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Research Article

Hepatoprotective Effect of *Typhonium Flagelliforme* against Thioacetamide Produced Liver Cirrhosis in Rats

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Abstract

Typhonium flagelliforme (*T. flagelliforme*) was utilized in outdated medication for handling numerous syndromes. This study aimed to investigate the hepatoprotection effects of *T. flagelliforme* against Thioacetamide (TAA) hepatotoxicity in rats. Thirty rats have arbitrarily separated into five groups. Collection 1 was intraperitoneal injected with distilled water thrice /week and fed (p.o) daily with 10% Tween 20 to eight weeks. Collection 2 to 5 i.p. injected with 200 mg/kg. TAA three times thrice per week for 8 weeks and fed 10% Tween 20 mg/kg, 50 mg/kg silymarin, 250 mg/kg and 500 mg/kg of *T. flagelliforme* extract daily for 8 weeks, respectively. Hepatotoxic assembly showed a suggestive rise in hepatic biochemistry markers together with a considerable lessening of proteins and albumin compared to normal assemblage. The hepatotoxic group displayed decreased Catalase (CAT) and Superoxide Dismutase (SOD) activities and increase lipid peroxidation (MDA). Macroscopy of hepatotoxic liver exhibited irregular, rough surface with micro and macro nodules, and histopathology-stained Hematoxylin and Eosin, and Masson's Trichome exhibited inflammation infiltration of lymphocytes, focal necrosis, fibrosis, and bile duct propagation. *T. flagelliforme*-fed groups have expressively reduced TAA toxicity in gross and histology as designated by fewer disturbances of hepatic tissue, slight fibrosis, and low-grade cell infiltration. Acute toxicity with a higher doses of 5 g/kg *T. flagelliforme* did not obvious any toxicological signs in rats. The rats were distinctly administered with two doses of *T. flagelliforme* with TAA showed a significant down-regulated of the alpha-smooth muscle act in (α-SMA) compared to the TAA control group. Thus, our results showed that the hepatoprotective effect of this plant might be due to reduced toxicity, inhibition of hepatocyte proliferation, down-regulated of the α-SMA, decrease enzyme markers, increase protein and albumin, increased endogenous enzymes, and reduced lipid peroxidation level.

Keywords: ***Typhonium Flagelliforme*; Liver cirrhosis; TAA; Histology; α-SMA; Liver function tests**

Introduction

T. flagelliforme curative herb which fits *Araceae*. This herb is widely utilized *in vitro* [1-3], and *in vivo* [4] due to its medicinal treatment properties for many diseases such as cancer, edema, injuries, coughs, pulmonary ailments, and bleeding [5]. Also, this plant widely utilizes South East Asia as a traditional remedy for many diseases [6]. *T. flagelliforme* has biologically active chemicals such as alkaloids, saponins, steroids, and glycosides [2]. Rodent tuber has potential components of anticancer and antiviral [7], anti-inflammatory, analgesic, and antihepatotoxic [8,9].

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Although the liver is a highly important organ for cleansing, diseases of the liver can be the greatest dangerous healthiness complications [10]. The most common liver diseases are cirrhosis hepatocellular carcinoma, viral hepatitis, and alcoholic hepatitis, which remain predominant disorders worldwide, and are strongly linked with jaundice [11]. In scientific literature, several studies have the well-known helpful influence of uncountable medicinal plants defending the liver from hepatotoxic damage of TAA in laboratory animals [10,12]. The most common hepatoprotection agent is silymarin, which is an herbal substance that has been cleansed from seeds of the *Silybum* marinum plant [13]. The latter is used broadly as a therapeutic supplement aimed at liver illnesses like hepatitis, fatty acid infiltration, and cirrhosis resulting from toxic chemical and alcohol effects [11]. Numerous training several academics utilized silymarin ordinary medicine hepatoprotective contrary to the hepatotoxicity of thioacetamide [14-16].

Thioacetamide (TAA) causes an increase in oxidative stress, attractive free radical-facilitated injury to proteins, lipids, and DNA [17]. TAA makes hepatic cells impairment subsequent its breakdown to thioacetamide sulphene and sulphone, by dangerous trail comprises CYP4502E1-intermediated bio-transformation [10]. Abundant studies by different co-researchers evidenced TAA has been used at the beginning of liver fibrosis [3,18,19].

The effectiveness of rodent tuber herb since traditional right necessity verified to aid progress novel medicines functioning in contradiction of liver syndromes. However, no work was started on the hepatoprotective achievement of this plant. The existing training is designed to assess hepatoprotection action *T. flagelliforme* on TAA-persuaded hepatic injuries in rats.

Materials and Methods

Ethics announcement

The current experiment was authorized through conscience team rodents' examination, Faculty Sciences Cihan University-Erbil, Ethical Number PM/07/05/2020/MMA. All animals for the duration of trials, obtained human attention by principles set forth "Director Maintenance Utilize research" organized nationwide School Science has issued nation-wide Institution healthiness.

Thioacetamide

TAA purchased Sigma-Aldrich, liquefied 10% Tween 20 also mixed whole liquefied. Then, 200 mg/kg body mass inserted rodent 3 periods weekly 8 weeks. TAA produced vicissitudes together with biology besides morphology structures similar to humanoid hepatic fibrosis [20].

Silymarin

Silymarin is a reference drug (International Laboratory, USA), which is used in normal medication in testing. Silymarin melted in double glass-distilled water, then gavage rodents in amount 50 mg/kg [21,22].

Plant preparations and extraction

T. flagelliforme fresh plants received from (Ethno Resources Sdn Bhd), detected when compared with the Voucher sample placed at Herbarium Garden, institute of Science Biology. Dried plants are processed to powder using Electrical Blender. One thousand millilitres of 95% ethanol were used to dissolve 300 gm of *T. flagelliforme* powder for 72 hours. After this period, the plant residue was cleared *via* clean muslin fabric, and then the mixture was filtered using mesh paper. Resulted suspension evaporated at a low-pressure lab rotary evaporator. Dried extract soaked in 10% Tween 20 then rats administrated a dosage of 250 mg/kg and 500 mg/kg (5 ml/kg) [23].

Acute toxicity test

Acute toxicity was obligatory for examination the safety of *T. flagelliforme*'s biologic activity is extremely advised to prevent any undesirable adverse side effects. Acute toxicity test was conducted according to Organization for Economic Cooperation and Development (OECD) guidelines, 2002. Experimental rats acquired from Animal House Experimental Unit of Cihan University-Erbil. Acute toxicity test was performed to fix toxic dose of *T. flagelliforme* extract. Rats were fed normal rat pellets ad libitum and tap water. Thirty-six rats (18 males and 18 females) assigned similarly each into 3 groups and administered vehicle (10% Tween 20); 2000 mg/kg and 5000 mg/kg of *T. flagelliforme*, respectively. These doses were selected based on the previous efficacy studies [24]. Experimental rats starved over-night (food) but allowed excess to water before to start treatment. Rats were watched for 30 min and 1, 2, 3, and 24 hrs for any toxic signs or death. Then rats fasted overnight on day14th and sacrifice on day 15th using general anesthesia, i.e. Ketamine (30 mg/kg, 100 mg/mL) and Xylazine (3 mg/kg, 100 mg/mL) [25]. Blood was collected by intracardiac puncture for liver and kidney function tests. All the rats were subsequently sacrificed by cervical dislocation. Histopathology of liver and kidney stained by H&E stain and analyzed for any structural changes [26].

Experimental animals and hepatoprotective activity

Rats weight approximately 180 gm to 200 gm were housed individually *via* wide-mesh wire bottoms to avoid coprophagia throughout the experimental time, at 25°C ± 2°C temperature, approximate moisture 55% - 65% and 12 hours' exposure light/dark rotation. All the rats were fed on tape water and a standard pellet. The experimental designed and authorized through Ethics Committee for Animal Research. Human care for whole experimental animals was applied and followed Maintenance Usage Animal which produced Nationwide College Knowledge issued through countrywide Institute of healthiness.

Thirty healthy adults' Sprague Dawley rodents were arbitrarily alienated into five clusters with six rats respectively. Rats clusters divisions besides treatment protocol were determined following the method of [22,27] with a few modifications; Group 1 (normal), which was treated by normal saline (5 mL/kg) injection for 3 weeks, and 10% Tween 20 *via* oral administration every day for 2 months. Group 2 (hepatotoxic) inoculated (i.p) (200 mg/kg) of TAA 3 periods weekly every day administrated orally by 10% Tween 20 for two months. Assembly 3 (reference drug) assumed 3 times weekly of TAA inoculation then daily administered Silymarin (50 mg/kg) for 8 weeks. Collection 4 and 5 were conventional TAA injections thrice/weekly for 2 months, daily oral administration of *T. flagelliforme* extract, respectively.

After the last treatment at the end of experimental time (two months), all animals fated 24 hours and then processed for general anesthesia using ketamine xylazine [25]. Blood is collected from intracardial puncture and stored in a gel-activated tube for liver functions test [28].

Biochemical parameters (liver function test)

Blood in clot-activator tubes was separated *via* centrifuge 10 minutes 2500 rpm. Spectrophotometer used for evaluation alanine aminotransferase aspartate aminotransferase, alkaline phosphatase, total bilirubin, total protein besides albumin. Biochemical parameters evaluated by Medicine Center [25].

Macroscopic appearance of liver

The liver assessment was done by opening the rat's abdominal and thoracic cavities. The livers showed significant macroscopic proof of pathological changes. Also, other organs showed pathological gross lesions but were excluded from the current study. All livers were separately washed in cold saline [29].

Histopathology of liver tissue

H&E stain & Masson Trichrome stain: Liver samples were washed in cold saline, cut 2 cm cubic, fixed in 10% phosphate-buffered formalin. Leica, Germany tissue processor machine was used to process the specimens. Five µm slices are routinely stained by H&E (hematoxylin and eosin) [25] in addition Masson trichrome stain [25]. Nikon microscope (Y-THS, Japan) was used to evaluate the liver slides.

Immunohistochemical staining: Poly-L-lysine-treated glass slides were used for α-smooth muscle actin (α-SMA) staining methods, as previously described in detail [3,30].

Hepatic homogenate endogenic (CAT, SOD) oxidative stress:

Neutral ice-cold phosphate buffer saline 10% (w/v) was used to wash rats' livers. Teflon homogenizer was used to homogenize liver samples (all steps done on ice), then centrifugation was detached. Clear supernatant collected verify antioxidant activity *via* SOD, CAT analyzes kits. Also, Oxidative stress, Malondialdehyde (MDA), assess kits were utilized to govern thiobarbituric acid reactive substance (TBARS, Chemical Compony) [31].

Statistic examination of information: Information analysis was showed mean ± SEM, One-Way ANOVA using Tukey post hoc assessment, SPSS software, and version 24. The p values statistical meaning at p<0.05.

Results

Acute toxicity test

Rats fed by *T. flagelliforme* at a dose of 2000 mg/kg and 5000 mg/kg were observed for 2 weeks. Rats were continuously active and there were no significant signs of toxicity, atypical symbols, alteration of behavioral patterns, body mass deviations, or gross discovery noticed throughout the entire experiment. There was no mortality in both dosages towards the end of 14 days. A histopathological investigation of the liver and kidney and blood biochemical markers showed no substantial alterations among the various groups Figure 1. Based on the findings of the current study, *T. flagelliforme* was not toxic at either dosage.

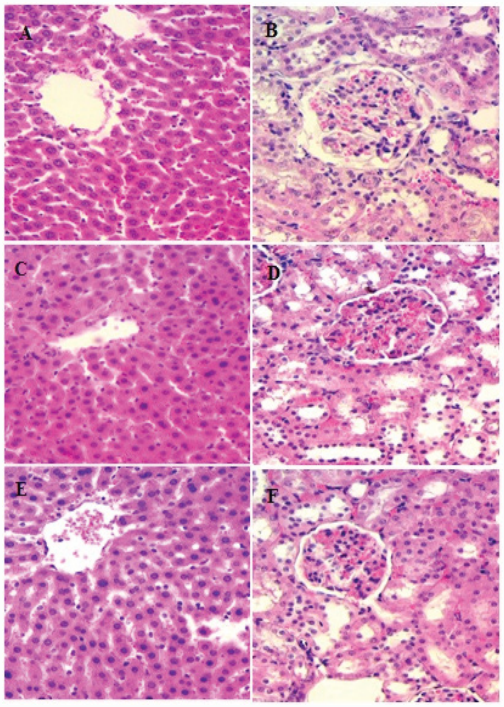

Figure 1: Histologic sections of liver besides kidney for acute toxicity experimentation. Rats fed 5 mL/kg vehicle (10% Tween 20) (A and B). Rats fed on 2000 mg/kg (5 mL/kg) Alpinetin (C and D). Rats fed on 5000 mg/kg of *T. flagelliforme* (E and F). No significant variations in liver and kidney structures between the experimental and control groups were seen (hematoxylin and eosin stain 40x).

Hepatic biochemical markers

The hepatotoxic effect of TAA was meaningfully augmented (P<0.001, mean ± SE) levels of ALT, ALP, total bilirubin AST, referred to as liver damage (Table 1). Moreover, the TAA cluster exhibited substantial decreases (P<0.001, mean ± SE) total protein albumin compared with the normal collection, demonstrating hepatocellular injury. *T. flagelliforme* and silymarin treated groups are significantly dropped (P<0.001, mean ± SE) enzyme ALT, ALP, total bilirubin AST. In addition, total protein total albumin values were elevated (P<0.001, mean ± SE) in *T. flagelliforme* and silymarin treatments in comparison with the TAA control group. Hence, *T. flagelliforme* revoked the hepatotoxic effect of TAA *via* reinstating typical liver activities. *T. flagelliforme* effectively prevented TAA-induced hepatotoxicity at a dosage of 250 mg/kg, whereas slightly affected at a dosage of 500 mg/kg.

Gross appearance of liver

The morphological changes of liver in all groups (Figure 2 (GA)) were evaluated and showed that normal control group liver was contained smooth surface with regular lobs (Figure 2, GA (a). TAA-induced hepatotoxic group liver was demonstrated unregularly surface with several macro and micronodules (Figure 2, GA (b)). TAA+silymarin treated group was presented smooth surface closed to normal group (Figure 2, GA (c)). TAA+*T. flagelliforme* 250 mg/kg TAA+ *T. flagelliforme* 500 mg/kg assemblages were exhibited liver with even superficial closely maintain hepatic usual architectural structure and form (Figure 2, GA (d, e)).

Histopathological examination of hepatocyte sections

A histopathological change of liver sections stained with hematoxylin and eosin is shown in Figure 3 (H&E). Liver slides of the normal group are demonstrated typical hepatocytes construction, preserved cytoplasm, distinguished nucleus and nucleolus with distinct regular plates of liver cells which are divided *via* sinusoidal capillaries and central vein (Figure 3, H&E (a)). Liver sections from the TAA group were showed irregular hepatocyte architecture resulting from the existence of reforming nodes. Moreover, the hepatic section is separated *via* a rubbery septum stretching the chief vein to the portal area. Hepatocytes presented severe damage, necrosis and extensive propagation of the bile duct, congested central vein, fatty changes, and granulocytes and monocytes which are presented surround the central vein due to the inflammation (Figure 3, H&E stain (b)). Silymarin+TAA, low and high dose of *T. flagelliforme*+TAA groups were illustrated relative protection from hepatocyte-disruptions induced by TAA. The hepatic cellular compositions showed a reduced amount of damage with a slight fibrotic septum. Insignificant penetration of lymphocytes was observed in these liver sections groups. Moreover, the histopathological sections demonstrated remarkable regenerative parenchymal nodules, which are boarded with fibrous tissue as well as noteworthy growth in the cells-fat storing, bile ducts, and Kupffer cells (Figure 3, H&E (c-e)). Hepatic tissues stain Masson trichrome to measure levels of tissue fibrosis. There was no collagen deposition observed in the normal control liver section (Figure 4, MT (a)). TAA group has presented a regeneration of bile duct with notable septa of dense fibers and increased the accumulation of collagen fibers surrounding the congested central vein, which are referred to severe fibrosis in the hepatic tissue (Figure 4, MT (b)). The silymarin and *T. flagelliforme* clusters illustrated a reduction in the number of fibrous septa and regeneration nodules. In addition, the collagen fibers in all these three groups were observed to be homologous, which indicated the hepatoprotection activity of *T. flagelliforme* extract (Figure 4, MT (c-e)).

Immunohistochemistry staining of hepatic tissue sections

Thioacetamide (TAA)-induced liver damage and the importance

Table 1: Influence *Typhonium flagelliforme* liver biochemistry markers TAA-produced hepatotoxic rats.

Animal Groups	ALP IU/L	ALT IU/L	AST IU/L	T. Bilirubin (µM/L)	T. Protein g/L	T. Albumin g/L
Normal	70.3 ± 0.6	30.4 ± 0.6	63.9 ± 0.7	1.2 ± 0.01	73.2 ± 0.7	32.9 ± 0.5
TAA + NS	193 ± 1.1*	130.3 ± 0.5*	172.5 ± 0.5*	5.1 ± 0.07*	45.8 ± 0.6*	13.2 ± 0.2*
Silymarin + TAA (50mg/kg)	62.4 ± 0.6#	28.1 ± 0.9#	62.5 ± 0.6#	1.4 ± 0.01#	68.1 ± 0.7#	29.4 ± 0.6#
LD + TAA (250mg/kg)	58.2 ± 0.8#	22.3 ± 0.6#	55.4 ± 0.5#	1.9 ± 0.03#	60 ± 0.8#	22.1 ± 0.6#
HD + TAA (500mg/kg)	54.3 ± 0.5 #	25 ± 0.4#	58.7 ± 0.7#	1.7 ± 0.05#	64.8 ± 0.4#	25.6 ± 0.6#

Effects of *T. flagelliforme* or silymarin on ALT, AST, and ALP actions, on level of total bilirubin, albumin, protein. Values stated mean ± SEM. Important alteration normal collection. *p<0.001, Substantial variance TAA control assembly at #p<0.001

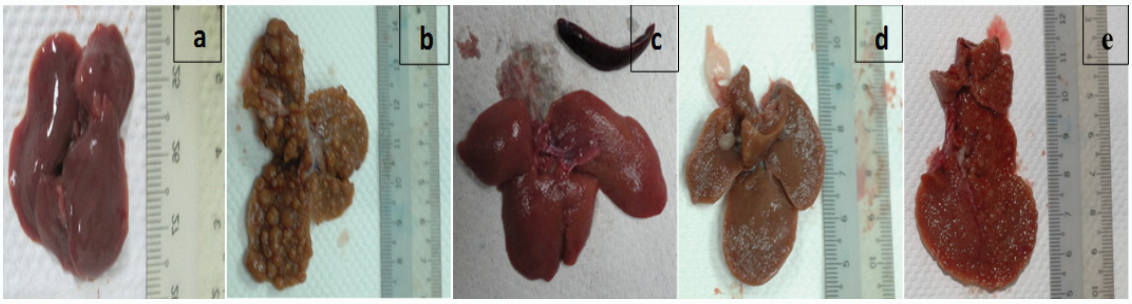

Figure 2: Macroscopically displays influences *T. flagelliforme* TAA-produced hepatic injury rats (a). Normal group expressions are even superficial. (b). Rats injected TAA demonstration several micronodules and macronodules in the hepatic parenchyma. (c). Rats inoculated TAA+ silymarin viewing usual flat external. (d). Rats inserted TAA+ *T. flagelliforme* 250 mg/kg and (e). Rats injected TAA+*T. flagelliforme* 500 mg/kg. *T. flagelliforme* ordinary even exterior and closely reserve hepatic ordinary anatomy outline advent.

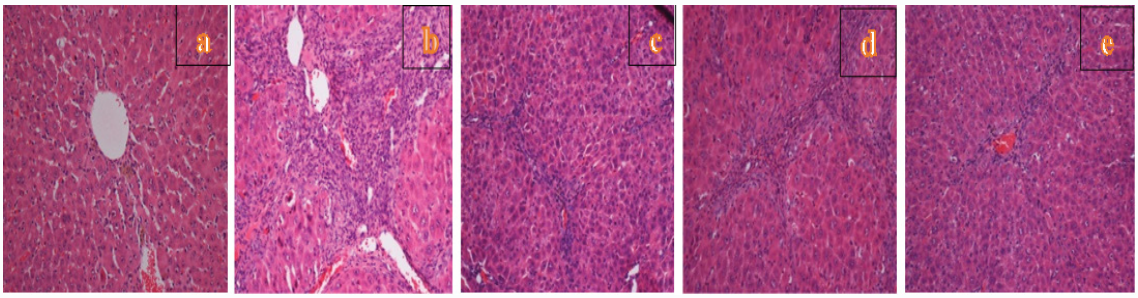

Figure 3: Histopathology slices of the livers stained with H&E stain. (a). Normal histology construction was understood as a hepatic ordinary collection. (b). Extensive organizational injury development pseudo lobules abundant fibrous septum and propagation bile duct central lobular damage hepatic TAA assembly. (c). The minor inflammatory fibrous septum was shown hepatic parenchyma hepatoprotection rats inoculated TAA+silymarin. (d). Partial conserved hepatic cells construction minor portion of injuries and thin fibrotic septum occurred in the liver of the rat injected TAA+250 mg/kg of the *T. flagelliforme*. (e). Partial conserved hepatocytes construction slight parts minor damage experiential hepatic rats inoculated TAA+500 mg/kg *T. flagelliforme* (H&E stains 10x).

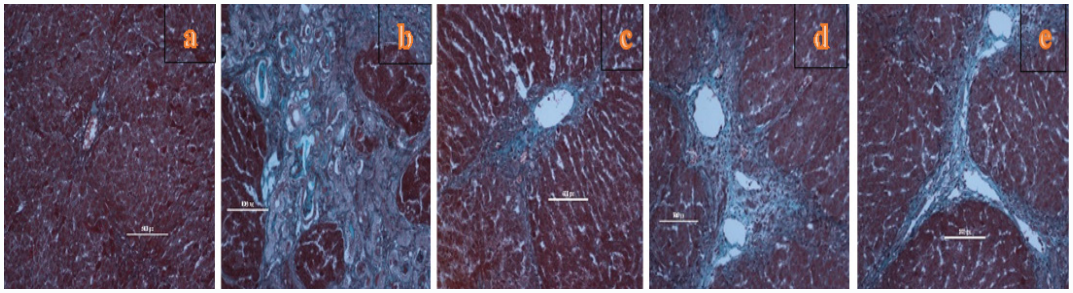

Figure 4: Histology slices of liver stained with Masson Trichrome. (a). Normal assemblage illustrations usual hepatic construction. (b). TAA cluster demonstrations propagation bile duct, compact fibrosis septum (c). Rats injected TAA+ silymarin expressions negligible fibrous septum. (d). Rat treated with TAA+250 mg/kg T. flagelliforme displays slight fibrous septum and uneven renewing nodes. (e). Rats inoculated TAA+500 mg/kg *T. flagelliforme* confirmations slight fibrous septum. Masson Trichrome stains (amplification 10x).

of *T. flagelliforme* extract were examined by the immunohistochemical staining of α-smooth muscle actin (α-SMA) expression in the liver parenchyma utilizing specific antibodies. The normal control group showed the down-regulation of α-SMA staining, which indicates no occurrence of cell regeneration (Figure 5). On the contrary, the TAA control group had an outstanding α-SMA appearance signifying up-regulation of these proteins with a higher level of hepatocyte fibrosis. The TAA control group elevated the mitotic figure index significantly, suggesting the proliferation of the regeneration of widespread hepatic damage induced by TAA. Rats fed 500 mg/kg *T. flagelliforme* extract had reduced hepatic cell revitalization in comparison to the TAA control group, as indicated by α-SMA appearance and a significant drop-off in the mitotic index. These results were comparatively similar to that of the silymarin-treated group. *T. flagelliforme* extract

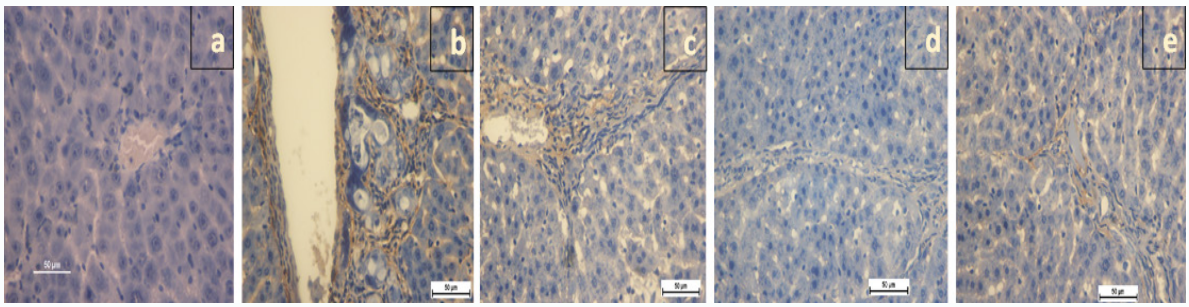

Figure 5: Immunohistochemistry: Effect of ethanolic extracts of *T. flagelliforme* on α-SMA staining of liver, (a). Normal control group, no α-SMA expression (down-regulation); (b). TAA-control group, α-SMA expression of hepatocytes (up-regulation); (c). TAA+Silymarin group, mild α-SMA expression (down-regulation); (d). TAA+250 mg/kg G. *T. flagelliforme* group, moderate α-SMA expression (down-regulation); (e) TAA+500 mg/kg *T. flagelliforme* group, mild α-SMA expression (down-regulation) (α-SMA stain, magnification 40x).

resisted hepatocyte fibrosis by down-regulating α-SMA expression. Rats fed with 250 mg/kg *T. flagelliforme* extract, however, exhibited mild to moderate expressions of α-SMA within the hepatocytes with a significant decrease in the mitotic figure index, but not analogous to the silymarin-treated group. These results suggest that *T. flagelliforme* extract had an estimable hepatoprotective effect by inhibiting the fibrosis of hepatocytes and ameliorating propagation.

Effect of *T. flagelliforme* on liver antioxidant enzymes (CAT and SOD) and oxidative stress (Malondialdehyde (MDA)) Levels

Liver homogenates of the TAA control group revealed meaningfully reduced SOD and CAT activities in contrast to rats fed with *T. flagelliforme*. *T. flagelliforme* significantly returned the SOD and CAT activities by protecting the tissues from the hepatotoxic effects of TAA. However, MDA amount increases in homogenized materials indicate a lesser director of lipid peroxidation. The MDA of liver tissue homogenate was knowingly high in the TAA control group. However, the administration of *T. flagelliforme* extract significantly decreased the level of MDA (Figure 6).

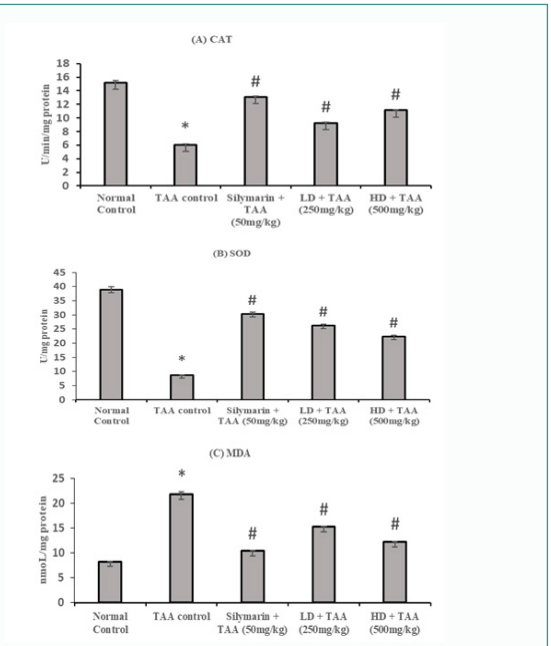

Figure 6: Effects of *T. flagelliforme* on antioxidant enzyme actions MDA amount liver. Actions of SOD, CAT, contented MDA, amount hepatic liver cells. Information stated mean ± SEM. (A) CAT (B) SOD (C). MDA. Substantial alteration normal collection at *p<0.001, Important change TAA assemblage at #p<0.001.

Discussion

The current investigation was initiated with an oral acute toxicity test of *T. flagelliforme* extract on experimental rats, the outcome revealed promising safety of this plant extract with no morbidity and mortality during the entire experimental period even at higher concentrations i.e. 5000 mg/kg of *T. flagelliforme* extract. Consistently, many studies by various investigators using different medicinal plant extracts displayed safe, and no symbol of toxic effect was reported [3,25,32].

In the present study, the hepatotoxic group was related to a visible increase in activities of liver markers in blood circulation such as ALP, ALT, and AST bilirubin levels. Raise hepatic function markers imitates hepatic impairment. Similarly, increases in liver markers activities and bilirubin levels in hepatotoxic group were previously reported by several researchers [3,17,33]. Morals meaningfully condensed nearly usual standards after nourishing with *T. flagelliforme* extract. With the consistency of the results of our study several co-workers who used various plant extracts showed decreased in liver function enzymes activities and bilirubin level has been previously reported elsewhere [13,34]. The hepatoprotective achievement may be due to its effect against cells leakage and injury of hepatocytes covering. TAA stated burden RNA initiative nucleus to the cytoplasm, initial exterior damage results upsurge serum hepatic pointers [4]. Current training, total protein and albumin quantities serum condensed TAA control cluster. However, silymarin or *T. flagelliforme* nourishing collections evoke these values in closely ordinary amount. Similarly, huge numbers of scientists displayed that rats' gavage silymarin or various plant extracts brought the albumin and protein to almost normal levels [11].

Accelerate the recovery of liver damage and significantly prevent the effects of TAA toxicity [28]. The outcomes of this study are also in line with earlier studies reported by numerousco-researchers using various medicinal plants in contradiction to TAA-induced liver injury in rats [13,28,32,35]. Results of the existing study displayed reduced collagen production synthesis in *T. flagelliforme* feeding, for example, Masson's trichrome stain. In agreement with the consequences of the present study, abundant studies which used diverse medicinal plant extracts exhibited a reduction in collagen fibers against TAA-induced liver cirrhosis [17,21,30,36,37]. In the TAA-induced hepatotoxic rats, TAA caused the production of Reactive Oxygen Species (ROS) leading to the stimulation of Hepatic Satellite Cells (HSC), a major factor for the ECM in chronic liver cirrhosis and the up-regulation of α-smooth muscle actin (α-SMA). The initiation of HSC comes with the cell propagation and upgrading of ECM production, and the

occurrence of α-SMA in myofibroblasts. The results of the current study revealed that *T. flagelliforme* extract supplementation caused the down-regulation of α-SMA compared to the TAA control group, which showed a significant up-regulation of α-SMA. *T. flagelliforme* extract significantly reduced the HSC activation by decreasing the rate of ROS production. Similar results have been reported on the efficiency of medicinal plants in the down-regulation of α-SMA in TAA-induced liver cirrhosis [3,13,32,35].

In the present study, Endogenous enzymes, SOD and CAT, in liver tissues homogenate suggestively condensed hepatotoxicity assemblage comparison ordinary cluster. Both enzymes become flagged by free radicals's resulting in liver weakening [34]. Meanwhile, *T. flagelliforme* expressively raised attentiveness serum CAT, SOD, *via* self-protective hepatic injurious influence free radicals likened TAA control collection. Analogous outcomes described formerly uncountable investigators [8,16,38].

MDA as a lipid peroxidation marker is a usual damaging procedure [17]. MDA level raised improved lipid peroxidation. Upsurge MDA initiating damages and tragedy of anti-oxidant protection to prevent the expansion of additional free radicals [3,18]. The existing search exhibited TAA yield increase in MDA amount has been promisingly condensed by *T. flagelliforme* feeding. Parallel results have been previously reported by various academics elsewhere [11,39]. Reduction of hepatic SOD and CAT activities in the hepatotoxic group might possibly explain elevated MDA. TAA produced liver fibrosis in rodents [40,41]. Nonetheless, rat's gavage with *T. flagelliforme* could dramatically hasten retrieval the hepatic damages suggestively prevent effect TAA intoxication. These results consistence former trainings stated abundant inventers utilizing diverse medicinal herbs [42]. Results of the existing study presented decrease collagen deposition in *T. flagelliforme* fed groups in tissue section-stained Masson trichrome staining. Similar to consequences of present study numerous investigators used many plant extracts confirmed reduction of collagen fibers compared to TAA control group [18,43].

Conclusion

According to the results the current study *T. flagelliforme* exposed significant hepatoprotective effect in reduction of TAA toxicity in rats as acknowledged by biochemical liver parameters, endogenous enzymes, macroscopically, histologically and immunohistochemistry. *T. flagelliforme* intensely raises the CAT&SOD activities, whereas significant reduction of hepatic MDA.

T. flagelliforme extract effectively prevent TAA-induced liver cirrhosis by the marked down-regulation of hepatic α-SMA appearance. The defensive result of *T. flagelliforme* against TAA-induced hepatotoxicity could be due to its capacity to avoid hepatocyte propagation, decrease oxidative stress and lipid peroxidation, and its antioxidant and free radical scavenger properties, Hepatoprotective effect of *T. flagelliforme* against TAA-induced hepatotoxicity might be attributed to its ability to avoid hepatic cells propagation, lessening oxidative stress lipid peroxidation, and its antioxidant free radical scavenger possessions.

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