INTRODUCTION

India has a rich culture of medicinal herbs and spices, which includes more than 2000 species and has a vast geographical area with high potential abilities for the Ayurvedic, Unani, and Siddha traditional medicines, but only very few have been studied chemically and pharmacologically for their potential medicinal value [1,2]. Annual incidence of drug-induced liver injury (DILI) has been estimated between 10 and 15/10,000 and 100,000 persons taking prescribed medicines [3]. Hence, natural products from medicinal plants need to be investigated by scientific methods for their hepatoprotective activity. The fruits of Mallotus philippensis (Mp) belonging to the family of Euphorbiaceae possess a wide variety of activities such as skin problem, bronchitis, antifungal, worm infestation (tapeworm) eye disease, cancer, diabetes, and diarrhea [4].

METHODS

Collection, identification, and authentication of the fruit

The fruits of Mp were purchased from local herbal dealer in Aligarh, India. It was identified by Dr. Athar Ali Khan, Taxonomist, Department of Botany, Aligarh. A voucher specimen bearing the number 433 was deposited in the herbarium of the Department of Botany, A.M.U, Aligarh, India.

Preparation of extract

The granulated fruits of Mallotus philippensis (100 g) were packed in a Soxhlet apparatus and subjected to continuous hot percolation for 8 h using 450 ml of methanol (95% v/v) as a solvent. The extract was concentrated to dryness under reduced pressure and controlled temperature and dried in a desiccator (yield 45.6 g, 15.20% w/w). The extract was suspended in 5% gum acacia and used for further experiments.

RESULTS

No toxicity profile was observed in rats after oral administration of the methanolic fruits extract at the dose of 2 g/kg body weight. The different dose of 300 mg/kg and 500 mg/kg administered with the extract of Mp. There was a significant (p<0.001) reduction in biochemical parameters with respect to control. Phytochemical screening of the fruits extract revealed the presence of tannins, alkaloids, flavonoids and saponins, and terpenoids.

CONCLUSION

It can be concluded that the hepatoprotective activity elucidated by Mallotus philippensis could be mainly due to the presences of high-value class of compound like the phenolic group as the major content in the plant.

Keywords: Mallotus philippensis, CCl₄, ATT, Biochemical parameters and histopathological studies.

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ABSTRACT

Objective: Mallotus philippensis (Mp) is locally known as kamala and is a large woody multipurpose medicinal tree belonging to the family of Euphorbiaceae. Mp possess a wide variety of activities such as skin problem, bronchitis, antifungal, worm infestation (tapeworm) eye disease, cancer, diabetes, and diarrhea. Hence, the present study was intended to evaluate methanolic fruits extract of Mp for hepatoprotective activities.

Methods: The hepatoprotective activity was studied by CCl₄ at the dose of 1 ml/kg of body weight in liquid olive oil in the ratio of 1:1 and ATT (isoniazid − 7.5 mg/kg, rifampicin − 10 mg/kg, and pyrazinamide − 35 mg/kg b.w.) induced models. Acute toxicity study and preliminary phytochemical screening were also studied to evaluate the toxicity.

RESULTS: No toxicity profile was observed in rats after oral administration of the methanolic fruits extract at the dose of 2 g/kg body weight. The different dose of 300 mg/kg and 500 mg/kg administered with the extract of Mp. There was a significant (p<0.001) reduction in biochemical parameters with respect to control. Phytochemical screening of the fruits extract revealed the presence of tannins, alkaloids, flavonoids and saponins, and terpenoids.

CONCLUSION: It can be concluded that the hepatoprotective activity elucidated by Mallotus philippensis could be mainly due to the presences of high-value class of compound like the phenolic group as the major content in the plant.

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The rats were divided into the seven groups of each containing six rats. 

- **Group I**: Control rats, which fed normal diet and water.
- **Group II**: Rats treated with CCl4 (1 ml/kg) once daily for 7 days.
- **Group III**: Rats treated with silymarin (50 mg/kg) + CCl4 (1 ml/kg) once daily for 7 days.
- **Group IV**: Rats treated with Mp (300 mg/kg, i.p.) + CCl4 (1 ml/kg) once daily for 7 days.
- **Group V**: Rats treated with Mp (500 mg/kg, i.p.) + ATT (1 ml/kg) once daily for 7 days.
- **Group VI**: Rats treated with Mp (300 mg/kg, i.p.) + ATT (1 ml/kg) once daily for 35 days.
- **Group VII**: Rats treated with Mp (500 mg/kg, i.p.) + ATT (1 ml/kg) once daily for 35 days.

**Statistical analysis**

Values were represented as mean±standard error of mean of three parallel data's.

**RESULTS**

**Preliminary phytochemical screening**

The preliminary phytochemical analysis of methanolic fractions of *M. philippensis* shows the presence of steroids, alkaloids, flavonoids, glycosides, saponins, tannin, and carbohydrate.

**DISCUSSION**

The present study reveals the hepatoprotective activity of *M. philippensis* against CCl4 and ATT-induced hepatic damage in rats. Liver damage is assessed by measuring the levels of serum transaminases such as AST, ALT, and ALP, which are released into the blood from damaged liver cells. They are also the indicators of liver damage (Shah and Gupte, 2004). The normalization of the elevated markers after administration of drugs is an indicator of their efficacy for regeneration of liver cells. It has been reported that serum transaminases return to normal level with the healing of liver parenchyma and hepatocytes [7]. We found that administration of CCl4 with or without fractions did increase the weight and volume of the liver relative to the body weight of the rats as compared to the normal control group, but the increase was

### Table 1: Acute toxicity study of methanolic extract of fruits of *Mallotus philippensis* based on OECD guidelines 423

| S. No. | Number of animals | Dose in mg/kg | Report |
|--------|-------------------|---------------|--------|
| 1      | 3                 | 5             | No death |
| 2      | 3                 | 50            | No death |
| 3      | 3                 | 300           | No death |
| 4      | 3                 | 2000          | No death |

### Table 2: Results of gross behavioral studies in rats on administration of *Mallotus philippensis* 2000 mg/kg/p.o

| Observation                                      | Effects                  | Up to 3 h | 3½ h | 4 h | 4½ h | 5 h | 5½ h | 6 h | 12 h | 24 h |
|--------------------------------------------------|--------------------------|-----------|------|-----|------|-----|------|-----|------|------|
| Respiration                                      | +                        | +         | +    | +   | +    | +   | +    | +   | +    | +    |
| Writing                                          | -                        | -         | -    | -   | -    | -   | -    | -   | -    | -    |
| Tremor                                          | -                        | -         | -    | -   | -    | -   | -    | -   | -    | -    |
| Convulsions                                      | -                        | -         | -    | -   | -    | -   | -    | -   | -    | -    |
| Hindlimb paralysis                               | -                        | -         | -    | -   | -    | -   | -    | -   | -    | -    |
| Sense of touch and sound                         | +                        | +         | +    | +   | +    | +   | +    | +   | +    | +    |
| Salivation                                       | +                        | +         | +    | +   | +    | +   | +    | +   | +    | +    |
| Diarrhea                                         | -                        | -         | -    | -   | -    | -   | -    | -   | -    | -    |
| Mortality                                        | -                        | -         | -    | -   | -    | -   | -    | -   | -    | -    |

*+: Normal, -: No effect

### Table 3: Effect of *M. philippensis* fractions on liver function test in CCl4-induced liver toxicity

| Groups              | AST (IU/ml) | ALT (IU/ml) | ALP (KAU/dl) | Bilirubin (mg/ml) |
|---------------------|-------------|-------------|--------------|-------------------|
| Group I             | 28.8±1.8    | 31.3±2.9    | 42.7±1.7     | 0.67±0.03         |
| Group II            | 180.8±1.9***| 166.8±6.0***| 80.7±4.3***  | 0.73±0.05         |
| Group III           | 55.2±3.3*** | 57.1±2.9*** | 52.3±2.2**   | 0.67±0.03         |
| Group IV            | 144.3±8.8** | 140.3±10.3  | 69.8±6.4     | 0.72±0.04         |
| Group V             | 111.0±12.3**| 123.3±10.7**| 56.0±6.4**   | 0.67±0.05         |
| Group VI            | 134.7±15.0**| 127.3±1.52  | 60.0±4.4*    | 0.70±0.05         |
| Group VII           | 88.0±7.4*** | 91.7±6.1*** | 56.7±5.5**   | 0.67±0.05         |

n=6; values were expressed mean±SEM; Group II was compared to Group I. Groups III to VII were compared to Group II. *p<0.01 versus CCl4 group; Significant; **p<0.001 versus CCl4 group; Highly significant data were analyzed by oneway ANOVA followed by Dunnett’s test

### Table 4: Effect of *M. philippensis* fractions on liver function test in ATT-induced liver toxicity

| Groups              | AST (IU/ml) | ALT (IU/ml) | ALP (KAU/dl) | Bilirubin (mg/ml) |
|---------------------|-------------|-------------|--------------|-------------------|
| Group I             | 28.5±0.98   | 31.4±2.34   | 43.3±1.2     | 0.73±0.04         |
| Group II            | 169.0±6.7***| 170.1±5.6***| 80.2±2.7***  | 3.47±0.49***      |
| Group III           | 56.4±3.3*** | 58.3±2.9*** | 51.4±2.2***  | 1.37±0.03***      |
| Group IV            | 124.0±9.5** | 119.7±6.7***| 67.3±4.8     | 2.82±0.14*        |
| Group V             | 106.2±10.5***| 106.5±9.6***| 62.5±3.6**   | 2.1±0.28**        |
| Group VI            | 122.2±9.6** | 130.5±8.9** | 58.3±2.9**   | 2.2±0.21**        |
| Group VII           | 104.2±11.2***| 99.2±10.3***| 56.2±1.5***  | 2.0±0.21**        |

n=6; values were expressed mean±SEM; Group II was compared to Group I. Groups III to VII were compared to Group II. *p<0.01 versus ATT group; Significant; **p<0.001 versus ATT group; Highly significant data were analyzed by oneway ANOVA followed by Dunnett’s test
not statistically significant. The weight and volume of the liver are increased in inflammation due to extravasations of fluid in extracellular compartment. The methanol fractions of \textit{M. philippensis} demonstrated significant hepatoprotective activity as shown by its ability to control the rise of serum transaminases. Although the effect was more at dose of 500 mg/kg for methanol fraction 123.3±10.7 IU/ml with 300 mg/kg dose, no significant hepatoprotective activity was observed for liver specific enzyme ALT. There was no significant rise in the bilirubin levels of negative control as compared to normal control group or any significant decrease in the levels of bilirubin in test groups as compared to negative control. The percentage hepatoprotection was good at 500 mg/kg b.w 32.1% for ALT. Our findings are in accordance with the observations [8]. Similarly, the methanol and ethyl acetate fractions of \textit{F. parviflora} showed significant hepatoprotective activity as shown by its ability of control the rise of serum transaminases. Although the effect was observed more at dose of 500 mg/kg of methanol fraction (124.2±9.9 IU/ml). There was no significant rise in the bilirubin levels of negative control as compared to normal control group or any significant decrease in the levels of bilirubin in test groups as compared to negative control. Methanol fraction of \textit{M. philippensis} demonstrated significant hepatoprotective activity in ATT-induced liver injury, as shown by its ability of limit the rise of serum transaminases. Highly significant decrease was observed in liver-specific ALT levels with the fraction at a dose of 500 mg/kg (106.5±9.6 IU/ml). There was an increase in the bilirubin levels in the negative control that was significantly prevented in all test groups as compared to negative control methanol 300 mg/kg 2.8±0.14 IU/ml and 500 mg/kg 2.1±0.26 IU/ml, \textit{M. philippensis} test groups the methanol fraction in the dose of 300 and 500 mg/kg b.w offered a protection of 36.3% and 45.9% for ALT. 

\textbf{CONCLUSION}

From the present work, we conclude that species of \textit{M. philippensis} are highly potential in biological activity. The preliminary screening of the samples revealed the presences of high-value class of compound like the phenolic group as the major content in the fruits.

\textbf{AUTHORS’ CONTRIBUTIONS}

Dr. Muthuramu T: Concept, design, collection of data, laboratory and animal investigations, interpretation of data, drafting a final report, and approval of the article to be published. Dr. Mujeeb Ur Rahman: Concept, design, collection of data, laboratory and animal investigations, interpretation of data, revising of article, and approval of the article to be published. Mr. Abdurohman Mengesha Yessu: Laboratory investigations, interpretation of data, and revising of article.

\textbf{CONFLICTS OF INTEREST}

All authors report no conflicts of interest regarding this manuscript.

\textbf{AUTHORS’ FUNDING}

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