Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env.Pharmacol. Life Sci., Vol 11[7] June 2022 : 01-12

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

ORIGINAL ARTICLE **OPEN ACCESS**

Hepatoprotective potential of *Prunus armeniaca* against the Aluminium Sulphate induced liver toxicity in rats

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ABSTRACT

The impact of an ethanolic extract of Prunus armeniaca seed on aluminium sulfate-induced liver damage in rats was investigated in this work. In this study, Prunus armeniaca was tested for hepatoprotective properties against aluminium sulfate-induced liver damage. The Aluminium sulphate (50 mg/kg, i.p) was administered except the normal control group, Ursodeoxycholic acid (250 mg/kg, p.o) was given to the standard group.Ethanolic extract Prunus armeniaca seed (200 and 400 mg/kg p.o) were given to the treatment groups, it reduced the level of various biochemical parameter of the liver which are responsible for the liver toxicity such as serum glutamyl oxaloacetate transaminase (SGOT), serum glutamyl pyruvate transaminase (SGPT), alkaline phosphatase (ALP), total protein (TP), total bilirubin (TB) and direct bilirubin (DB), High density lipoproetin (HDL), Low density lipoprotein (LDL), Total cholesterol (TC), Alkaline phosphate (ALP), Triglyceride, Total bilirubin (TBL) and Direct bilirubin (DBL). Later were the all the experimental animal were sacrificed and the histopathology examination of liver was performed for all the groups. The hepatoprotective action of the ethanolic extract of Prunus armeniaca seed is also confirmed by histology of the liver slice. As a result, the current research strongly supports the therapeutic claim of the plant Prunus armeniaca, which has strong antioxidant and hepatoprotective properties.

Keywords: *Prunus armeniaca seed, Aluminiumsulphate, ethanolic extract, Hepatoprotection.*

Received 11.12.2021 Revised 01.05.2022 Accepted 01.06.2022

INTRODUCTION

The liver is the largest and most biochemically complex organ in the adult human body, weighing roughly 3 pounds and taking up much of the right side of the body, including the diaphragm, abdominal-pelvic area, and behind the ribs. It is a basic organ that is only found in vertebrates[1]; it plays an important role in metabolism and has a variety of physiological functions in the body, including plasma protein synthesis, bile production, triglyceride cholesterol production, glycogen storage, RBC lysis, hormone production, and detoxification. It also filters and preserves chemicals digested by the digestive system before they reach the body's other organs via the systemic circulatory system[2,3].

The most important metabolic function of the liver is detoxification or inactivation and excretion of toxic chemicals, drugs, and hormones, both those produced by the body and those obtained from outside sources. Due to the liver's large reserve capacity, even minor cell injury does not result in measurable changes in its function. However, some of its functions are so sensitive that abnormalities begin to appear depending on the nature and severity of the insult [4].

Al plays a role in neurodegenerative diseases such Alzheimer's disease, Parkinson's dementia, and hepatotoxicity. Free-radical generation appears to have a role in Al's toxicity, at least in part. When Al is exposed for a long time, it causes changes in the neurological, skeletal, respiratory, and haematological systems[6,7]. The accumulation of aluminium in the liver is linked to a variety of biochemical changes, including the release of enzyme markers of liver damage and changes in the oxidant status [8,9].

Prunus armeniaca (apricot) belongs to the Rosaceae family, with a genus Prunus containing roughly 98 species of commercial value. This category encompasses all stone fruits. Prunophora is a subgenera of Prunophora (plums and apricots)[10]. Apricot is also known as "moon of the loyal" and "Egg of the sun" by the ancient Persians.*Prunusarmeinaca* fruit is one of the most well-known crops in the world, because to its high vitamin and mineral content. Apricot trees are rarely common since they can only thrive in specific areas with ideal environmental conditions.

The *Prunus armeniaca* has long been used in traditional medicine to treat a variety of ailments. A decoction of the plant bark has been used to treat inflamed skin as an astringent. In folk medicine, apricots are used to cure hemorrhages, infertility, eye inflammation, and cramps. Vaginal infections can be treated with apricot kernel paste. In cosmetics, the kernel oil is used to protect the skin from UV rays. It has been utilized in cosmetics such as hair oil, body oil, biodiesel manufacturing, and medicinal drugs [11](Laxative and expectorant). The poisonous hydrogen cyanide found in bitter apricot kernels has been used to treat asthma, cough, and constipation in very tiny doses[12] Carbohydrates, vitamins C and K, -carotene, niacin, and thiamine are all found in the fresh apricot fruit. Also isolated were organic acids, phenols, volatile chemicals, esters, and terpenoids[13]. Apricot kernels are high in dietary protein [14]there's also a lot of oil and fiber in there. Including a prior study, sweet apricot kernels contain more oil than bitter kernels, and oleic and linoleic acids account for roughly 92 g/100 g of the total fatty acids available. Depending on the variety, apricot kernels contain the poisonous cyanogenic glycoside amygdalin. Hydrolysis of amygdalin produces glucose, benzaldehyde, and hydrocyanic acid. In the presence of -glucoronidase, an enzyme present in the human intestine, cyanide is released by enzyme[15].

Cos of the presence of cyanogenic glycosides (mostly amygdalin) in the seed,*Prunus armeniaca* has anticancer properties [16].*Prunus armeniaca* hexane extract has been shown to have antimutagenic activity [17]. With the reference medicine Prednisolone, the seed kernel also demonstrated anti-inflammatory activity[18]. It has been observed that an aqueous and ethanol extract from *Prunus armeniaca* fruit possesses antitubercular activity comparable to that of Rifampicin[19].*Prunus armeniaca* kernel oil has been found to have antibacterial effects [20]. The ethanolic extract of *Prunusarmeinaca* fruits has antihelmintic properties [21]. According to a study, eating the fruit *Prunus armeniaca* on a daily basis protects against UV radiation[22]. The hepatoprotective efficacy of *Prunus armeniaca* kernel againstdimethylnitrosamine-induced hepatotoxicity was also demonstrated [23].

Prunus armeniaca has a high concentration of phytoconstituents, according to early phytochemical analysis. In light of this research, the current study was created to conduct pharmacological testing. The seed ethanol extract was studied for its preventive, hepatoprotective properties. So it was concluded from the current investigation clearly support the medicinal claim of the plant *Prunus armeniaca* possessing the good hepatoprotective activity.

MATERIAL AND METHOD

Plant Collection

In the month of July, the fruits of *Prunus armeniaca* were obtained in District Sirmour, Himanchal Pradesh, India. The NISCAIR, New Delhi, recognized the fruits and tree. The seeds were retrieved by manually breaking the fruit into two halves. These seeds were dried in the shade before being coarsely pulverised by hand. The seeds and plant were identified by the NISCAIR New Delhi.

Extraction Methodology [24,25]

The plant's seed parts were washed thoroughly with tap water, dried at room temperature, and ground into a coarse powder. By using the Soxhlet extraction method, the powder was extracted separately with solvents such as Petroleum ether (60-80), Chloroform, ethanol and water. To achieve thick sticky extract, the extracts were evaporated and dried into the desiccators and concentrated the extract to dryness, which was then stored in the refrigerator until further research could've been performed.

Drugs and Chemicals

All the chemicals used for the study were of analytical grade. Ethanols (Modern Scientific Meerut, India), Ursodeoxycholic acid (wockhardt, India) were used.

In-vivo hepatoprotective activity

Animals

Animals were procured from Animal House, IFTM University, Moradabad. Animals were approved by Institutional Animal Ethic Committee (IAEC), IFTM University.

From which approval number were given for this work. The young healthy adult Wistar Albino rats were taken in equal numbers per group (n= 6). At the commencement of the study the weight variations of animals were used and kept minimal not exceeded ± 20% of the mean weight of each animal. The Wistar albino rats, weighing 200-250gm, were used for the present study. They were housed in the cleaned propylene cage and were maintained under the standard laboratory condition (25 $\pm$ 2^0C with dark/light cycle 12/12h).They were feed with standard commercial food pellets diet (Hindustan lever, India) and water *ad libitum*. The animals were acclimatized to laboratory condition for one month to experiment. All procedure describe were reviewed and approved by the Institutional Animal Ethics Committee (IAEC), IFTM University.

Drug solutions preparation

According to the prior literature, the dried form of ethanolic extract of *Prunus armeniaca* seed was dissolved in corn oil (1 ml/kg bw) to make a solution, which was then given for 30 days. Because it promoted conginative impairment in animal screening models, Aluminium Sulphate (50mg/kg, i.p route) was used as an inducing agent for 30 days in the current study. Ursodeoxycholic acid (1 ml/kg bw) was dissolved in corn oil and a new solution was prepared every day during the experiment.

Acute oral toxicity studies

In Albino rats, the acute toxicity of sample extract and it was measured. Prior to the experiment, the animals were fasted for the night. For toxicity studies, the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) used the fixed dose [Organisation for Economic Co-operation and Development (OECD) Guideline no. 423, Annexure 2d][26] method of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA). In this experiment, the animals were divided into six groups, each with six animals. The first group was treated with 0.5 percent w/v sodium carboxy methyl cellulose and was considered normal (CMC). Groups 2, 3, 4, 5, and 6 were given a single graded dose of ethanol extract of *Prunus armeniaca* seed (1000, 2000, 3000, 4000, and 5000 mg/kg bw orally, respectively). The monitoring of parameters began soon after the sample was administered. Animals were spotted at 0hr,1hr, 2hrs, 4hrs, 6hrs, 8hrs, 24 hrs and 72hrs (with special attention given during the first four hour). Observation includes mortality and clinical signs, which includes changes in skin, fur, eyes and mucous membranes. The gross behaviours like body positions, locomotion rearing, tremors and gait were observed. The effect of plant extracts on passivity group strength, pain response, stereotype, vocalization, righting reflex, body weight and intake was also observed.

Experiment Procedure.

Aluminium induced hepatotoxicity.[27]

A total of 42 rats were equally divided into 7 groups (n = 6).

Group-I which served as normal group, were give Saline (1ml/kg/d orally) for 30 d.

Group-II Liver damage was induced in rats (Negative control), rats were administered twice with AluminiumSulphate (50 mg/kg/d) dissolved in (1 ml/kg bw) saline were injected i.p. double dose per week to induced hepatotoxicity for 30 d.

Group-III, IV were treated with ethanolic extract of *Prunus armeniaca* seed in the dose 200mg/kg, 400mg/kg (dissolve in corn oil 1 ml/kg bw) orally with Aluminium sulphate same procedure like group II for 30 d.

Group-V, VI were treated with ethanolic extract of *Prunus armeniaca* seed dissolvedin corn oil (1 ml/kg bw) for 30 d.

Group-VII Hepatotoxicity induced rats were treated with Ursodeoxycholic acid (250mg/kg/ bw) dissolved in corn oil (1 ml/kg bw) for 30 d.

Group I served as normal group and received normal saline (1ml/kg) orally for 30 days, Group II served as toxic group received Aluminum sulphate (50mg/kg) dissolved in (1ml/kg bw) saline injected by I.P, double dose per week to induced the hepatotoxicity for 30 days. Group III & IV served as test group and treated with the ethanolic extract of *Prunus armeniaca* seed in dose of 200 mg/kg, 400 mg/kg (dissolve in corn oil 1ml/kg bw) orally with aluminiumsulphate same procedure like in group II for the 30 days.

Group V and VI served as test control group which were treated only withethanolic extract of *Prunus armeniaca* seed in the dose of 200mg/kg and 400mg/kg respectively(dissolved in corn oil) given orally for 30 days.

Group VII received Ursodeoxycholic acid (250mg/kg) dissolved in corn oil (1ml/kg; bw) for the 30 days regularly.

Serum biochemistry

The b.w of rats of each group were measured before the experimental trial and 30 d after the extract administration. Twenty- four hour after the last dosage of drug administration, all the Animals were sacrificed by cervical dislocation after an overnight fasting and the blood were collected in plain and heparinised tubes by retro orbital puncture before sacrifice for the biochemical assay. Liver weights of all rats were measured after the sacrifice. Liver was isolated and washed with saline. Blood samples were centrifuged for 10 m at 2500 rpm and the serum was separated then stored at 4^{o}C until further investigations. Fresh serum samples were stored at -20^{0} C for identifyingthe biochemical parameters viz. SGOT, SGPT, CRT, TP, GGTP, TBA, ALP, TBL, DBL were estimated by using standard kits available commercially.

Histopathological studies

Quickly excised the livers of the animals and it was fixed into the formalin (10%) and embedded into paraffin. 4- 6 µm sections which were stained by the haemotoxylin and eosin dye (H & E) for

histopathological architecture of the liver. In short, liver sections approx (4-6 µm thickness) that were embedded by the paraffin and dewaxed by the distilled water for the 2 m. After that at room temperature, the liver sections were stained from the haemotoxylinfor 5 m. following 15 m, the sections of liver were counterstained from the eosin dye for 2 m, dehydrated by the alcohol, rinsed with the xylene and blocked from eosin. Studies with hemotoxylin and eosin staining of liver sections were examined under the microscope. For the histological study, the staining procedure was carried out by the hematoxylin, which is a basic dye, stains the nuclei into blue and eosin, acidic die, stains gives the pink color for the cytoplasm.

Statistical analysis

The data obtained from hepatoprotective activity were expressed as mean $\pm$ SEM. The graph were drawn, and the statistical analysis was carried out by using, the Graphpad prism software version 5.0. Results data were showed as the mean $\pm$ SEM. For data group statical evaluation mean were evaluated by one way study of variance (ANOVA) followed by Dunnet,s t3 test, $p< 0.05$, $p< 0.01$ was recognized significant.

RESULTS AND DISCUSSIONS

Acute oral toxicity study

As per OECD Guideline 423, the LD_{50} for *Prunus armeniaca*seed extract was found to be 2000 mg/kg.

Table1.Acute oral toxicity study for the ethanolic*extract* of *Prunus armeniaca* seed.

S. No	Observed activity	Ethanolic extract of *Prunus armeniaca* seed (2000 mg/kg)
1	Skin colour	Normal
2	Fur colour	Normal
3	Eyes colour	Normal
4	Mucus membrane (Nasal)	Normal
5	Respiratory rate	Normal
6	Hyperactivity	Normal
7	Eye twitching	Normal
8	Catalepsy	Normal
9	Irritation	Normal
10	Convulsions	Normal
11	Ataxia	Normal
12	Erythema	Normal
13	Edema	Normal
14	Catatonia	Normal
15	Gripping Strength	Normal
16	Pinneal reflex	Normal
17	Torch reflex	Normal
18	Lacrimination	Normal

In-vivo hepatoprotective activities

During the research, the ethanolic extract of *Prunus armeniaca* seed was found to have hepatoprotective properties against $Al_2(S0_4)_3$ -induced liver injury in wistar albino rats.

The activity of the marker enzymes SGOT, SGPT, TP, GGTP, Total bile acid, HDL, LDL, TC,Triglyceride, ALP, TBL, and DBL was considerably increased ($P<0.05$) after treatment of the experimental rats with Aluminium sulphate 50 mg/kg/d; I,P. The levels of albumin, TP, and HDL all decreased significantly.

The toxic effect of $Al_2(S0_4)_3$ on rats was gradually reversed in extract-treated groups, with significant reductions in serum SGOT, SGPT,CRT,GGTP, Total bile, LDL, ALP, TBL,DBL, TC, and triglyceride. The levels of albumin, TP, and HDL all increased significantly. Only the ethanolic extract-treated animals demonstrated a significant reduction in serum liver marker enzymes, while significant increases in Albumin, TP, and HDL levels were seen in comparison to the Ursodeoxycholic acid-treated animals (standard group).

Table 2. Effect of ethanolic extract of *Prunusa rmeniaca* seed on body weight and liver weight in $Al_2(SO_4)_3$induced rats.

Group treatment	Dose (mg/kg)	Initial body weight (gm)	Final body weight (gm)	Change in% body weight	Final liver weight (gm)
Normal group	1 ml	285.71 ± 11.07	317.69 ± 15.60	11.19	5.34 ± 0.40
Control group	50	270.28 ± 5.69^{ns}	272.30 ± 17.82**	0.74	8.96 ± 0.67**
$Al_2(SO_4)_3$+ *Prunus armeniaca* 200 mg/kg	200	273.79 ± 16.53^{ns}	290.26 ± 18.34*	5.91	6.62 ± 0.40**
$Al_2(SO_4)_3$ + *Prunus armeniaca*400 mg/kg	400	275.68 ± 14.15^{ns}	305.16 ± 17.22^{ns}	10.69	5.94 ± 0.26^{ns}
*Prunus armeniaca*200 mg/kg	200	276.806 ± 18.78^{ns}	291.16 ± 21.89*	5.18	6.60 ± 0.70**
*Prunus armeniaca*400 mg/kg	400	278.96 ± 17.09^{ns}	307.956 ± 4.07^{ns}	10.39	5.89 ± 0.31**
Standard(Ursodeoxycholic acid 250 mg/kg)	250	280.23 ± 25.41^{ns}	310.39 ± 14.17^{ns}	10.76	5.46 ± 0.28^{ns}

Results are expressed as mean ± SEM n= 6, n= represent the non significant changes * p ≤0.05 represent less significant changes, ** p ≤0.01 represent significant changes compared with normal rats by one wayAnova followed by Dunett's test.

Table 3.Effect of ethanolic extract of *Prunus armeniaca* seed on some biochemical parameters of $Al_2(SO_4)_3$ intoxicated rats.

Treatment	SGOT (U/L)	SGPT (U/L)	Albumin (g/dl)	CRT (mg/dl)	Total protein (g/dl)	GGTP (U/L)	Total bile acid (µmol/L)
Normal group	9.33 ± 1.59	10.12 ± 7.35	4.69 ± 0.36	0.79 ± 0.07	8.59 ± 0.96	13.04 ± 2.65	0.94 ± 0.07
Control group	78.59 ±7.96**	65.86 ±14.008**	1.74 ± 0.40**	1.78± 0.02**	1.67 ± 0.93**	82.44 ± 5.94**	3.03 ± 0.28**
$Al_2(SO_4)_3$+ *Prunus armeniaca* 200 mg/kg	30.29 ± 6.07**	34.89 ± 7.26**	2.98 ± 0.37**	1.25 ± 0.49**	6.24 ± 0.24**	34.03 ± 9.96**	1.73 ± 0.15**
$Al_2(SO_4)_3$ + *Prunus armeniaca*400 mg/kg	25.10 ± 16.17*	29.75 ± 6.00*	4.07 ± 0.18*	0.97 ± 0.013ns	7.42 ± 0.30**	26.72 ± 9.56^{ns}	1.19 ± 0.10*
*Prunus armeniaca*200 mg/kg	28.43 ± 8.38**	33.65 ± 6.74*	3.02 ± 0.24**	1.24 ± 0.11**	6.31 ± 0.07**	32.02 ± 7.16**	1.57 ± 0.042**
*Prunus armeniaca*400 mg/kg	22.95 ± 3.93*	28.61 ± 4.82*	4.10 ± 0.36*	.93 ± 0.08^{ns}	7.27 ± 0.10**	25.02 ± 3.6^{ns}	1.24 ± 0.13**
Standard(Ursodeoxycholic acid 250 mg/kg)	23.39 ± 5.52^{ns}	29.66 ±5.14^{ns}	4.46 ± 0.21^{ns}	.88 ±0.06^{ns}	7.52 ± 0.17**	19.43 ± 5.53^{ns}	1.08 ± 0.08^{ns}

Results are expressed as mean ± SEM n= 6, ns represent the non significant changes, * p ≤0.05 represent less significant changes, ** p ≤0.01 represent significant changes were highly significant changes compared with normal rats by one way ANOVA followed by Dunetttest, $Al_2(SO_4)_3$;Aluminiumsulphate, SGOT; Serum glutamic oxaloacetictransmminase, SGPT; Serum glutamic pyruvic transminase, CRT; Creatinine, GGTP; Gamma glutamyltreanspeptidase

Table 4.Effect of *Prunus armeniaca* seed on some other biochemical parameters of $Al_2(SO_4)_3$ intoxicated rats.

Treatment	HDL	LDL	TC	Triglyceride	ALP	TBL	DBL
Normal group	60.03 ± 13.67	53.53 ± 1.44	90.88 ± 1.44	80.84 ± 4.25	186.36 ± 2.33	0.39 ± 0.12	0.10 ± 0.10
Control group	16.11 ± 3.20**	170.45 ± 6.13**	246.88 ± 55.09**	132.99 ± 10.18**	459.48 ± 7.52**	2.65± 0.15**	1.43± 0.03**
$Al_2(SO_4)_3$+ *Prunus armeniaca* 200 mg/kg	42.38 ± 9.96^{ns}	88.90 ± 24.96*	154.48 ±33.23**	97.00 ± 6.16^{ns}	339 .04 ± 0.70**	.88 ± 0.28**	0.26 ± 0.18^{ns}
$Al_2(SO_4)_3$ + *Prunus armeniaca*400 mg/kg	54.20 ± 14.74^{ns}	72.40 ± 11.27^{ns}	101.40 ±16.23^{ns}	87.95 ± 7.42^{ns}	264.42 ± 0.20^{ns}	0.58 ± 0.20^{ns}	0.17 ± 0.01^{ns}
Prunus armeniaca 200 mg/kg	44.56 ± 12.38^{ns}	86.64 ± 20.38*	151.67 ±32.10**	99.05 ± 9.91^{ns}	328.63 ± 4.00*	.87 ± 0.11**	0.25 ± 0.17^{ns}
Prunus armeniaca 400 mg/kg	56.18 ± 8.67^{ns}	70.09 ± 15.54^{ns}	100.10 ±14.98**	86.31 ±11.17^{ns}	254.19 ± 3.34^{ns}	0.56 ± 0.18ns	0.16 ± 0.06^{ns}
Standard(Ursodeoxycholic acid 250 mg/kg)	56.42 ± 9.39^{ns}	63.11 ± 12.29^{ns}	92.42 ±1.71^{ns}	82.81 ± 11.00^{ns}	206.63 ± 1.65^{ns}	0.49 ± 0.14^{ns}	0.16 ± 0.07^{ns}

Results are expressed as mean ± SEM n= 6, ns represent the non significant changes * p ≤0.05 represent less significant changes, ** p ≤0.01 represent significant changes compared with normal rats by one way ANOVA followed by Dunett test HDL; High density lipoprotein, LDL; Low density lipoprotein, TC; Total cholesterol, ALP; Alkaline phosphatase, TBL; Total bilirubin, DBL; Direct bilirubin.

Animals treated with $Al_2(SO_4)_3$ and doses of ethanolic extract of *Prunus armeniaca* seed (200 mg/kg and 400 mg/kg) showing the gradual decrease in hepatic toxic lesions, reduced sized neutrophil infiltration and recovery of normal hepatocytes. Sections from the animals treated with ethanolic extract of *Prunus armeniaca* seed (200 mg/kg and 400 mg/kg) showing the unnoticeable difference with the normal group of animals. While comparison of all groups which are treated by the *Prunus armeniaca*(200 mg/kg and 400 mg/kg), the *Prunus armeniaca* (400 mg/kg) gives the more signified results and ethanolic extracts recovered the damaged hepatic cell to normal almost after the administration of *Prunus armeniaca* at the dose of 400 mg/kg, which indicates that *Prunus armeniaca* plant possess the good anti-hepatotoxic nature.

Histological sections which were obtained from the animals's liver treated with $Al_2(SO_4)_3$ and Ursodeoxycholic acid (standard drug ; 250 mg/kg) demonstrating the defending against the liver tissues with no pathological hepatic lesions occurred by the $Al_2(SO_4)_3$.

Consequence stated that treatment from *Prunus armeniaca* seed 400mg/kg was showed the highly significant value against the hepatotoxicity induced by $Al_2(SO_4)_3$.

It's estimated from the overall consequences of antioxidant stress activity, biochemical enzyme parameters and histopathological evaluations, it could be reconfirmed that in ethanolic seed extracts of the *Prunus armeniaca* at dose of 400 mg/kg was showed the maximum potent hepatoprotective activity in $Al_2(SO_4)_3$ induced hepatotoxicity. The potential action may be occurred due to its chemical composition, phytochemical and antioxidant compounds available in the extract. Treatment withthe*Prunus armeniaca* seed extract (at dose 400 mg/kg) and returned the damaged liver to moderately normal. Currently it could be sure that *Prunus armeniaca* seed 400 mg/kg was the most efficient and proved the highly potent and effective for the $Al_2(SO_4)_3$ induced liver toxicity. Histological studies from the sections of the animals's liver that were treated with the $Al_2(SO_4)_3$ and Ursodeoxycholic acid (standard drug; 250 mg/kg) showed the protecting action against the hepatic tissues along with no pathological hepatic lesions occurred by $Al_2(SO_4)_3$.

Normal Group (Group I)

The histology of liver sections revealed normal hepatic architecture. The liver is covered by a thin connective tissue capsule (Glisson capsule). Each lobule consists of normal sinusoids and radiating cords of hepatic parenchymal cells with central vein. Lobules are indistinctly separated from one another. Normal portal areas contained portal vein, hepatic artery, bile duct and lymphatic vessel. The normal bile duct is lined by simple columnar epithelium

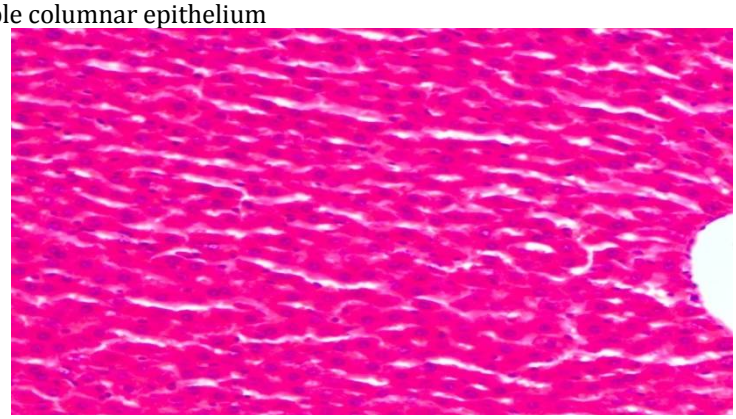
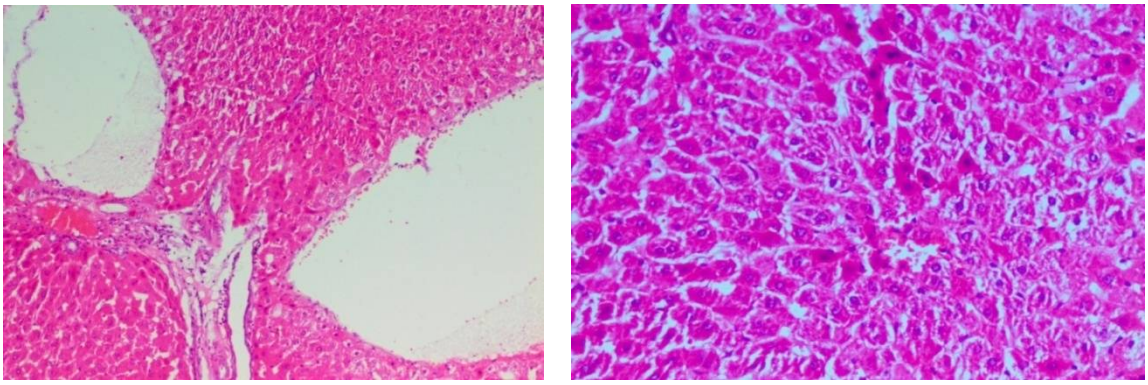


Fig1. Histological characteristics in Normal Group. Normal hepatic architecture with normal sinusoidsand radiating cords of hepatic parenchymal cells with central vein. Lobules are indistinctly separated from one another. H&E, X200.

Control Group (Group II)

Marked dilatation of central vein with severe engorgement of RBCs was noticed. Portal areas contained marked congestion in portal vein and hepatic artery with mononuclear cell infiltration. Necrosis of hepatocytes with focal areas of inflammatory cell infiltrate especially mononuclear cell infiltration was noticed. Sinusoidal spaces were dilated and engorged with RBCs. Individualization of hepatocytes with atrophy of hepatic parenchymal cells was noticed. Infiltration of inflammatory cells was noticed around the portal areas. Few binucleated cells were noticed.



(a) **(b)**

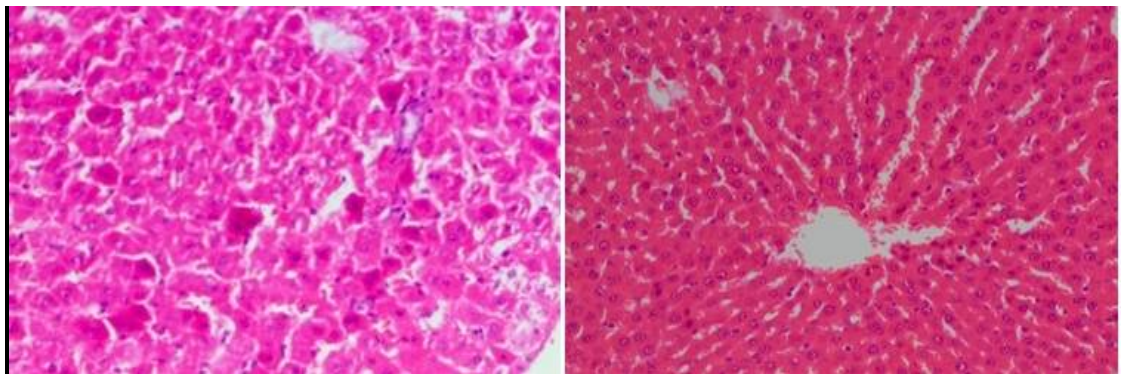
Fig2(a) & 2(b). Histological characteristics in Control Group,

(a): Marked dilatation of central vein with congestion and infiltration of inflammatory cells around the portal areas and atrophy of hepatocytes. H&E, X100.

(b): Necrosis of hepatocytes with swollen eosinophilic cytoplasm. Few binucleated cells were noticed. H&E, X200.

***Prunus armeniaca* (200 mg/kg +$Al_2(SO_4)_3$ induced hepatotoxicity (Group III)**

Pathological changes were reduced in this treated group when compared to control group. Moderate regenerative changes in hepatic parenchyma evidenced by increased size and number of hepatocytes (hypertrophy and hyperplasia of hepatocytes), variation in the size of hepatocytes, moderate number of binucleated cells, hyperchromatic nucleus and mitotic figures were observed. The amount of necrosis of hepatocytes was reduced in treated group. Moderate congestion and dilatation in central vein, portal vein and hepatic artery were observed. Inflammatory reaction in liver parenchyma significantly reduced. Sinusoidal spaces contained RBCs.



(a) **3(b)**

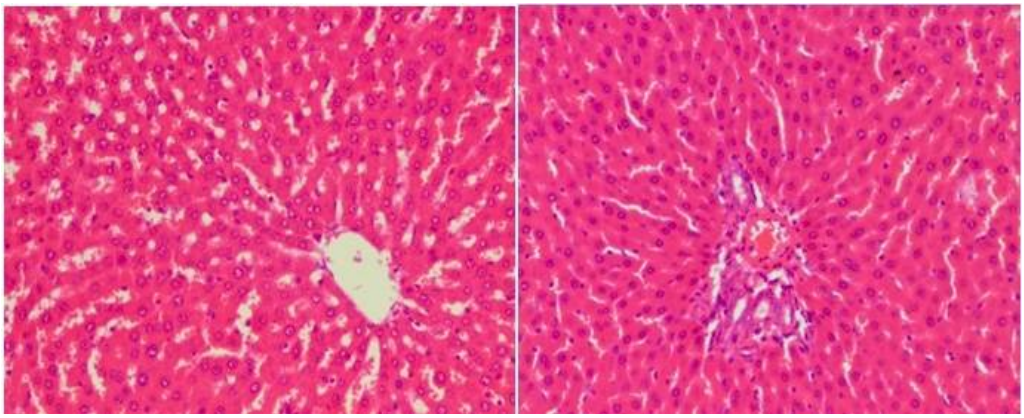
Fig3 .Histological characteristics in *Prunus armeniaca* (200mg/kg)+$Al_2(SO_4)_3$ induced hepatotoxicity (Group III)

(a): Regenerative changes like binucleated cells, hyperchromatic nucleus, hypertrophy of hepatocyte and variation in the size of hepatocytes. H&E, X200.

(b): Moderate congestion and dilatation in central vein and sinusoidal spaces with hyperplasia of hepatocytees. H&E, X200.

***Prunus armeniaca* Group (400 mg/ kg + $Al_2(SO_4)_3$) (Group IV)**

Pathological changes were significantly reduced in this treated group when compared to control and*Prunus armeniaca* [200 mg/ kg + $Al_2(SO_4)_3$]group. Liver parenchyma showed normal architecture in most of the places. Significant regenerative changes in hepatic parenchyma evidenced by increased size and number of hepatocytes (hypertrophy and hyperplasia of hepatocytes), variation in the size of hepatocytes, numerous binucleated cells, hyperchromatic nucleus and mitotic figures were observed. The amount of necrosis, and congestion and dilatation in central vein, portal vein and hepatic artery was significantly reduced in treated group. Sinusoidal spaces were contained RBCs with increased Kupffer cell activity.



(a) **(b)**

Fig 4(a) &4(b). Histological characteristics in *Prunus armeniaca*(400 mg/kg) treated Group against $Al_2(SO_4)_3$ induced hepatotoxicity

Fig 4(a): Hypertrophy and hyperplasia of hepatocytes with increased Kupffer cell activity. H&E, X200.
Fig 4(b): Moderate congestion in portal areas with hypertrophy and hyperplasia of hepatocytes with increased Kupffer cell activity. H&E, X200.

***Prunus armeniaca* Group (200 mg/ kg only) (Group V)**

Only *Prunus armeniaca* [200 mg/ kg] extract treated group showed normal architecture of liver as that of normal group. However, in few areas portal inflammation and mild sinusoidal congestion and dilatation were noticed.

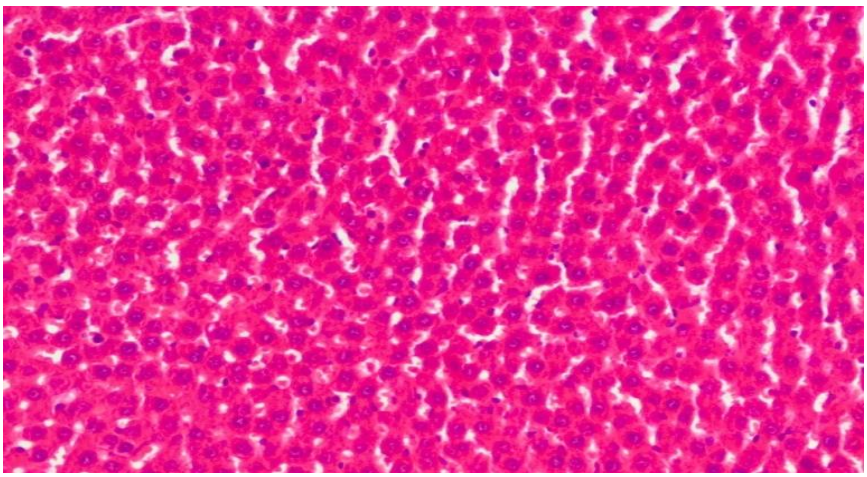


Fig 5.Histological characteristics in *Prunus armeniaca*(200 mg/kg) treated Group. Normal hepatic architecture with normal sinusoidsand radiating cords of hepatic parenchymal cells with central vein. Lobules are indistinctly separated from one another. H&E, X200

***Prunus armeniaca* Group (400 mg/ kg only) (Group VI)**

Only *Prunus armeniaca* [400 mg/ kg] extract treated group showed normal architecture of liver as that of normal group. However, at places hyperplasia of hepatocytes and Kupffer cells were noticed.

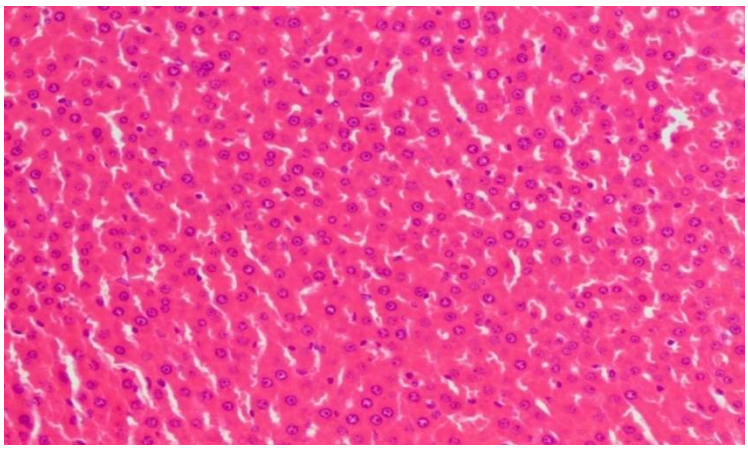


Fig 6. Histological characterstics in *Prunus armeniaca*(400 mg/kg) treated Group only Normal hepatic architecture with normal sinusoidsand radiating cords of hepatic parenchymal cells. Lobules are indistinctly separated from one another. H&E, X200.

Standard Group (Ursodeoxycholic acid (UDC) 250 mg/ kg + $Al_2 (SO_4)_3$) (Group VII)

Pathological changes were significantly reduced in this treated group when compared to control group. Liver parenchyma showed normal architecture in most of the places. Significant regenerative changes in hepatic parenchyma evidenced by increased size of cells (cytomegaly), variation in the size of hepatocytes, numerous binucleated cells, hyperchromatic nucleus and mitotic figures were observed. The amount of necrosis was significantly reduced in treated group. Mild congestion and dilatation in central vein, portal vein and hepatic artery were observed. Inflammatory reaction in liver parenchyma was also significantly reduced. Sinusoidal spaces were minimal.

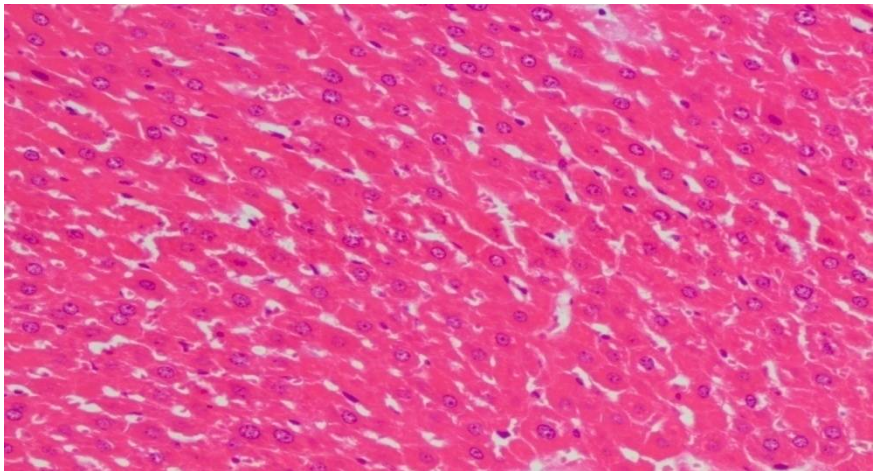


Fig 7. Histological characteristics in Ursodeoxycholic acid (UDC) 250 mg/ kg treated Group against $Al_2 (SO4)_3$ induced hepatotoxicity

Fig7. Regenerative changes like hypertrophy and hyperplasia of hepatocytes and Kupffer cells. H&E, X200.

Statistical analysis

The data finded from the *In vivo* antioxidant parameter and hepatoprotective activity were expressed as mean $\pm$ SEM. The graph were drawn, and the statistical analysis was carried out by using, the Graphpad prism software version 5.0. Results data were showed as the mean $\pm$ SEM. For data group statical evaluation mean were evaluated by one way study of variance (ANOVA) followed by Dunnet,s t3 test, $p< 0.05$, $p< 0.01$ was recognized significant.

The current study explored the effect of ethanolic extract of *Prunus armeniaca* seed on $Al_2(SO_4)_3$- induced hepatotoxicity in rats.

Table 5.Histopathological changes in *Prunus armeniaca* treated rat liver, against the aluminium sulphate induced hepatotoxicity in rats. Histopathological grading of liver lesions

Group	Necrosis of hepatocytes	Dilatation and congestion in central vein	Sinusoidal dilatation and congestion	Portal area inflammation	Inflammatory nodule in hepatic parenchyma	Kupffer cell hyperplasia	Regenerative changes (Hypertrophy and hyperplasia of hepatocytes, binucleated cells, etc.)
Aluminiumsulphate ($Al_2(SO_4)_3$)Group							
Normal	-	-	-	-	-	-	-
Control	+++	+++	+	+++	+++	+	+
$Al_2(SO_4)_3$ + *Prunus armeniaca*200 mg/kg	++	++	++	++	+	++	++
$Al_2(SO_4)_3$ + *Prunus armeniaca*400 mg/kg	+	+	++	++	-	+++	+++
*Prunus armeniaca*200 mg/kg	-	-	+	+	-	-	-
*Prunus armeniaca*400 mg/kg	-	-	-	-	-	+	-
Standard(Ursodeoxycholic acid 250 mg/kg)	+	+	++	++	-	+++	+++
Lesions absent – (-); mild – (+); moderate – (++); intense – (+++)							

DISCUSSION

The current study explored the effect of ethanolic extract of *Prunus armeniaca* seed on $Al_2(SO_4)_3$- induced hepatotoxicity in rats.

Prunus armeniaca extract was subjected to biochemical estimation to determine the ability of *Prunus armeniaca* extract to show hepatoprotective effect.The behaviour of wistar albino rats was assessed using general observations of each animal immediately after the drug was administered at hourly intervals (0 hr, 1 hr, 2 hr, 4 hr, 6 hr, 8 hr, 24 hr, and 72 hr). Any anomalies or changes noted could be a sign of toxicity. The test animals' behaviour did not change significantly before or after receiving an oral dosage of ethanolic extract of *Prunus armeniaca* seed at any dose level (Table. 1), Table 2.Represents the changes in liver weight before and after treatment during the experiment.

Hepatoprotective activity is a common feature of the global population; to illustrate this condition, an $Al_2(SO_4)_3$ induced animal model can be used as a natural model of hepatoprotective activity, with oxidative stress followed by hepatoprotective activity, similar to that seen in patients with liver diseases.

In addition, the current study used $Al_2(SO_4)_3$ to screen out the hepatoprotective activity of plant extract in rats, because previous reports suggest that $Al_2(SO_4)_3$ increases the levels of SGOT, SGPT, ALP, TP, GGTP, Total bile acid LDL, TC, TBL, DBL and triglyceride, while decreasing the levels of HDL, Albumin, and TP.

In contrast, rats treated with ursodeoxycholic acid and *Prunus armeniaca* extract had lower levels of SGOT, SGPT, ALP, TP, GGTP, Total bile acid, LDL, TC, TBL, DBL, and triglyceride, as well as higher levels of HDL, albumin, and TP. The findings support the traditional assertion, particularly in regards to *Prunus armeniaca*'s hepatoprotective qualities.

This research revealed that the $Al_2(SO_4)_3$-induced group had higher levels of SGOT, SGPT, ALP, TP, GGTP, total bile acid, LDL, TC, TBL, DBL, and triglyceride, indicating liver injury. The effect of ethanolic extract of *Prunus armeniaca* seed was supplied at the dose (200, 400 mg/kg) revealed a decrease in the levels of SGOT, SGPT, ALP, TP, GGTP, Total bile acid, LDL, TC, TBL, DBL, and triglyceride and an increase in the levels of HDL, TP, and albumin inside the rats (Table 3 & 4).

Prunus armeniaca'shepatoprotective and antioxidant properties were compared to that of the standard refrence drug Ursodeoxycholic acid. The percentage of hepatoprotection was estimated and showed in Fig. 1 to 7 in terms of changes in specific biochemical parameters and antioxidant enzyme activities.

Histological studies: the test drug's hepatoprotective activity against Aluminum sulphate-induced injury was validated by histopathological examination. Fig 1 to 7 show the effects of intraparotneal

administration of aluminiumsulphate. Normal hepatic architecture was seen in liver sections from normal rats, with the heptic architecture, where the hepatocytes are organised around the central vein, and blood sinusoids. Figure 1.(In Normal group) Each liver cell has a limiting membrane, a big nucleus in the centre, and conspicuous nucleoli. In Figure 2a,2b(In Control group)Periportal inflammation is caused by mononuclear cells, the majority of which are lymphocytes areas of piecemeal necrosis, apoptosis, and steatosis, as well as bile stasis in focal areas had been also seemed.

At doses of 200 mg/kg P.O. and 400 mg/kg P.O., *Prunus armeniaca* seed extract produced only modest degenerative alterations in hepatocytes without causing entrilobular necrosis. Steatosis is visible in a concentrated area, showed by Figure3a,3b and 4a,4b . Fig 3a, 3b and 4a, 4b showedthe patchy interstitial aggregation of lymphocytes without necrosis or apoptosis. The normality of hepatic cells, central vein, and portal vein was observed in the liver segment of *Prunus armeniaca* (400 mg/kg) p.o treated rats. In filtration, there are no inflammatory cells. Plate Fig3 also shows no steatosis. The significant result was recorded using *Prunus armeniaca* seed extract at 400 mg/kg p.o. There is no evidence of liver cell necrosis/apoptosis at lower doses (200mg/kg p.o), which is a major improvement.

Only *Prunus armeniaca* seed extract at doses of 200 mg/kg p.o. and 400 mg/kg p.o. resulted in a significant improvement in hepatocytes, as shown in Fig 5 and 6. The group that received the test drug at the 400 mg/kg dose was more powerful than the lower dose, as seen in Figure 5 and Figure 6.

A rat liver slice treated with Ursodeoxycholic acid (250 mg/kg p.o.) revealed no substantial portal/periportal inflammation. There is no evidence of necrosis or apoptosis in the liver cells. Figure7 shows a few clogged and dilated central veins.

Table 5 showed the summarized form of the histopathological study, which reconfirmed the investigation that the *Prunuaarmeniaca* had the potent antioxidant as well as the good hepatoprotetcive potency.

CONCLUSION

We conclude that the plant extracts have hepatoprotective activity based on the findings of this investigation. The current study's findings also revealed that ethanolic extracts of *Prunus armeniaca* seed, the plant, could be a more useful as a medicinal agent in preventing however, more research is needed to investigate the underlying processes of hepatoprotective activity and identify the active components responsible for these pharmacological effects.

FUTURE PROSPECTS

Our research envisage that the plant *Prunus armeniaca*is possesses hepatoprotective potential against the hepatotoxicity induced by the $Al_2(SO_4)_3$administration in wistar albino rats. On the other hand further researches are necessitating to exploring the potential mechanism of action. All at once, the above stated plants can be prepared in a appropriate dosage form either individually or in the form of polyherbal formulation, its pharmacological assessment by using appropriate animal models after that clinical trials based on the human volunteers are also proposed.

ACKNOWLEDGEMENT

We, the authors are thankful to Dr M.P PandeyVice-Chancellor and management of the IFTM University for providing facilities encouragement.

CONFLICT OF INTEREST

There is no conflict of interest.

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CITATION OF THIS ARTICLE

V Raj, M Mani, P Kumar, N Verma. Hepatoprotetive potential of *Prunus armeniaca* against the Aluminium Sulphate induced liver toxicity in rats. Bull. Env. Pharmacol. Life Sci., Vol 11[7] June 2022 : 01-12.