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Hepatoprotective activity of methanolic extract of *Malva parviflora* against paracetamol-induced hepatotoxicity in mice

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Abstract

Malva parviflora (cheeseweed) is traditionally used as hepatoprotective. The current study was conducted to determine its hepatoprotective activity of aqueous methanolic extract of whole plant. Two doses of plant (250 and 500 mg/kg) were administered in paracetamol intoxicated mice and results were compared with silymarin. Observational parameters were ALT, AST, ALP and total bilirubin. The results showed that the extract of *M. parviflora* produced significant ($p<0.001$) reduction in liver enzymes and total bilirubin. Results were supported by histopathological investigation, phyto-chemical screening and detection of hepatoprotective constituents (kaempferol and apigenin) by HPLC. So, the current study showed that aqueous methanolic extract of *M. parviflora* possesses hepatoprotective activity.

Introduction

Almost 80% people all over the word depend upon traditional medicines to cure their major and minor ailments. Plants are always been an inspirational source for many researcher in medicine. The problem of resistance and tolerance to the existing drugs has created a decreased efficacy of these drugs in use. This problem has been tried to be overcome by increasing the drug delivery to the target site by the use of polymers (Khalid et al., 2009; Hussain et al., 2011) or through nanotechnology (Naz et al., 2012; Ehsan et al., 2012), synthesis of new drugs, either by the use of proteomics (Qadir, 2011), or synthesis from lactic acid bacteria (Masood et al., 2011), or marine microorganisms (Javed et al., 2011). However, now a days, the trend is also being changed to the use of herbal products or extracts to control the diseases. The plant kingdom still holds many species containing substances of medicinal value which have yet to be discovered: Large numbers of plants are constantly being screened for their possible pharmacological value particularly for their anti-inflammatory (Qadir, 2009), hypotensive (Qadir, 2010), hypoglycemic, amoebicidal, anti-fertility, cytotoxic, antibiotic (Amin et al., 2012), spasmolytic, bronchodilator (Bashir et al., 2013), antioxidant (Janbaz et al., 2012) and hepatoprotective properties (Ahmad et al., 2012). Many plants have been identified as hepatoprotective like *Trianthema decandra* (Balamurugan and Muthusamy, 2008), *Cocculus hirsutus* (Thakare et al., 2009), *Carica papaya* (Sadeque and Begum, 2010), *Carissa spinarum* (Hegde and Joshi, 2010), *Convolvulus arvensis* (Ali et al., 2013), *Dodonaea viscosa* (Khan et al., 2013), *Trichodesma sedgwickianum* (Saboo et al., 2013), *Oflpomoea staphylina* (Bag and Mumtaz, 2013), Khamira Gaozaban Ambri Jadwar Ood Saleeb Wala (Akhtar et al., 2013), *Cestrum nocturnum* (Qadir et al., 2014a), *Viola odorata* (Qadir et al., 2014b), *Chenopodium murale* (Saleem et al., 2014) and *Morus nigra* (Mallhi et al., 2014).

Malva parviflora L. (family Malvaceae) is herb native to Africa, Asia and Europe. It common name is cheeseweed and locally known as Sonchal. Pharmacologically, it has been reported to be antibacterial (Shale et al.,

2005), antidiabetic (Gutierrez, 2012), antifungal (Wang et al., 2001). Traditionally *M. parviflora* is used for the treatment of inflammation, pain and liver injuries (Afolayan et al., 2010). The plant contains phenolic and flavonoid compounds (Farhan et al., 2012). Traditional importance and phytochemical profile of the plant appeal its use in liver injury. Therefore, the current study was conducted to scientifically determine hepatoprotective potential of *M. parviflora.*

Materials and Methods

Plant material

The plant was collected from Faisalabad and identified by Dr. Mansoor Hameed, Department of Botany, University of Agriculture, Faisalabad. The voucher specimen was deposited in the herbarium of College of Pharmacy, for future reference. Powdered plant was soaked in aqueous methanol (70:30). After 7-10 days solution was filtered and the filtrate was evaporated with the help of rotary evaporator to get the extract.

Estimation of hepatoprotective activity

Swiss albino mice of both sexes weighing 22-35 g were kept under standard laboratory conditions (25 ± 2°C with dark and light cycle of 12/12 hours). These were fed with standardized pellet diet and water *ad libitum*. All the animals were divided into five groups having 5 animals each. Group I was Control, receiving distilled water only. Group II served as paracetamol control, receiving paracetamol p.o. 250 mg/kg dissolved in water for 7 days. Group III, silymarin control in which silymarin was given as reference drug 50 mg/kg daily for 7 days and paracetamol was administered 3 hours after silymarin. Group IV received aqueous methanolic (70:30) extract of *M. parviflora* at doses 250 mg/kg p.o. for 7 days and received paracetamol 250 mg/kg 3 hours after extract dose. Group V received aqueous methanolic extract of *M. parviflora* at doses 500 mg/kg p.o. for 7 days and received paracetamol 250 mg/kg 3 hours after extract dose. At the 8th day, blood samples were collected to estimate ALT, AST, ALP and total bilirubin; and livers from animals were separated for histopathological examination (Ali et al., 2013).

Phytochemical screening

The phytochemical screening of various active compounds in the extract was accomplished by methods used by Farhan et al., 2012.

HPLC analysis

For qualitative separation of compounds, SYKAM HPLC system was used equipped with S-1122 Solvent Delivery System, S-3210 UV/VIS Detector, S-5111 Injector Valve Bracket, pump (1500 series), Column oven and pre-packed C-18 column (250 × 4.5 mm, 5 um particle size). Data was analyzed by using Sample-Clarity Light software. Acetonitrile-water (1:1) with few drops of acetic acid (1%) was used as mobile phase with flow rate of 1 mL/min; and compounds were detected at 254 nm (Saddique et al., 2011).

Statistical analysis

All the data were subjected to one-way ANOVA by SPSS for statistical analysis. Results were represented as mean ± SE.

Results

Effect of aqueous methanolic extract of *M. parviflora* (AMMP) on liver enzymes and total bilirubin is given in Table I. Aqueous methanolic extract of *M. parviflora* with 250 mg/kg reduces elevated ALT by 53% ($p<0.001$)), AST by 53% ($p<0.01$), ALP by 27% ($p<0.001$) and TBR by 53% ($p<0.001$) as compared to paracetamol control. At 500 mg/kg dose, elevated ALT reduced by 55% ($p<0.001$), AST by 57% ($p<0.001$), ALP by 30% ($p<0.001$) and TBR by 53% ($p<0.001$) as compared to paracetamol control. There is insignificant ($p>0.05$) difference between two doses with exception of AST whose reduction is higher with 500 mg/kg ($p<0.001$) as compared to 250 mg/kg ($p<0.01$). These results are also comparable to that of silymarin ($p<0.001$, as compared to paracetamol control). Histopathological examination of liver sections also supported biochemical investigation as shown in Figure 1. Results of the phytochemical screening are given in Table II.

Table I

Effect of aqueous methanolic extract of *Malva parviflora* on liver enzymes and total bilirubin

Treatment groups	ALT (IU/L)	AST (IU/L)	ALP (IU/L)	TBR (g/dL)
Normal (D/W)	32.8 ± 02.0	36.5 ± 03.6	216.2 ± 09.9	0.8 ± 0.0
Paracetamol Control (250 mg/kg)	112.1 ± 4.1	101.2 ± 09.1	413.4 ± 21.7	2.0 ± 0.2
Silymarin (50 mg/kg) + Paracetamol	41.6 ± 03.0^b	39.8 ± 07.8^b	266.4 ± 32.6^a	0.9 ± 0.1^a
Extract (250 mg/kg) + Paracetamol	52.6 ± 04.4^b	47.6 ± 04.9^a	300.6 ± 10.4^a	0.9 ± 0.0^a
Extract (500 mg/kg) + Paracetamol	51.0 ± 05.6^b	43.8 ± 03.2^b	287.6 ± 09.8^a	0.9 ± 0.0^a

$^a p<0.01$, $^b p<0.001$

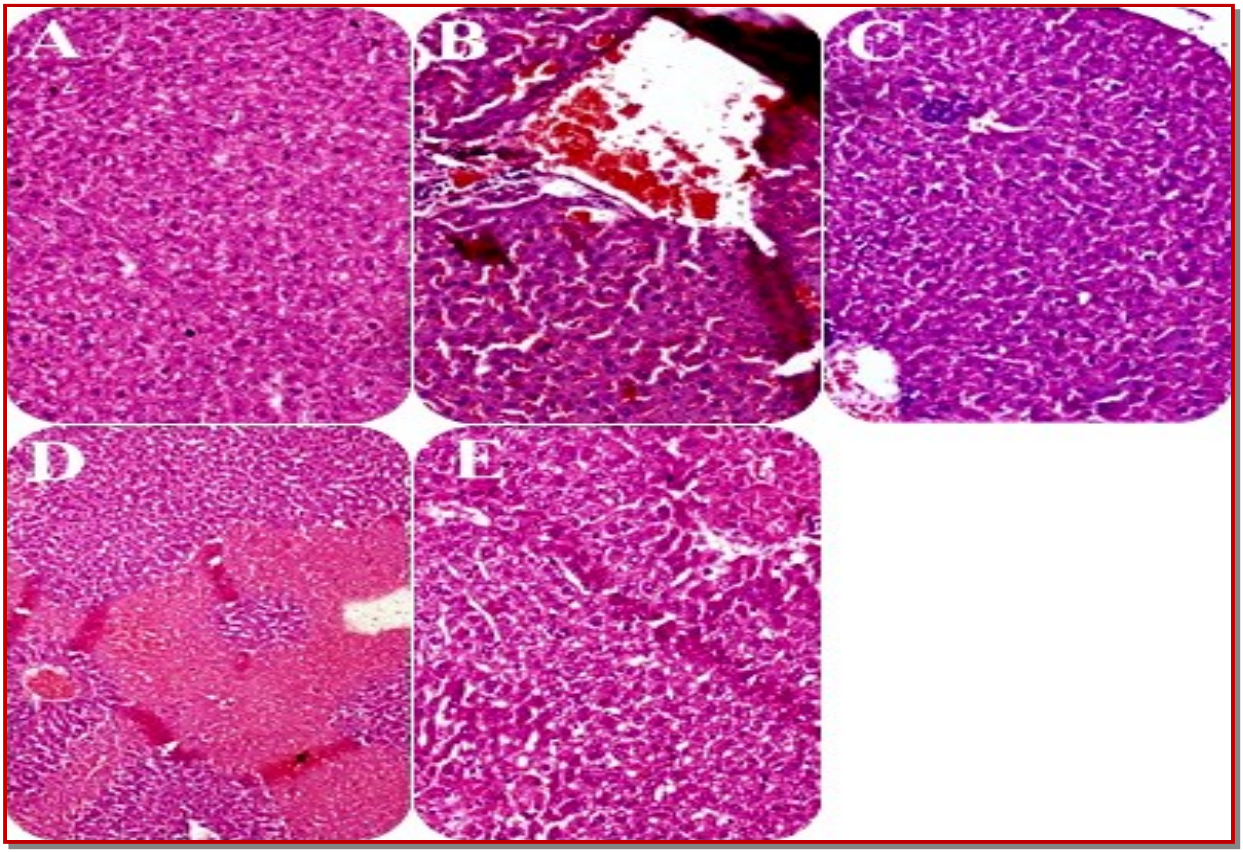

Figure 1: Histopathological pictures of (A) Normal hepatocytes (B) Paracetamol treated group, marked inflammation, necrosis, sinusoidal constrictions and ballooning (C) Silymarin treated group, improvement in necrosis, inflammation, ballooning and moderate dilatation of sinusoids (D) Extract 250 mg/kg treated group, mild inflammation, ballooning and moderate sinusoidal dilatation (E) Extract 500 mg/kg treated group, moderated inflammation, mild ballooning, mild necrosis and moderate sinusoidal dilatation

Table II

Phytochemical screening of whole plant of *Malva parviflora*

Constituents	Inferences	Constituents	Inferences	Constituents	Inferences
Phenols	++	Alkaloids	+	Coumarines	-
Flavonoids	++	Resins	+	Volatile Oils	-
Saponins	+	Tannins	+	Terpinoids	-

+++ = high amount after added of reagent immediately; ++ = moderate amount after 5 min of reagent added; + = low amount after 10 min of reagent added and - = absent of active compound after 20 min

Discussion

M. parviflora is an endangered species of Malvaceae in Pakistan. It has traditional use for hepatitis and jaundice in rural areas of Central Punjab, Pakistan. Its leaves are also edible and cooked with leafy vegetables for its taste, in other countries it is also used for salad dressing. The number of plants of this family has been reported to have hepatoprotective activity. Depending pon its broad use in medicine, hepatoprotective traditional use, edible importance, phytochemistry and relevancy with other hepatoprotective plants of family, this plant was evaluated for its hepatoprotective use.

Aqueous methanolic extract of *M. parviflora* reduces elevated ALT by 53 and 55% ($p<0.001$), AST by 53 and 57% ($p<0.01$, $p<0.001$; 250 and 500 mg/kg respectively), ALP by 27 and 30% ($p<0.001$) and TBR by 53% ($p<0.001$) with 250 and 500 mg/kg doses respectively in hepatotoxic mice and results are significant when compared to paracetamol control. There is insignificant ($p<0.9$) difference between two doses with exception of AST whose reduction is higher with 500 mg/kg ($p<0.001$) as compared to 250 mg/kg ($p<0.01$). These results are also comparable to that of silymarin ($p<0.001$). It seems high dose provides better results but not in all observational parameters so further studies

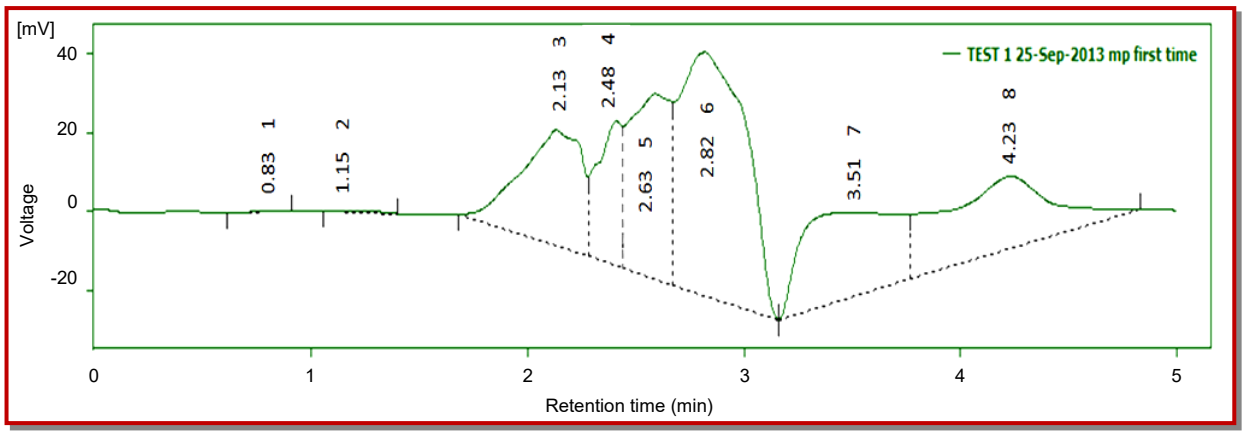

Figure 2: HPLC chromatogram of aqeous methanolic extract of *Malva parviflora*

are required to postulate this claim.

Flavonoids are important compounds in plants and have previously reported to have hepatoprotective activity (Ali et al., 2013). In our study moderate amount of flavonoids was present in whole plant. Qualitative determination of these flavonoids by HPLC confirmed the presence of kaempferol and apigenin (Figure 2). kaempferol (Song et al., 2003) and apigenin (Oh et al., 2004) have already been reported to have hepatoprotective activity. Therefore, hepatoprotective activity of the plant may be due to these compounds.

Conclusion

The aqueous methanolic extract of whole plant of *M. parviflora* possesses hepatoprotective activity.

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Ethical Issue

Experimental protocols were approved by Ethical Review Committee of the Institute.

Conflict of Interest

Authors declare no conflict of interest

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