

Protective role of *Avena fatua* against drug-induced liver toxicity

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Abstract: The study was conducted to examine the protective potential of ethanol seed extract (ESEt) of *Avena fatua* (wild oats) against antituberculosis drug (ATD)-induced hepatotoxicity in rats. Four groups of rats ($n=6$) were used. Of which, three groups were given ATD (Rimstar 900mg/15kg) and divided them into hepatotoxic control (distilled water 1mL/kg), positive control (silymarin 200mg/kg) and test group (ESEt 800mg/kg). The fourth was the normal control group treated only with distilled water (1mL/kg). All treatments were orally administered in their respective groups for 26 days. On the 27th day, rats were decapitated. Body and liver weights were measured whereas serum and liver samples were collected for biochemical and histopathological assessments. The rats treated with silymarin and ESEt showed a significant decrease ($p<0.05$, 0.01 & 0.0001) in liver enzymes including alanine & aspartate transaminases, gamma glutamyltranspeptidase and alkaline phosphatase. ESEt also improved total bilirubin (particularly indirect bilirubin), total protein, albumin and low density lipoprotein cholesterol levels in test group. The hepatoprotective ability of extract was also evident by histological study of liver tissues of the test group that showed normal architecture as compared to liver of ATD treated hepatotoxic control group displayed heterogeneous hepatocytes, inflamed central vein, fatty deposits, enlarged sinusoid, Kupffer's cells infiltration, hypertrophy and fibrosis. In conclusion, ESEt of *A. fatua* is hepatoprotective in nature which may be due to the presence of total phenols and flavonoids already reported from the seeds of this plant.

Keywords: Antituberculosis drug, hepatotoxicity, *Avena fatua*, alanine transaminase, aspartate transaminase.

INTRODUCTION

Diet plays an essential role in human health. Food not only provides energy and nutrients but also contributes therapeutic effects to the biological system thus referred to as functional foods. These foods are used as such or in fortified form by enhancing their nutritional values to provide beneficial effects like improving health by delaying the onset or minimizing the chronic complications of metabolic diseases besides fulfilling the basic dietary requirements of the body (Gupta and Mishra 2021). Foods derived from plants and other sources are rich in bioactive compounds that play a crucial role in preventing many chronic diseases such as diabetes, cardiac, gastrointestinal, liver and neurodegenerative diseases (Teodoro 2019).

The liver is the largest organ in the mammalian body and executes several vital functions such as storage metabolism of nutrients and bile secretion. It also involves cleaning of compounds and metabolic wastes from the body (Smith *et al.*, 2020). It is the first internal organ to be subjected to orally administer foreign substances or drugs, hence highly vulnerable to damage. Among the liver problematic acquired factors, drugs like analgesics, antibiotics, antituberculosis, antipsoriatic, anticholesterolemic (statins) and chemotherapeutic agents induce acute hepatotoxicity (Shakya 2020). These drugs

are life-saving but their long-term use can cause liver dysfunction by producing oxidative stress and mitochondrial damage which results in lipid peroxidation, inflammation, and activation of the immune system (Lei *et al.*, 2021). Therefore, drug induced liver injuries are one of the debatable topics nowadays. According to different population, several studies showed that antituberculosis drug-induced hepatotoxicity during treatment is about 2% to 28 % (Zhu *et al.*, 2021).

Tuberculosis is the second most common cause of death worldwide (Sahu *et al.*, 2020). The most frequently used antituberculosis drugs are isoniazid, rifampicin, pyrazinamide and ethambutol reported having hepatotoxic effects (Molla *et al.*, 2021). The primary mechanism that appears to be responsible for these drug-induced liver problem is idiosyncratic reactions which may be metabolic or hypersensitive. Hypersensitive idiosyncrasy is often associated with skin rashes, fever, eosinophilia and/or lymphadenopathy (Sernoskie *et al.*, 2021). However, in most cases metabolic idiosyncrasy is observed like antituberculosis drug isoniazid after passing through liver metabolism in the presence of *N*-acetyltransferase 2 converts into acetyl isoniazid which hydrolyzed to form acetyl hydrazine that later oxidized by cytochrome P4502E1 to form *N*-hydroxy acetyl hydrazine which dehydrates to produce acetyl diazine, which is a toxic metabolite and may split into more reactive ions such as acetyl onium ion, acetyl radical and ketene which covalently bind with liver macromolecules and induce

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liver injury (Ramappa and Aithal 2013). Rifampicin also accelerates this metabolic pathway when given with isoniazid (Mwila and Walker 2020). Pyrazinamide facilitates free radical-induced hepatotoxicity by inhibiting cytochrome P450 and nicotinamide adenine dinucleotide (Cao *et al.*, 2017). Conclusively, antituberculosis drugs induce oxidative stress by generating reactive metabolites and altering mitochondrial redox in hepatotoxicity (Yew *et al.*, 2018). The treatment with antituberculosis drugs is typically lasts for 4 to 6 months or little more depending on patient's condition. During this treatment liver dysfunction is apparent. However, this side effect is gradually reverted after the treatment but there is no particular medicine available to subside this unwanted effect during the treatment. There is an immediate requirement for a better, safe and effective therapy for minimizing the acute hepatotoxicity induced by antituberculosis drugs. The functional foods or their active components can be played an important role and are used as complementary medicine to lower the side effect caused by the antituberculosis drugs on liver.

Oat or common oat (*Avena sativa*) is a species of cereal grain and its oatmeal finds a prominent place on the breakfast table of many people globally. Previous studies reveal that *A. sativa* (common oats) exhibits several biological functions like anti-microbial, anti-inflammatory, anti-diabetic, anti-oxidant, anti-atherogenic, vasodilation, anti-asthmatic, immunomodulatory and anti-cancer activities (Gheith and El-Mahmoudy, 2019). Besides these health benefits, oats also have the hepatoprotective property (Debnath *et al.*, 2019). *Avena fatua* commonly known as “Wild oat or Jungli Jau” among the *Avena* species. However, few active components of *A. fatua* have been reported. The pharmacological effects of this species have been scarcely discovered. According to studies, *A. fatua* seeds act upon nerves as a sedative, prevent constipation and serve as psychostimulants (Abbas *et al.*, 2012). Studies have shown that seeds of *A. fatua* contain flavonoids, saponins, tannins, steroids, glycosides, alkaloids and terpenoids (Saeed *et al.*, 2016). It has also been reported that wild species of oats have higher oil content than cultivated oats (Leonova *et al.*, 2008). A literature survey reveals that hepatoprotective activity of seeds of *A. fatua* has not been reported yet. Therefore, the present study evaluated the hepatoprotective activity of ethanol seed extract of *A. fatua* against antituberculosis drug-induced acute liver toxicity in rats.

MATERIALS AND METHODS

Sampling and authentication of plant material

Dry seeds of the experimental plant *Avena fatua* (wild oat) were purchased and validated by an authoritative taxonomist (voucher no. KU/BCH/SAQ/09) and kept in the Department of Biochemistry, University of Karachi, Pakistan.

Preparation of ethanol seed extract and its percent yield

According to the method described by Qureshi *et al.*, 2019 where 40g of the ground seeds powder was soaked in 1000ml of 95% ethanol (Sigma-Aldrich, St Louis, USA) overnight at room temperature then filtered with What man filter paper No. 42 (125mm) twice and finally filtrate was reduced by using a rotary vacuum evaporator at 40°C to obtain a brown colored gummy material and marked as ethanol seed extract (ESEt). The percent yield of this extract was calculated by using the formula given by Adam *et al.*, 2019.

$$\text{Percent Yield (\%)} = \frac{Y}{A} \times 100$$

Where, Y = Obtained ESEt (g), A = total seeds powder (g) used for extraction.

Experimental animals

Female albino *Wistar* rats weighing between 150-220 g were purchased from the authentic breeding house of Dow University of Health Sciences (DUHS), Karachi and kept separately in standard plastic cages in a room (23 ± 2°C, 12 h of light/dark cycle) of conventional animal house of the Department of Biochemistry. The rats were allowed to have a standard laboratory diet and water *ad libitum*. They were handled carefully, following international standard guidelines approved by the ethical committee of University of Karachi (BASR/No.03625/Sc; dated October 27, 2017).

Antituberculosis drug, positive control and dissolving medium

Antituberculosis drug (ATD) named Rimstar (900mg; Sandoz Pvt. Ltd) was used to induce hepatotoxicity in experimental rats at 900mg/15kg. Rimstar is a combination of four drugs including Rifampicin 150 mg, Isoniazid 75 mg, Pyrazinamide 400mg and Ethambutol 275mg. In contrast, Silymarin (Silver 200mg/kg; Abbott Laboratories Pakistan Ltd) is a well-known hepatoprotective medicine and used as a positive control at 200mg/kg. Dimethyl sulphoxide [DMSO (0.05%); Fisher Scientific, UK] was used as a dissolving medium (vehicle) for the preparation of the dose (800mg/kg) of ESEt of *A. fatua*. All treatments were done orally for 26 days consecutively in overnight fasted condition.

Experimental protocol with grouping and dosing of rats

Rats were divided into six groups randomly (6 rats in each group), they fasted overnight. Group I served as normal control and received distilled water (1 mL/kg/day). Group II served as hepatotoxic control and received distilled water (1mL/kg/day) + ATD (Rimstar 900mg/15kg/day). Group III served as positive control which received silymarin(200mg/kg/day)+ATD(Rimstar900mg/15kg/day) Group IV served as test group that received ESEt (800mg/kg/day) + ATD (Rimstar 900mg/15kg/day). All treatments were given orally for 26 days consecutively in overnight fasted condition. After 24 hr of the last dose of

each treatment in each group, rats were decapitated to collect whole blood to separate serum which used for estimating liver-specific biochemical parameters. Whereas liver tissues were dissected out for histo-pathological examination.

Physical, biochemical and histo-pathological assessments

Initial and final day body weights (IDBW and FDBW) of rats of each group were measured by using electronic digital weighing balance to calculate percent body weight change (PBWC) through the formula given by Qureshi *et al.*, 2016 $PBWC = \{(FDBW - IDBW) / IDBW\} \times 100$

Similarly, liver index (LI) was calculated by the formula given by Qureshi *et al.*, 2019 after measuring the liver weight (LW) of each rat of each group:

$$LI = \left\{ \frac{LW(g)}{FDBW(g)} \right\} \times 100$$

Liver-specific biochemical parameters include alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyltranspeptidase (GGT), total bilirubin (TB), direct bilirubin (DB), total protein (TP), and albumin (ALB) were estimated in serum by using commercially available enzymatic reagent kits (Randox, UK) on the automatic analyzer (Beckman coulter AU- 480). However, indirect bilirubin (IB) and low density lipoprotein-cholesterol (LDL-c) were computed using formula given in Randox reagent kits. The percent loss or gain in parameter was also calculated using the formula given by Qureshi *et al.*, 2019.

$$\text{Percent gain/loss} = \left\{ \frac{(\text{treated group} - \text{hepatotoxic group})}{\text{hepatotoxic group}} \right\} \times 100$$

Liver tissues were dissected from each rat, soaked in 10% formalin in separate bottles and sent to Dr. Essa's diagnostic laboratory, Abul Hassan Isphahani road, Karachi for histo-pathological examination (Qureshi *et al.*, 2019). The photographs of histological slides were taken using a system microscope (Olympus BX51) equipped with a digital camera (Olympus DP72).

STATISTICAL ANALYSIS

For the interpretation of the overall effect of treatments on all the parameters, statistical analysis was done by one-way analysis of variance (ANOVA) followed by LSD (least significant difference) test at $p < 0.05$ using a statistical package SPSS Version 17.0. The outcomes of the current study were expressed as mean $\pm$ standard deviation (SD) and were considered significant at $p < 0.05$, $p < 0.01$, $p < 0.001$ and $p < 0.0001$ when compared with the hepatotoxic control group.

RESULTS

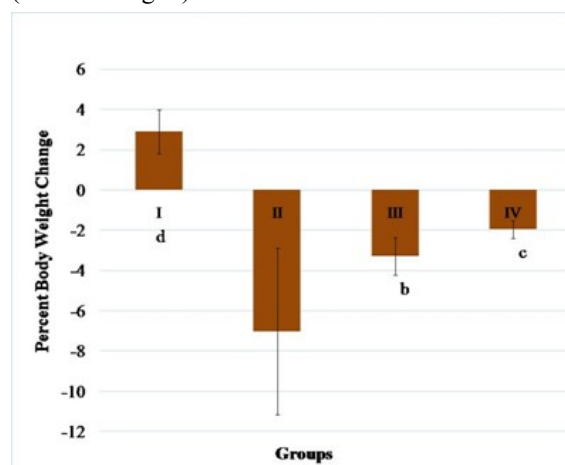
The percentage yield of ESEt of *A. fatua*

The percent yield of ESEt of *A. fatua* was 18.01 ± 1.40 g/100g of ground seeds powder.

Protective effect of ESEt on ATD-induced hepatotoxic rat model

Physical parameters

The results showed a drastic decline in percent body weight change in hepatotoxic control (group II) as compared to normal control (group I). No doubt rats of positive control (group III) and test treated with ESEt (group IV) also displayed a decline ($p < 0.01$ & $p < 0.005$) in percent body weight change but the decline was much less than observed in the hepatotoxic control group (Fig. 1). Similarly, a prominent drop was observed in liver weights and liver index of hepatotoxic group II compared to normal control group I. On the contrary, liver weights and liver index of positive control group III and ESEt treated test group IV were found to improve ($p < 0.05$ & $p < 0.005$) as compared to group II, a noticeable improvement was observed by ESEt in the test group (table 1 & fig. 2).



Each bar represents the mean $\pm$ SD (n = 6). b, c and d indicate $p < 0.01$, $p < 0.005$ and $p < 0.0001$ when compared with ATD treated hepatotoxic control group II.

Fig. 1: Effect of ESEt on Percent body weight

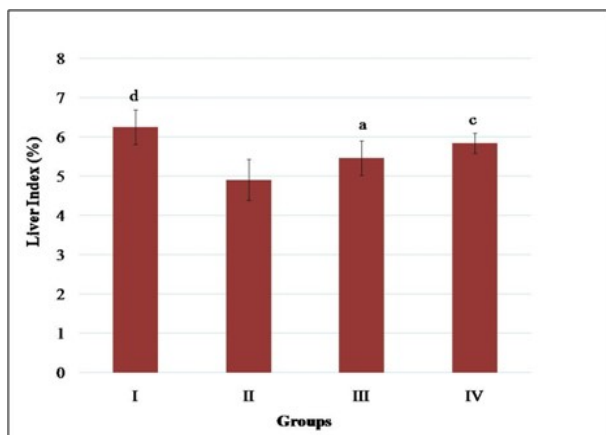
Liver-specific biochemical parameters

As compared to normal control group I, the rats of hepatotoxic control group II revealed an elevation in levels of liver specific enzymes such as ALT, AST, ALP and GGT. Whereas ESEt treated test group IV showed noteworthy percent reduction ($p < 0.05$, $p < 0.01$ & $p < 0.0001$) in levels of four of these enzymes. Silymarin in positive control group III was only found effective in reducing the levels of ALT, ALP and GGT (table 1). ATD intoxication also increased bilirubin profile particularly indirect bilirubin (IB) in hepatotoxic control group II

compared with normal group I. On the other hand, three of the bilirubin including TB, DB and IB were significantly found to decrease ($p < 0.0001$) in positive control group III and prominently in ESEt treated test group IV (table I). TP and ALB levels decreased in ATD hepatotoxic control group II while the levels of both these parameters (TP & ALB) became upgraded ($p < 0.005$ & $p < 0.0001$) in ESEt treated test group IV (table 1). The LDL-c was also elevated in hepatotoxic control group II. However, LDL-c levels were observed too much decrease ($p < 0.0001$) in positive control group III and ESEt treated test group IV (table 1).

Histopathological examination of hepatic tissues

The liver histology of hepatotoxic control group II showed dreadful structural deterioration, heterogeneous hepatocytes, enlarged /inflamed central vein with RBCs, ballooning (fatty deposits), enlarged sinusoid, Kupffer cells infiltration, hypertrophy and fibrosis compared with the liver section of normal control group I. However, the liver sections of treated groups showed reversal in structural integrity compared with hepatotoxic group II. Histological examination of ESEt treated test group IV exhibited most significant improvement in the liver tissue architecture as compared to the positive control group III (fig. 3).



Each bar represents the mean $\pm$ SD (n = 6). a, c and d indicate $p < 0.05$, $p < 0.005$ and $p < 0.0001$ respectively, when compared with ATD treated hepatotoxic control group II.

Fig. 2: Effect of ESEt on liver index

DISCUSSION

Consumption of healthy food is one of the keys to the well-being of humans. Plant- derived functional foods have grown globally, believing that natural is better, safer and more beneficial than synthetic drugs (Turrini *et al.*, 2020). Plants have phytochemicals that contain curative properties and are now being used to treat various diseases including hepatic diseases (Jima and Megersa

2018). Among acquired factors, few life-saving drugs like antituberculosis drugs induce hepatotoxicity as their side effect (Singh *et al.*, 2016). The focus on plant-derived products has increased globally due to their health promoting effects. Thus, in the present study, ethanol seed extract (ESEt) of *A. fatua* was assessed for its protective effect against acute hepatotoxicity induced by antituberculosis drug (ATD) in rats. The extract's potency was also compared with a known hepatoprotective medicine named silymarin, which proved to be helpful in different liver problems (Federico *et al.*, 2017).

Early detection of hepatic disease is a challenge but very necessary. Symptoms of drug- induced liver injury manifest from an asymptomatic increase in liver enzymes to non-specific symptoms such as malaise, nausea, jaundice, abdominal pain, etc (Sandhu and Navarro, 2020). Besides these, loss of appetite and weight reduction are also associated with liver problems induced by drug toxicity. The study depicted a significant decline in the body weight of ATD (Rimstar 900mg/15 kg) treated hepatotoxic control group compared to the normal control group treated with only distilled water (1mL/kg).

This weight reduction may be due to the gastrointestinal disturbance, commonly induced of ATD and observed in the initial few weeks of tuberculosis treatment, resulting in inadequate food intake (Warmelink *et al.*, 2011). Similarly, a significant decrease in liver weight and its index was observed in the same hepatotoxic control group that was also a reflection of liver impairment that due to oxidative stress, usually induced by ATD that could result in tissue protein degradation (Li *et al.*, 2015). However, the test group treated with ESEt 800mg/kg showed percent gain in body weight and normalization in liver weight and its index. It proves that *A. fatua* has an excellent potential to minimize the toxic effects induced by ATDs on the liver.

According to the literature, the liver enzymes levels are normally increased during tuberculosis treatment with drugs like isoniazid, rifampicin, etc (Jabbar *et al.*, 2020). Elevated levels of serum transaminases including ALT and AST are the indicators of altered integrity of hepatocytes, leading to leakage of these intracellular enzymes in serum. The increase levels of AST and ALT reveal hepatocellular damage whereas elevated levels of ALP and GGT indicate hepatobiliary obstruction and cholestatic liver injury due to inflammation in cholangiocytes (Levick 2017). Same scenario was observed in the present study where ATD (Rimstar 900mg/15kg) treated hepatotoxic control group displayed an increase in serum levels of ALT, AST, ALP and GGT.

Conversely, alleviation in these liver enzymes was observed in silymarin (200mg/kg) and ESEt (800mg/kg) treated positive control and test groups respectively. Of

Table 1: Effect of ESEt on physical and liver-specific biochemical parameters

Parameters	Group I	Group II	Group III	Group IV
IDBW (g)	176.0 ± 16.78	187.5 ± 10.61	190.3 ± 7.78	180.3 ± 6.25
FDBW (g)	181.2 ± 17.85	174.5 ± 14.80	184.0 ± 6.00	175.6 ± 4.45
LW (g)	11.46 ± 0.51 ^d	8.63 ± 0.99	10.10 ± 1.05 ^c	10.31 ± 0.38 ^c
ALT (U/L)	36.16 ± 3.92 ^d	54.00 ± 5.76(+ 49.33%)	45.33 ± 8.77 ^a (-16.05%)	35.66 ± 8.31 ^d (-33.96%)
AST (U/L)	183.83 ± 86.37 ^b	287.00 ± 69.24(+ 56.14%)	240.16 ± 17.18(-16.37%)	197.66 ± 26.08 ^b (-31.30%)
ALP (U/L)	147.83 ± 8.37 ^d	229.83 ± 17.03 (+55.48%)	164.66 ± 11.80 ^d (-28.37%)	107.33 ± 17.61 ^d (-53.30%)
GGT (U/L)	10.50 ± 0.54 ^c	14.00 ± 3.16(+33.33%)	11.50 ± 0.83 ^b (-17.85%)	4.0 ± 0.00 ^d (-71.42%)
TB (mg/dL)	0.35 ± 0.20 ^d	1.21 ± 0.21(+ 245.71%)	0.43 ± 0.18 ^d (-64.46%)	0.13 ± 0.01 ^d (-89.25%)
DB (mg/dL)	0.20 ± 0.12 ^d	0.83 ± 0.18(+ 315.00%)	0.26 ± 0.13 ^d (-68.67%)	0.08 ± 0.01 ^d (-90.36%)
IB (mg/dL)	0.15 ± 0.10 ^d	0.38 ± 0.09(+ 153.33%)	0.16 ± 0.05 ^d (-57.89%)	0.04 ± 0.00 ^d (-89.47%)
TP (g/dL)	8.06 ± 0.65 ^b	6.21 ± 0.30(-22.95%)	6.46 ± 0.32(+4.02%)	8.91 ± 2.04 ^d (+43.31%)
ALB (g/dL)	3.86 ± 0.05 ^a	3.23 ± 0.13(-16.32%)	3.60 ± 0.08(+11.45%)	4.32 ± 0.96 ^c (+33.74%)
LDL-c (mg/dL)	13.66 ± 1.50 ^d	20.66 ± 1.86(+ 51.24%)	12.00 ± 1.89 ^d (-41.91%)	10.00 ± 2.19 ^d (-51.59%)

Each value represents the mean ± SD (n = 6). Where a, b, c & d indicate $p < 0.05$, $p < 0.01$, $p < 0.005$ & $p < 0.0001$ respectively when compared with ATD treated hepatotoxic control group II. Values in parenthesis with negative (-) / positive (+) sign indicate the percent reduction or gain in each parameter.

which ESEt showed more prominent percent reduction in ALT (-33.96%), AST (-31.30%), ALP (-53.30%) and GGT (-71.42%) levels in test group.

Hyperbilirubinemia is another best reflection of altered liver function, indicating that hepatic cells are losing their conjugating function and showing their inability to convert indirect bilirubin (IB) into direct bilirubin (DB) (Ruiz *et al.*, 2021). Increased IB level are primarily found in hemolysis and disorder of bilirubin metabolism and increased DB indicates hepatocellular damage or cholestasis (Liu *et al.*, 2020). A study revealed that isoniazid, rifampicin, pyrazinamide and ethambutol increased in serum bilirubin concentration, especially indirect one (Zhao *et al.*, 2020). ATD named Rimstar 900mg/15 kg, which is a combination of four antituberculosis drugs including Rifampicin 150 mg, Isoniazid 75 mg, Pyrazinamide 400mg and Ethambutol 275mg was used as a hepatotoxic agent in this study that also showed an increase in levels of TB (total bilirubin), DB and particularly IB in the hepatotoxic control group. Whereas ESEt (800mg/kg) treated test group showed an excellent percent reduction ranging from -89.25 to -90.36% in three of these bilirubin (TB, DB and IB).

Hepatic parenchymal cells are active in synthesizing albumin, fibrinogen, globulin and other coagulation factors (Carvalho and Machado 2018). Various studies showed a decrease in total protein (TP) especially albumin (ALB) levels indicate the deterioration in the protein synthesizing ability of liver (Carvalho and Machado 2018). ATD treated hepatotoxic control group also showed decreased levels of TP and ALB. On the other hand, treatment with ESEt of *A. fatua* improved liver protein synthesizing ability in rats of the test group by displaying percent gain in TP (+ 43.31%) and ALB (+ 33.74%) levels.

Many crucial substances required for the body are synthesized by the liver such as cholesterol wrapped up in the cell membrane of hepatocytes and then transported to the extra-hepatic tissues in the form of low density lipoprotein-cholesterol (LDL-c). The liver not only synthesizes cholesterol but is also responsible for lipoprotein synthesis and metabolism, thus any damage like cirrhosis and necrosis in liver cells can cause variation in lipid profile (Hashik and Kezhakkut 2017). Several studies revealed that treatment with antituberculosis drug-induced free radicals constitute oxidative stress that damages liver cells (Yew *et al.*, 2018). Increased LDL-c levels are the clear echo of oxidative stress in the body (Varghese and Ali, 202). In the present investigation, LDL-c level was monitored and found significantly elevated in hepatotoxic control rats treated with ATD (Rimstar 900mg/15kg). However, the rats treated with silymarin and ESEt of *A. fatua* displayed a liver protective effect by observing a significant percent reduction in LDL- c levels.

Histopathological examination of liver tissues revealed heterogeneous hepatocytes, enlarged /inflamed hepatic central vein with RBCs, ballooning (fatty deposits), Enlarged hepatic sinusoid, Kupffer cells infiltration, Hypertrophy and fibrosis in liver slides of ATD treated hepatotoxic control rats. However, all these features were slightly subsided in positive control group III treated with silymarin (200mg/kg) but chiefly disappeared in liver tissues of the test group treated with ESEt (800mg/kg). This improvement indicates the promising participation of ESEt of *A. fatua* in restoring the typical architecture of the hepatic tissue. The possible mechanism of hepatoprotective action of ESEt of *A. fatua* may be due to its already reported total phenols and flavonoids that showed more than 70% antioxidant potential in a study published by Saeed *et al.*, 2018. Though to find out a

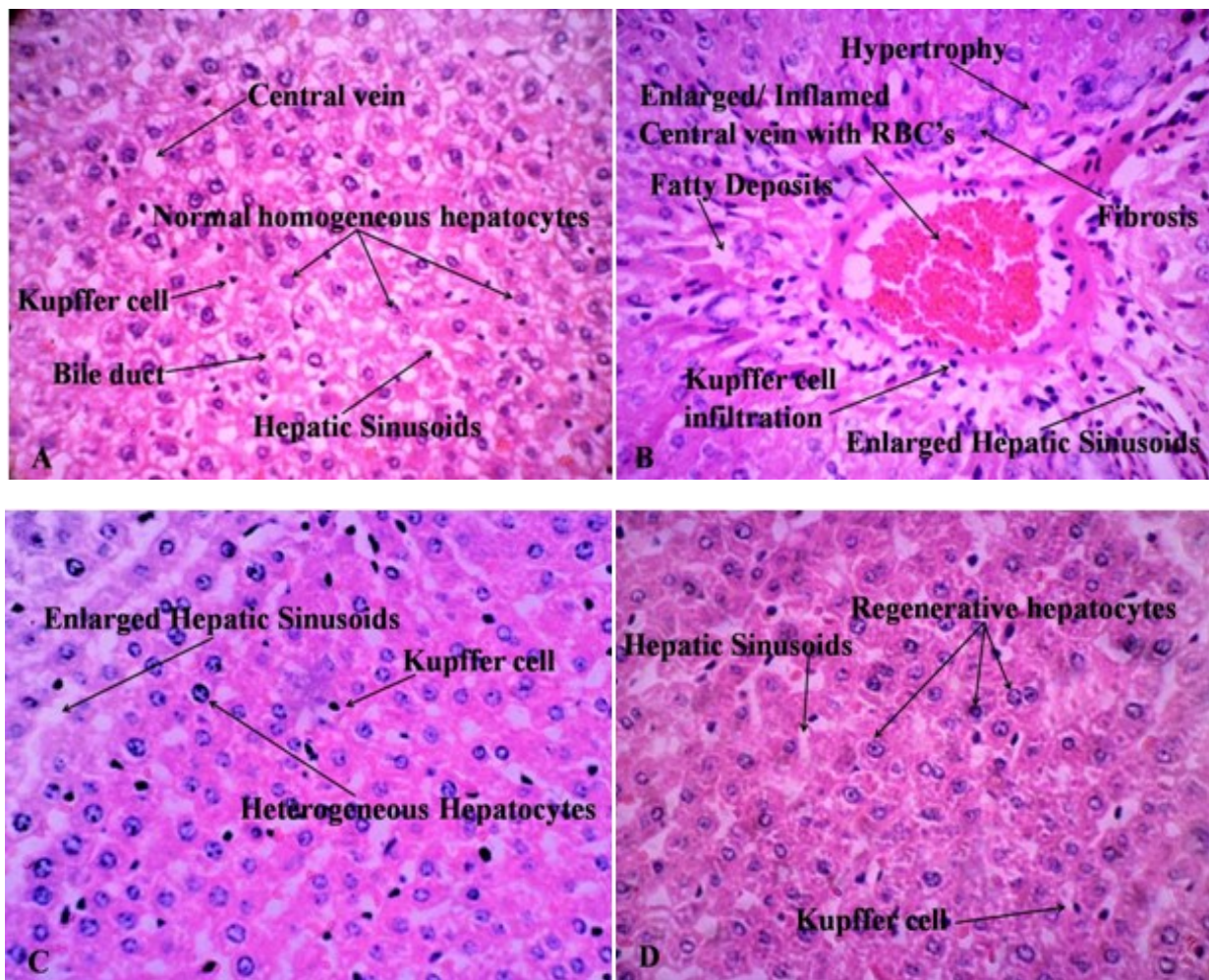


Fig. 3: Effect of ESET on histology of liver tissues. A. Liver tissue of normal control group I. B. Liver tissue of ATD (Rimstar 900mg/kg) hepatotoxic control group II showing heterogeneous hepatocytes, enlarged /inflamed hepatic central vein with RBCs, ballooning (fatty deposits), enlarged hepatic sinusoid, Kupffer cells infiltration, hypertrophy and fibrosis. C. Liver tissue of silymarin (200mg/kg) treated positive control group III showing slight improvement in liver structure. D. Liver tissue of ESET (800mg/kg) treated test group IV showing rejuvenation in normal architecture of the hepatic tissue.

particular compound from seeds of this plant chiefly involved in liver protective activity would be the dimension of new research.

CONCLUSION

The present study proves that ESET of *A. fatua* has an excellent hepatoprotective potential against liver toxicity induced by the antituberculosis drug. This effect was evident by observing improvement in physical and liver-specific biochemical parameters. Histopathological examination of liver sections also supported these findings by showing betterment in liver anatomy.

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