

Hepato- and Nephroprotective Effects of Ethanolic Extract of Seeds of *Macrotyloma uniflorum* on Paracetamol-induced Hepato- and Nephrotoxicity in Rats

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ABSTRACT

Objectives: The present study is planned to investigate the hepato- and nephroprotective effects of ethanolic extract of seeds of *Macrotyloma uniflorum* (EEMU) on paracetamol (PCM)-induced hepato- and nephrotoxicity in Sprague-Dawley rats. **Materials and Methods:** Hepato- and nephroprotective effects of EEMU were studied against PCM-induced hepatotoxicity and nephrotoxicity in rats. The rats were divided into seven groups viz., control, EEMU 400 mg/kg, PCM, PCM + Vitamin C 200 mg/kg, PCM + EEMU 100 mg/kg, PCM + EEMU 200 mg/kg and PCM + EEMU 400 mg/kg. The animals in groups III to VII were administered with PCM (750 mg/kg) once daily for seven days to induce hepato- and nephrotoxicity. EEMU and Vitamin C were administered once daily per orally for 7 days. On day 8, the animals were anaesthetized and blood samples were collected and used for estimation of biochemical parameters. Later the animals were sacrificed and liver and kidney were collected from all the animals for antioxidant assay and histopathological analysis. **Results:** The animals administered with EEMU (400 mg/kg) didn't show any significant changes in the biochemical parameters and histological features. The animals administered with PCM showed a significant increase in the levels of AST, ALT, ALP, bilirubin and urea compared with that of the control group. Whereas the animals administered with Vitamin C and EEMU (at 200 and 400 mg/kg) prevented PCM-induced changes in biochemical parameters and histological features. In the antioxidant assay, the animals administered with EEMU, PCM + Vitamin C and PCM + EEMU 400 mg/kg, didn't show any significant changes in the levels of reduced glutathione when compared with that of the control group. **Conclusion:** EEMU exhibited a significant hepatoprotective effect at the dose levels of 100, 200 and 400 mg/kg against PCM-induced hepatotoxicity in rats. EEMU did not show any significant nephroprotective effect at the same dose levels on PCM-induced nephrotoxicity in rats.

Keywords: Medical herbs, Nutrition, Hepatic injury, Renal failure, Toxicity.

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INTRODUCTION

Chronic exposure to chemical and long-time use of drugs for therapeutic purposes may cause systemic organ dysfunctions. The liver and kidney are major organs involved in drug metabolism and excretion. Any damage to these organs may result in the accumulation of the drug or its metabolites and causes toxicity.¹ The liver and kidney are the organs highly prone to get affected by chemicals and toxins during the elimination process.

Hepatotoxicity/liver injury/ hepatic injury are caused by more than a thousand chemical molecules and drugs and drug-induced liver injury is relatively common for acute liver disease.² The hepatic injury can be classified into hepatocellular (elevated aminotransferases out of proportion to alkaline phosphatase), cholestatic (elevated alkaline phosphatase + Gamma-glutamyl transferase [GGT] + bilirubin out of proportion to Aspartate transaminase



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[AST] and Alanine transaminase [ALT]) and mixed, and elevated levels of alanine aminotransferase and Alkaline phosphatase (ALP) are key indicators for hepatic injury. The elevated levels of aminotransferase and ALP were found in approx. 8% of the general population, with up to 30% elevation resolving after 3 weeks.³ Risk factors of hepatotoxicity include age (elderly population has more probabilities of getting hepatic damage), gender (female gender are the most susceptible for toxicity of drugs), alcohol consumption, concomitant administration of drugs, previous or underlying hepatic diseases and genetic disorders (polymorphism in cytochrome p450 enzymes).⁴

Nephrotoxicity is a renal dysfunction caused by drugs, chemicals, industrial, or environmental toxic agents.⁵ Cisplatin, aminoglycosides, mercury, arsenic, lead and cocaine are known for their nephrotoxic effect and also some of the pathological events such as hypertension, obesity, sepsis, liver failure and diabetes are causing kidney damage.⁶ The renal function alteration is assessed by the glomerular filtration rate, blood urea nitrogen, serum creatinine, or urine output.⁶

The prevalence of liver and renal failure is increasing every year which is mainly driven by population ageing, the use of more drugs as well as other pathological conditions including hypertension and obesity. Due to increases in disease burden, an increased number of adverse events (AEs) and therapeutic failure, the search for drugs from newer sources/ alternative sources is important. The herbs are one of the easily available sources of drugs. Many drugs are discovered from natural sources including herbs and they have been widely used as a pharmacotherapeutic agent to treat many diseases and AEs. According to the World health organization (WHO), there are more than 80% of the population especially those in developing and developed countries have relied on traditional plant-based medicines for their primary healthcare needs.⁷ *Macrotyloma uniflorum* is one of the promising herbs known for its nutritional benefits and its pharmacological activities are not completely explored.

M. uniflorum (Family: Fabaceae) is commonly known as horse gram/ Madras gram and native to tropical southern Asia. *M. uniflorum* is a potential grain legume having excellent nutritional values and remedial properties. Food legumes are the second most common crop category after cereals, which have long been a vital ingredient of a well-balanced human diet.⁸ Phytoconstituents of *M. uniflorum* includes anthocyanins (prevent diabetes), flavonoids (prevention of heart disease and stroke), phenolic acid (act as antioxidants, anti-inflammatory agent), haemagglutinins (helps in blood clotting),

tannins (reduce blood pressure and serum lipid level) and phytic acid (acts as an antioxidant), and they are known for their pharmacological activity.⁹ The seeds of *M. uniflorum* have antioxidant, antihyperlipidemic, antimicrobial, diuretic, antiurolithiatic activities and are used for the management of coronary heart diseases.^{10,11} The hepato- and nephroprotective effects of ethanolic extract of seeds of *M. uniflorum* are not clear. Hence the present study is planned to investigate the hepato- and nephroprotective effects of ethanolic extract of seeds of *M. uniflorum* on paracetamol (PCM)-induced hepato- and nephrotoxicity in Sprague-Dawley (SD) rats.

MATERIALS AND METHODS

Collection of seeds of *M. uniflorum*

The seeds of *M. uniflorum* were purchased in a local market in Sungai Petani, Malaysia.

Extraction

The seeds of *M. uniflorum* were powdered and extracted with ethanol by using a Soxhlet extractor. The powdered seeds of *M. uniflorum* was packed in a Soxhlet extractor and extracted with 95% ethanol at $75 \pm 5^\circ\text{C}$. The extraction was carried out for 72 hr or for 3-4 cycles. The ethanolic extract of seeds of *M. uniflorum* (EEMU) was filtered, and the filtrate was concentrated into a dry mass by using simple distillation under reduced pressure using rotary evaporator (Rotavapor® R-210, BUCHI Corporation). The ethanol extract of *M. uniflorum* was stored in the fridge until use.

Hepato- and nephroprotective effects of EEMU

Healthy, adult, female SD rats, weighing 180 ± 15 g, were obtained from Central Animal house, AIMST University, Malaysia. The animals were housed in large, spacious polyacrylic cages at an ambient room temperature with a 12-hr-light/12-hr-dark cycle. The animals were fed with water and normal rats pellet diet *ad libitum*. The study was carried out with prior ethical approval (AUAEC/FOP/2020/08 and AUAEC/FOP/2020/09) from AIMST University Human and Animal Ethics Committee (AUHAEC), and the study was conducted according to the Animal Research Review Panel guidelines.

Hepato- and nephroprotective effects of EEMU were studied against PCM-induced hepato- and nephrotoxicity. The animals were divided into seven groups, each of six animals as follows.

Group I: Control

Group II: EEMU 400 mg/kg

Group III: PCM 750 mg/kg

Group IV: PCM 750 mg/kg + Vitamin C 200 mg/kg

Group V: PCM 750 mg/kg + EEMU 100 mg/kg

Group VI: PCM 750 mg/kg + EEMU 200 mg/kg

Group VII: PCM 750 mg/kg + EEMU 400 mg/kg

Hepato- and nephrotoxicity were induced by administering PCM (750 mg/kg) per oral.¹² PCM, EEMU and Vitamin C were suspended in 0.5% w/v Carboxymethyl cellulose (CMC) solution. The control group was administered with CMC. The animals in groups II and III were administered with EEMU 400 mg/kg and PCM 750 mg/kg, respectively for seven consecutive days. The animals in groups III to VII were administered with PCM + Vitamin C 200 mg/kg, PCM + EEMU 100 mg/kg, PCM + EEMU 200 mg/kg and PCM + EEMU 400 mg/kg, respectively for seven consecutive days. On day 8, the animals were anaesthetized and the blood sample was collected from retro-orbital sinus and serum was separated. The serum samples were used for the estimation of the biochemical parameters. Later, the animals were sacrificed and liver and kidney samples were collected from all the animals for antioxidant assay and histopathological analysis.¹³

Body weight analysis

The body weight of the experimental animals was monitored at regular intervals.

Biochemical analysis

At the end of the study, the blood samples were withdrawn from all the experimental animals through retro-orbital plexus puncture in plain glass tubes for biochemical analysis under diethyl ether anaesthesia. The blood samples were centrifuged at 3000 rpm for 20 min, and serum was separated and stored at -20°C until further biochemical analysis. The serum sample was used for estimation of biochemical markers such as glucose, AST, alanine aminotransferase (ALT), ALP, total bilirubin, creatinine, and urea using a biochemical analyzer (Reflotron Plus System, Hoffmann-La Roche, USA).

Organ weight analysis

At the end of the experiment, the experimental animals were sacrificed under mild anaesthesia followed by cervical dislocation. The animals were dissected and liver and kidney were harvested. The absolute organ weight of the liver and kidney were measured and relative organ weights were calculated. Kidney/body weight ratio (K/BW ratio) calculated mathematically.¹⁴

$$\frac{\text{K}}{\text{BW}} \text{ ratio} \left(\frac{\text{g}}{\text{kg}} \right) = \frac{\text{Absolute weight of kidney}}{\text{Weight of whole animal}}$$

Antioxidant Assay

Reduced Glutathione (GSH) estimation: Liver homogenate was added with an equal volume of 20% trichloroacetic acid contacting 1 mM ethylenediaminetetraacetic acid (EDTA) to precipitate the tissue proteins and allowed to stand for 5 min. Later, the reaction mixture was centrifuged at 2000 RPM for 10 min. In a 200 μL of supernatant, 1.8 mL of Ellman's reagent was added and absorbance was measured spectrophotometrically (Model UV 1800, Shimadzu, Japan) at 412 nm against blank. Absorbance values were compared with a standard curve generated from known GSH. The results of GSH concentrations were expressed as μg of GSH per mg of protein.¹⁵

Histopathological analysis

The liver and kidney samples were collected, rinsed in normal saline, and sectioned into small pieces. The sectioned tissue was then fixed in 10% formalin, dehydrated stepwise with increasing concentration of ethanol solution (50% to 100%), and embedded in paraffin. Using a microtome, tissue sections of 4/5- μm thickness were produced, fixed overnight on the slide, subsequently stained with hematoxylin and eosin (H&E). Later, the slides were examined under light microscope.

Data Analysis

Data were expressed as mean \pm standard error of the mean (SEM) and analyzed using one-way Analysis of variance (ANOVA) followed by Turkey's multiple comparison *post-hoc* test. A $p < 0.05$ was considered statistically significant.

RESULTS

Effect on body weight analysis

The rats administered with PCM showed decreases in body weight when compared with that of the control group, but the results were not significant. The rats administered with PCM + Vitamin C and PCM + EEMU at the dose of 100, 200 and 400 mg/kg did not show any significant changes in body weight when compared with that of the control group. The animals administered with EEMU 400 mg/kg alone also did not show any significant changes in body weight when compared with that of the control group. The effect of the PCM, EEMU 400 mg/kg, PCM + Vitamin C and PCM + EEMU on body weight was presented in Figure 1.

Effect of EEMU on biochemical parameters

The animals administered with PCM + Vitamin C and PCM + EEMU (100, 200 and 400 mg/kg) did not

show any significant changes in the glucose levels when compared with that of the control group. The animals administered with and PCM + EEMU (400mg/kg) showed an increase in blood glucose level compared with that of the PCM administered group, but the results were not significant (Table 1).

The animals administered with PCM showed a significant increase in the AST, ALT, ALP total bilirubin and urea levels compared with that of the control group. The animals administered with PCM + Vitamin C and PCM + EEMU (at 200 and 400 mg/kg) showed significant increases in the level of total bilirubin compared with that of PCM administered group. The animals administered with PCM + EEMU (100 mg/kg) showed significant decreases in the level of AST and total bilirubin compared with that of control group. The effect of EEMU on biochemical parameters was presented in Table 1.

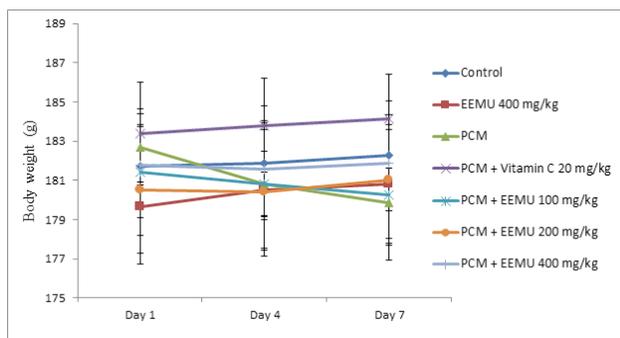


Figure 1: Effect of EEMU and PCM + EEMU on body weight.

All the values are mean ± SEM (n=6). PCM: Paracetamol; EEMU: Ethanolic extract of seeds of *M. uniflorum*.

Effect of EEMU on organ weight

The animals administered with PCM did not show any significant changes in absolute and relative organ weights of liver and kidney when compared with that of control group. In K/BW ratio analysis, no significant changes were observed (Table 2).

Effect of EEMU on oxidative stress parameter

In the antioxidant assay, the PCM and PCM + EEMU (100 and 200 mg/kg) administered animals showed significant decreases in the levels of GSH when compared with that of the control group. The animals administered with EEMU, PCM + Vitamin C and PCM + EEMU 400 mg/kg, didn't show any significant changes in the levels of GSH when compared with that of the control group (Figure 2).

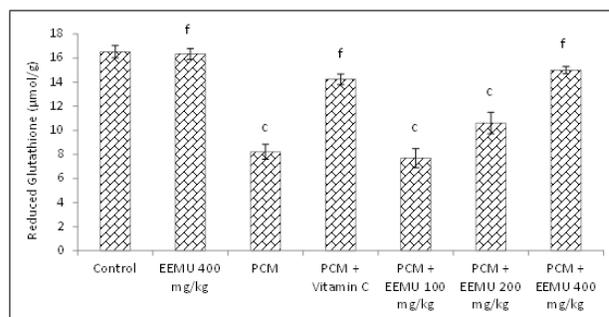


Figure 2: Effect of EEMU and PCM + EEMU on reduced glutathione.

All the values are mean ± SEM (n = 6). *P<0.001 compare with that of control; #P<0.001 compare with that of PCM (One-way ANOVA followed by Turkey's *post hoc* test).

PCM: Paracetamol; EEMU: Ethanolic extract of seeds of *M. uniflorum*.

Table 1: Effect of EEMU on biochemical parameter.

Treatment Groups	Glucose (mg/dL)	AST (U/L)	ALT (U/L)	ALP (U/L)	T. Bilirubin (mg/dL)	Urea (mg/dL)	Creatinine (mg/dL)
Control	88.08 ± 5.10	215.00 ± 12.68	102.92 ± 10.36	121.67 ± 8.15	0.97 ± 0.09	29.22 ± 2.75	0.50 ± 0.02
EEMU 400 mg/kg	84.97 ± 7.40	220.83 ± 11.84###	125.00 ± 12.14	125.17 ± 6.66##	0.98 ± 0.05###	30.67 ± 2.03#	0.51 ± 0.01
PCM	83.12 ± 9.73	365.50 ± 11.59***	153.37 ± 14.83*	172.17 ± 7.18***	1.90 ± 0.15***	45.32 ± 3.61*	0.89 ± 0.14
PCM + Vitamin C 20 mg/kg	86.92 ± 3.13	224.00 ± 10.00###	91.08 ± 7.96##	151.67 ± 9.34	1.19 ± 0.11###	35.50 ± 2.77	0.66 ± 0.12
PCM + EEMU 100 mg/kg	90.88 ± 4.63	254.33 ± 22.16###	139.20 ± 14.88	142.33 ± 2.91	1.43 ± 0.08*#	41.08 ± 3.73	0.84 ± 0.15
PCM + EEMU 200 mg/kg	86.88 ± 6.26	225.33 ± 13.67###	137.83 ± 9.41	135.83 ± 7.33#	1.05 ± 0.09###	40.92 ± 4.20	0.56 ± 0.03
PCM + EEMU 400 mg/kg	95.22 ± 6.03	211.50 ± 10.81###	124.67 ± 8.80	131.50 ± 7.66##	1.04 ± 0.07###	31.67 ± 2.45	0.52 ± 0.01

All the values are mean ± SEM (n=6). ***P<0.001 compare with that of control (One-way ANOVA followed by Tukey's *post hoc* test). ** P<0.01; ### P<0.001 compare with that of PCM 750 mg/kg group (One-way ANOVA followed by Tukey's *post hoc* test).

PCM: Paracetamol; EEMU: Ethanolic extract of seeds of *M. uniflorum*; T. Bilirubin: Total bilirubin.

Table 2: Effect of EEMU on relative and absolute organ weight of liver.

Treatment Groups	Absolute organ weight of		Relative organ weight of		K/BW ratio (g/kg)
	Liver (g)	Kidney (g)	Liver (g)	Kidney (g)	
Control	5.93 ± 0.17	0.87 ± 0.02	3.25 ± 0.13	0.48 ± 0.02	4.77 ± 0.18
EEMU 400 mg/kg	5.80 ± 0.13	0.89 ± 0.02	3.18 ± 0.04	0.49 ± 0.01	4.91 ± 0.07
PCM	5.85 ± 0.13	0.88 ± 0.02	3.30 ± 0.05	0.50 ± 0.01	4.99 ± 0.09
PCM + Vitamin C 20 mg/kg	6.20 ± 0.12	0.88 ± 0.01	3.35 ± 0.05	0.47 ± 0.01	4.75 ± 0.11
PCM + EEMU 100 mg/kg	5.87 ± 0.16	0.85 ± 0.01	3.25 ± 0.06	0.47 ± 0.01	4.71 ± 0.10
PCM + EEMU 200 mg/kg	5.88 ± 0.07	0.89 ± 0.01	3.24 ± 0.07	0.49 ± 0.01	4.89 ± 0.10
PCM + EEMU 400 mg/kg	5.77 ± 0.10	0.89 ± 0.02	3.16 ± 0.08	0.49 ± 0.02	4.90 ± 0.19

All the values are mean ± SEM (n=6). PCM: Paracetamol; EEMU: Ethanolic extract of seeds of *M. uniflorum*.

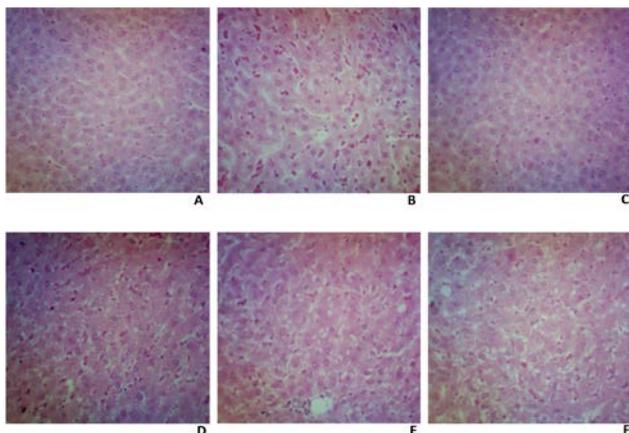


Figure 3: Photomicrograph of a section of liver of animals administered with EEMU/PCM/PCM + Vitamin C or EEMU (H&E, x400).

(A) EEMU 400 mg/kg administered animal showing the normal configuration of liver lobules. (B) PCM 750 mg/kg administered animal showing mild lymphocytic infiltration with focal spill over into the liver parenchyma. (C) PCM + EEMU 100 mg/kg administered animal showing mild degeneration of hepatocytes. (D) PCM + Vitamin C 200 mg/kg administered animal showing normal liver parenchyma cells. (E) PCM + EEMU 200 mg/kg administered animal showing normal configuration of liver lobules with mild degeneration of hepatocytes. (F) PCM + EEMU 400 mg/kg administered animal showing the normal liver parenchyma cells. PCM: Paracetamol; EEMU: Ethanolic extract of seeds of *M. uniflorum*.

Effect of EEMU on histology of liver and kidney

The liver of the PCM administered animals showed mild lymphocytic infiltration with focal spill over into the liver parenchyma. The liver of the control animals and the animals administered with EEMU 400 mg/kg, PCM + Vitamin C 200 mg/kg and PCM + EEMU 400 mg/kg showed normal liver parenchyma cells, no tract of inflammation, no evidence of hydropic degeneration of fatty change, no inflammation and no neoplastic process as well (Figure 3).

The kidney of control and PCM/ PCM + Vitamin C or PCM + EEMU showed normal renal cortex and medulla. The cortex shows normal glomeruli and the medulla shows normal renal tubules. No other significant pathology was observed.

DISCUSSION

In the present study, the hepato- and nephroprotective effect of EEMU was studied against the PCM-induced hepato- and nephrotoxicity in the rats. EEMU exhibited a significant hepatoprotective effect at the dose levels of 100, 200 and 400 mg/kg and did not show any significant nephroprotective effect at the same dose levels. But the EEMU reduces the PCM-induced elevated levels of urea and creatinine.

PCM is a widely used antipyretic and analgesic agent and produces acute liver damage when accidental overdoses are consumed. The liver hepatocytes metabolize PCM *via* microsomal Cytochrome P450 (CYP450) into non-toxic byproducts. In PCM overdose, PCM is converted by CYP450 into its toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI) subsequently excreted after glutathione conjugation. The covalent binding of NAPQI to the sulphhydryl group of protein results in cell necrosis and decreases in the levels of glutathione in the liver cause hepatotoxicity.^{16,17} Glutathione depletion in the mitochondria and cell cytosol results in decreased excretion of reactive oxygen species and peroxynitrite. Decreased levels of glutathione with an increased formation of free radicals stimulate lipid peroxidation. Malondialdehyde levels increase as a result of lipid peroxidation, and this reflects tissue damage.

Further, PCM toxicity causes acute tubular necrosis in the kidney, which is one of the main reasons for acute renal failure.¹⁸

In the present study, EEMU was administered at the dose level of 400 mg/kg and observed its effect on biochemical parameters and histology of liver and kidney. EEMU alone did not cause any alteration in the biochemical parameters, histology of organs such as liver and kidney and any toxic effects. Priyanga *et al.*, studied the acute toxic effect of ethanolic leaf extract of *M. uniflorum* at the dose levels of 50, 250, 500, 1000 and 2000 mg/kg and did not observe any significant undesirable effect of ethanolic leaf extract of *M. uniflorum* in female albino rats.¹⁹ Wijenayake *et al.*, reported an increase of Serum glutamic oxaloacetic transaminase (SGOT) with chronic administration of aqueous seed extract of *M. uniflorum* in pregnant female rats. In the same study, the chronic administration of aqueous seed extract of *M. uniflorum* did not induce overt signs of toxicity and renal toxicity at the dose level of 6.17 g/kg.²⁰ Ethanolic and water extracts of *M. uniflorum* reduced high-fat diet-induced alterations in SGOT and Serum glutamic pyruvic transaminase (SGPT) levels. And also reduces high-fat diet-induced hypercholesterolemia in rats.²¹

EEMU also prevented oxidative stress induced by the PCM. Oxidative stress is an important mechanism for the development of PCM toxicity. PCM overdose causes a reduction in glutathione peroxidase activity. At therapeutic doses, PCM is metabolized by conjugation reactions with glucuronate and sulfate. NAPQI, a metabolite of PCM is detoxified by either spontaneous or enzyme-catalyzed reaction with glutathione resulting in an acetaminophen-glutathione conjugate and 3-(glutathion-S-yl) acetaminophen. In PCM overdose, the glucuronidation and sulfation pathways are saturated, PCM is being oxidized to NAPQI in much higher extent and glutathione stores become depleted. The depletion of glutathione causes oxidative stress.²² The antioxidant effect of dietary phenolic extracts of seeds of *M. uniflorum* is already reported elsewhere.²³ The antioxidant effect of *M. uniflorum* is may be due to the presence of phenolic compounds and flavonoids. In the previous study, EEMU exhibited the presence of total phenolic content of 63.48 mg gallic acid equivalent/g and total flavonoid content of 15.44 mg rutin equivalent /g.²⁴ The antioxidants are playing a major role in preventing the free radicals-induced pathological changes and cardiovascular and metabolic diseases.

M. uniflorum is an excellent source of carbohydrates, protein, dietary fibre, and micronutrients. However, its flour usage has been limited due to the presence

of certain anti-nutrient effects from phytate, tannins and trypsin inhibitors.²⁵ Further studies are required to understand the mechanism of action of EEMU on the prevision of oxidative stress induced by PCM.

CONCLUSION

Ethanolic extract of seeds of *M. uniflorum* exhibited significant hepatoprotective effect at the dose levels of 100, 200 and 400 mg/kg against paracetamol-induced hepatotoxicity in rats by reducing paracetamol-induced elevated levels of liver enzyme, oxidative stress and by preventing histological changes in the liver. In the present study, ethanolic extract of seeds of *M. uniflorum* did not show any significant nephroprotective effect at the same dose levels on paracetamol-induced nephrotoxicity in rats.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

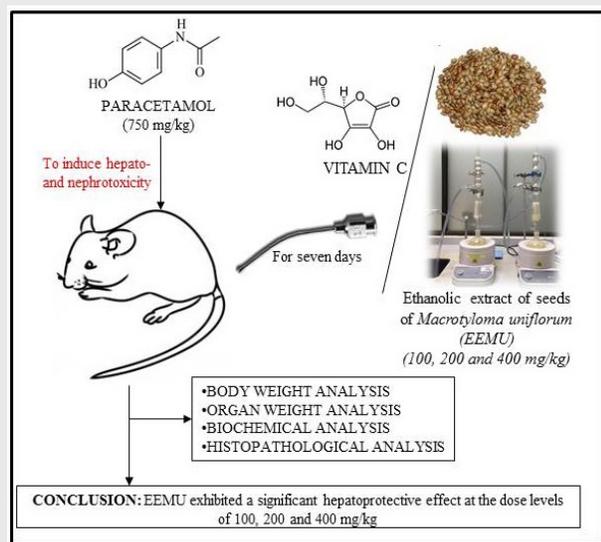
AEs: Adverse events; **ALT/ SGPT:** Alanine aminotransferase/ Serum glutamic pyruvic transaminase; **ANOVA:** Analysis of variance; **AST/ SGOT:** Aspartate transaminase/ Serum glutamic oxaloacetic transaminase; **CMC:** Carboxymethyl cellulose; **CYP450:** Cytochrome P450; **EEMU:** Ethanolic extract of seeds of *M. uniflorum*; **g:** Gram; **GGT:** Gamma-glutamyl transferase; **GSH:** Reduced Glutathione; **K/Bw ratio:** Kidney/body weight ratio; **Kg:** kilogram; **Mg:** milligram; **min:** Minutes; **NAPQI:** N-acetyl-p-benzoquinone imine; **PCM:** Paracetamol; **SD:** Sprague-Dawley; **SEM:** standard error of the mean; **T. Bilirubin:** Total bilirubin; **WHO:** World health organization.

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PICTORIAL ABSTRACT



SUMMARY

Macrotyloma uniflorum is a legume native to tropical southern Asia having excellent nutritional values and remedial properties. In the present study, ethanolic extract of seeds of *M. uniflorum* exhibited a significant hepatoprotective effect against paracetamol-induced hepatotoxicity.

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