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PHYTOCHEMICAL AND PHARMACOLOGICAL SCREENING OF MOMORDICA DIOICA FOR HEPATOPROTECTIVE ACTIVITY IN RATS

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Abstracts
The present study was designed to evaluate hepatoprotective activity of *Momordica dioica* (*M. dioica*) in Wistar albino rats using Anti Tuberculosis drugs induced hepatic damaged experimental animals. Isoniazid and Rifampicin-induced was administered a 100 and 50 mg/kg bw dose to induce hepatotoxicity. *M. dioica* (300 and 500mg/kg, p.o) and Silymarin 100mg/kg, p.o. were administered once daily for 30 days. The degree of hepatoprotection was measured using morphological parameters of changing in weight of liver, Biochemical parameters in serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum alkaline phosphatase (SALP), bilirubin. The histopathological parameters of histological changes in the liver architecture like architecture of hepatic lobules, swelling of liver cell, fatty changes, focal necrosis, inflammatory cell infiltration around portal areas, kupffer cell hyperplasia etc. The result of this study indicated that the *M. dioica* has got a hepatoprotective action against Isoniazid and Rifampicin induced hepatic damage in experimental animals.

Keywords: Isoniazid and Rifampicin, *M. dioica* and Silymarin

INTRODUCTION

The liver is a vital organ having a wide range of functions including detoxification, protein synthesis and production of biochemical necessary for digestion. It is involved with almost all the biochemical pathways related to growth, fight against disease, nutrient supply, energy provision and reproduction [1]. Liver is the key organ to maintenance, performance and regulating homeostasis in the body. But liver is continuously and variedly exposed to exogenous substances like environmental toxins, drugs and alcohol which can eventually lead to various liver disorders, generally presenting as a distinct patterns of diseases such as hepatocellular, cholestatic (obstructive), or mixed type of liver disorders [2].

Almost all types of liver injuries may lead to hepatic failure and ultimately death. Thus liver diseases are one of the most fatal diseases in the world today [3]. Till date available modern drugs have not been able to come up with a satisfactory answer for liver disorders because of high cost and additional adverse effects. It is therefore necessary to search for alternative drugs for the treatment of liver diseases to replace the currently used drugs of doubtful efficacy and safety.

M. dioica Roxb (Family: Cucurbitaceae) is commonly known as spine gourd or teasle gourd is an annual or perennial climber. It has native of tropical regions on Asia with extensive distribution in China, Japan, parts of South East Asia, and India. It is used as a vegetable in India, tender fruits and deseeded mature and ripe fruits cooked as vegetable [4]. It is known as *Kakora* in Hindi. Many research literatures including ancient *Ayurveda* an Indian system of traditional medicine demonstrate its medicinal values. The roots are used in head trouble, treating urinary calculi. The leaves having aphrodisiac and anthelmintic properties. The fruit was used as stomachic; treating constipation, and the powder or infusion of the dried fruits, when introduced into the nostrils produces a powerful errhine effect and provokes a copious discharge from the schneiderian mucous membrane[5]. The leaves have reported for having strong antioxidant, hepatoprotective action[6]. *M. dioica* fruits proved to be effective in controlling drug induced nephrotoxicity, and curing renal damages[7]. A recent study concludes that the ethanolic extract of *M. dioica* seeds possesses marked nephroprotective and curative activities and facilitates the treatment of acute renal injury induced by gentamicin a potent nephrotoxin[8]. The extract of the dried roots of this plant was successfully evaluated for its abortifacient and estrogenic activity[9]. Our studies is investigated the hepatoprotective properties of the ethanolic extract *M. dioica* fruits on Isoniazid and Rifampicin-induced liver damage in animals models.

COLLECTION OF PLANT MATERIAL:

Fresh fruit of *M. dioica* Roxb. (Family: Cucurbitaceae), were procured from local vendor Hyderabad, Telangana. Fruits are authenticated by authenticated by Dr.Vijaya Bhasker Reddy, Assistant Professor, Department of Botany , Osmania university, Hyderabad. A voucher specimen (No.OUAS-164).

PREPARATION OF EXTRACTION

The fresh fruits around 2kg shade dried for 15 days; fruit material was powdered using mixer grinder and passed through sieve no 85. Weight About 150gm of dried fruit powder was subjected to soxhlet's apparatus extraction using ethanol solvent for 72 hrs. The extract were concentrated in rotary flash evaporators and stored in refrigerator

Preliminary phytochemical analysis: the extracts were then subjected to preliminary phytochemical analysis to assess the presence of various phytoconstituents [10].

Experimental animals procured

Adult wistar rats of male 9 to 11 week age, weighing 160–180gm were procured from Mahaveera enterprises, Hyderabad. Animals were housed in standard laboratory conditions at 25°c with 12 hr light-dark cycle with free access to chow and water *ad libitum*. The research protocol was approved by (HKES/COP/MTRIPS/IAEC/105/2022)

Evaluation of HepatoProtective Activity:

Hepatic injury: A dose of 50 mg/kg and 100 mg/kgb.w Isoniazid and Rifampicin respectively in Aqueous 1% CMC through oral for 28days.

The study design is divided into 5groups, six rats in each. After 28 days of treatment study, animals were sacrificed and the following are weight of liver and liver profile for biochemical enzymes parameters such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), and liver histopathology.[11-13]

Group No	No. of Rats	Treatment	Dose
1	6	Control-Aqueous 1% CMC	10ml/kg b.w
2	6	Positive control – INH + RIF	50 mg/kg +100 mg/kg btw,
3	6	INH + RIF+ *M. dioica*	50 mg/kg +100 mg/kg btw+300mg/kg
4	6	INH + RIF+ *M. dioica*	50 mg/kg +100 mg/kg btw+500mg/kg
5	6	INH + RIF + Silymarin 100	50 mg/kg +100 mg/kg btw +5mlg/kg

Table1: Treatment of *M. dioica* on INH+RF induced liver injury

After 28 days of treatment study, animals were sacrificed and the following morphological and biochemical parameters such as

1. Weight of liver,
2. Histopathology of liver,
3. Biochemical enzymes parameters such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP)[11-14]

Histopathological Investigation:

The liver tissues were excised out, washed with the cold saline, fixed in 10% buffered formalin for 12 hours and processed and stained with hematoxylin and eosin dye for photomicroscopic observations.

Statistical Analysis:

The results were expressed as mean ± SEM. The data was analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test. A value of $P < 0.05$ was considered as statistically significant.

RESULTS:

Preliminary Phytochemical Screening:

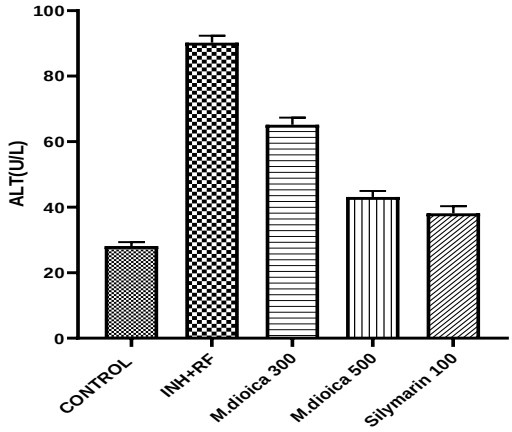
The preliminary phytochemical studies were performed for testing different phytochemical constituents present in *M. dioica* . The observations showed the presence of alkaloids, flavonoids, steroids, Carbohydrate,aminoacids, tannins and poly phenolics, which were found in extract.

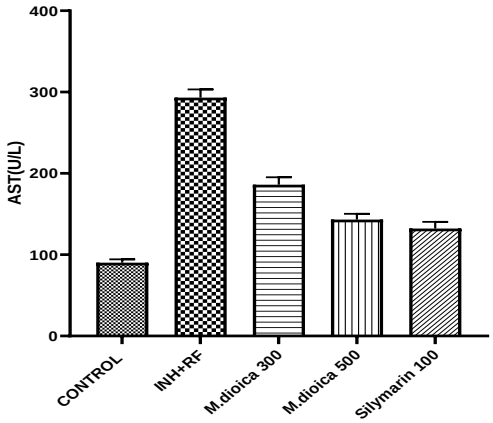
Effect of ethanolic extract of *M. dioica* on liver weight in rats

Anti-TB drug INH+RF treated group significantly decrease the liver weight compared to control group. *M. dioica* treatment markedly ameliorated the effect of anti-TB drug on liver weight. Impact of *M. dioica* was comparable to the effect of Silymarin on hepatic weight.

Effect of *M. dioica* extract on liver function tests

INH+RF administration increased the level of AST, ALT, ALP, TP, and TB in serum compared to the control group. The hepatotoxicity induced with INH+RF was ameliorated by the co-administration of *M. dioica* to INH+RF administered in rats. The protective effects of *M. dioica* on AST, ALT, ALP, TP, and TB were produced in a concentration dependent manner. The level of AST, ALT, ALP, TP, and TB in the serum of Silymarin administered groups remained unaffected compared to the control group as shown in (figure1)





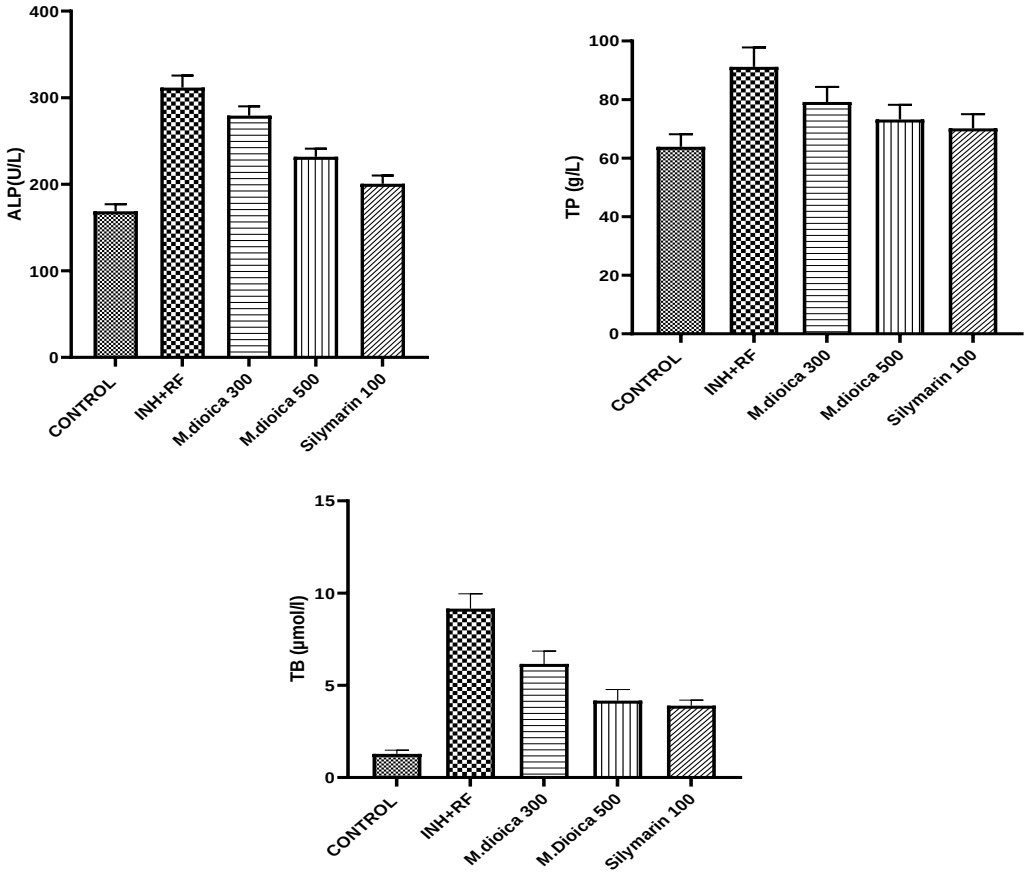
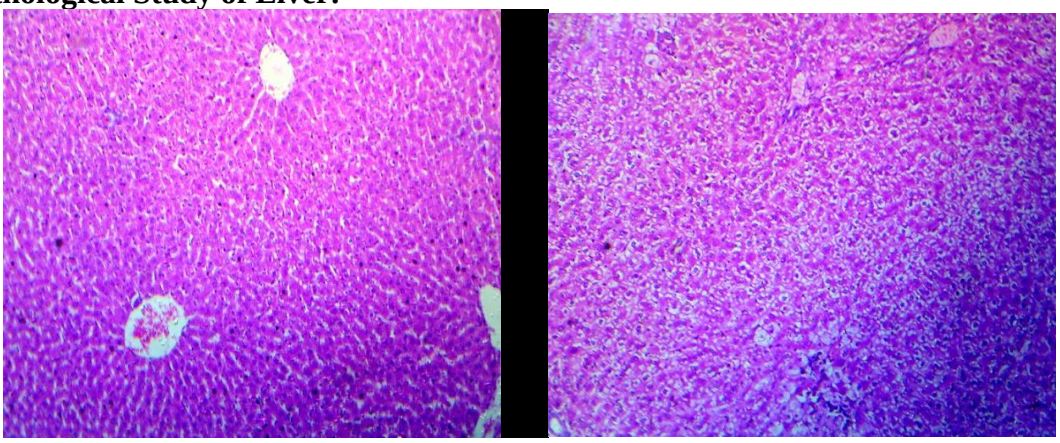
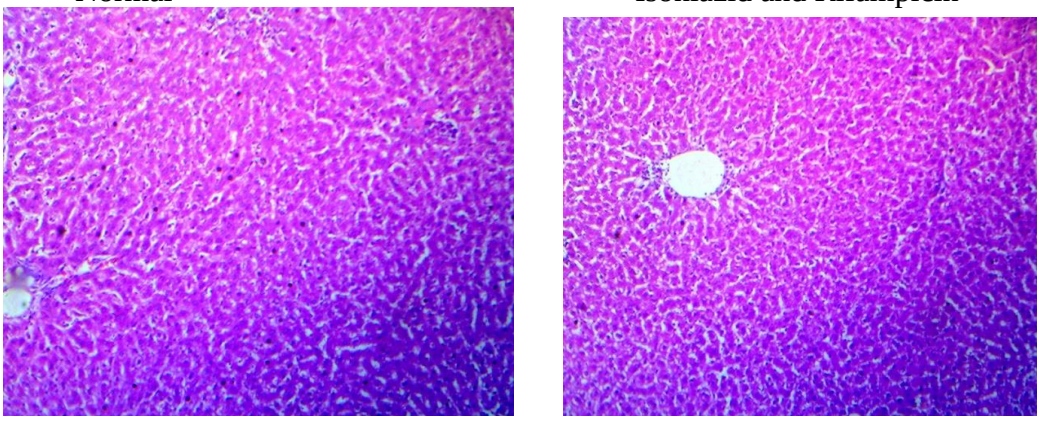


Figure:1 Effect of *M. dioica* in liver function on Isoniazid and Rifampicin induced Liver Toxicity

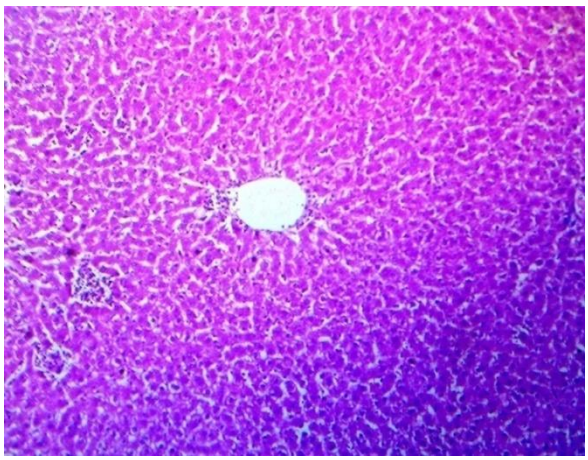
Histopathological Study of Liver:



Normal Isoniazid and Rifampicin



M. dioica 300 *M. dioica* 500



Silymarin

Photograph1 : Effect of *M. dioica* on histopathological of liver changes in albino rat.

Normal: The histological profile of the hepatic tissue of the placebo control animals showed a normal lobular architecture. Normal hepatocytes were arranged in single cell cords radiating away from a central vein .

Isoniazid and Rifampicin : animal treated with Isoniazid and Rifampicin showed disturbed liver architecture, exhibiting central lobular necrosis with tiny vacuoles, and fatty infiltrations .

***M. dioica* 300 and 500**: pretreated with *M. dioica* 300 and 500 extract respectively, retained normal hepatic tissue architecture, so received significant protection from Isoniazid and Rifampicin -induced hepatic damage, Group animals treated with Silymarin alone, show any significant hepatic tissue architectural changes.

DISCUSSION

the Antitubercular drugs induced hepatotoxicity is found to be mediated through oxidative stress and free radical damage to hepatocytes[15]. Liver enzymes ALP, AST, ALT, TP and TB increases in hepatic damage due to leakage of enzymes from damaged hepatocytes into vascular compartment. Liver damage leads to decrease in synthetic capability leading to fall in serum protein levels.[16] Administration of antitubercular drugs also resulted in degeneration, necrosis and fibrotic changes in rat liver. Concurrent administration of *M. dioica* along with antitubercular drugs significantly prevented the rise in level of Serum ALP, AST, ALT, TP and TB ,Administration of *M. dioica* reduced degeneration, necrosis and fibrosis and shows regeneration. *M. dioica* contains a variety of flavonoids,phenolic compounds and terterponoids, which act as antioxidants, scavenging and eliminating free radicals. The researchers found that consuming more *M. dioica* increased the level of polyphenolic and flavonoids antioxidants in the blood. In this study, the antioxidant and hepatoprotective effect of *M. dioica* against Antitubercular drugs induced hepatotoxicity in rats was shown by measuring antioxidant enzyme activities.

Conclusions

Anti-TB drugs are the most common group of drugs that are known to cause severe hepatotoxicity worldwide and overall, hepatotoxicity attributed to anti-TB drugs has been reported in 5–28% of people treated with anti-TB drugs. *M. dioica* contains a variety of flavonoids,phenolic compounds and terterponoids, which act as antioxidants, scavenging and eliminating free radicals. The researchers found that consuming more *M. dioica* have hepatoprocetive effect.

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CONFLICT OF INTEREST
We have no conflict of interest to declare.

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