacidonphaseIandphaseIIenzymesinlivertissueofcontrolandexperimentalrats.

	Control	30%Ethanolalone	30% Ethanol+quinic acid (50mg/kg b.w)	Quinic acid (50mg/kg b.w) alone
CytochromeP450(µmol/mgprotein)	0.94±0.13[a]	1.58±0.15[b]	1.05±0.15[c]	0.93±0.18[a]
Cytochromeb5(µmols/mgprotein)	0.75±0.16[a]	1.84±0.21[b]	0.98±0.18[c]	0.77±0.11[a]
NADPH-cytochromeP450reductase*	4.62±1.18[a]	8.96±1.34[b]	5.74±1.31[c]	4.55±1.65[a]
NADPH-cytochromeb5reductase[+]	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/mgprotein)	1.66±0.23[a]	0.71±0.31[b]	1.44±0.13[c]	1.68±0.19[a]
DTD(µmolsof2,6-dichlorophenolindophenol reduced/min/mgprotein))	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/mgprotein)	11.36±2.47[a]	5.68±1.69[b]	10.65±1.95[c]	11.47±2.13[a]

One unit of enzyme activityis defined as that causing the oxidation of 1 mole of NADPH/min/mg protein. [+] One unit of enzyme activityis defined as that causing the reduction of 1 mole of ferriccyanide/min/mg/protein. Values are means ±SD of 6 rats from each group. Values not sharing commonalphabetsassuperscript are significantly different from each other at the level of $P<0.05$(ANOVAfollowed by DMRT).

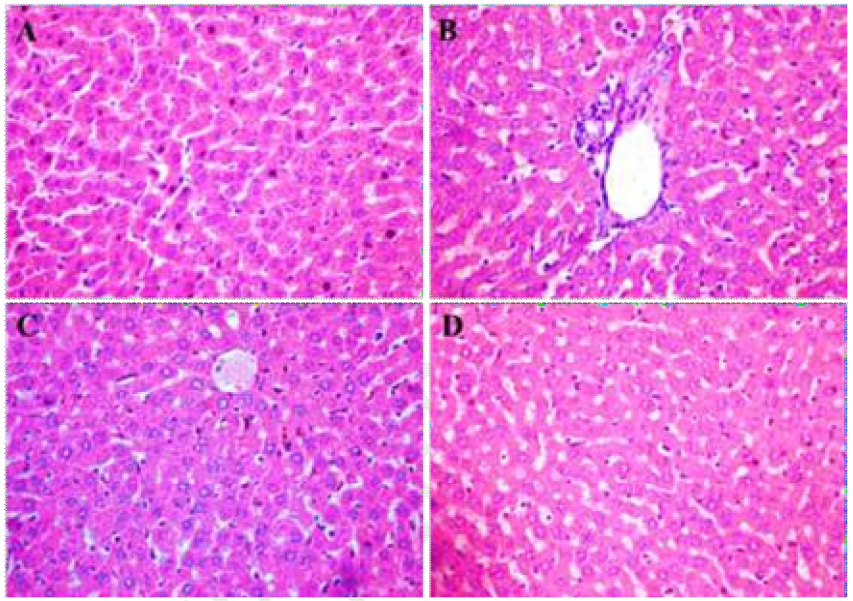

Fig.2: Histopathological changes of liver tissue of control and experimental rats. A)Control, B) 30% Ethanol, C)30% Ethanol+quinicacid (50mg/kg b.w) D) Quinic acid (50mg/kg b.w) alone.