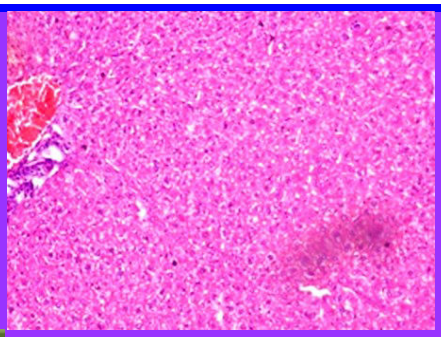

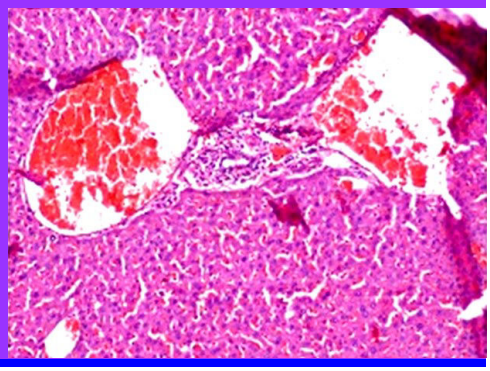

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Hepatoprotective potential of *Convolvulus arvensis* against paracetamol-induced hepatotoxicity

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Abstract

Convolvulus arvensis is traditionally used as laxative. Its decoction is used in cough, flu, jaundice and in skin diseases. It is also used to treat the painful joints, inflammation and swelling. The current study was conducted to determine its hepatoprotective activity. The results showed that extract of *C. arvensis* (200 and 500 mg/kg) produced significant ($p<0.05$) decrease in paracetamol induced increased levels of liver enzymes and total bilirubin. Histopathological investigation and detection of active constituent, qurecetin by HPLC also supported the results. So the current study showed that ethanolic extract of *C. arvensis* possess hepatoprotective activity.

Introduction

Convolvulus arvensis is a creeping weed with wide distribution in Asia (Kaur and Kalia, 2012) belonging to family Convolvulaceae. The plant, if not climbing it can form 5 cm thick carpets-off the ground. The length of the stem can be up to 2 m in length. It is locally known as "Leli" (Iqbal et al., 2011). The ethanolic extract of aerial part of plant *C. arvensis* possess high amount of flavonoids including quercetin (Kaur and Kalia, 2012).

Traditionally it is used as laxative. Its decoction is used in cough, flu, and jaundice and in skin diseases (Iqbal et al., 2011; Thakral et al., 2010). It is also used to treat the painful joints, inflammation and swelling (Kaur and Kalia, 2012). The reported scientific effects of *C. arvensis* are antioxidant (Elzaawely and Tawata, 2012), immune-stimulatory, anti-angiogenesis, cytotoxic (Kaur and Kalia, 2012).

Hepatoprotective effects of different plant extracts have been studied. Some of the recent studies include hepatoprotective activity of *Trianthema decandra* (Balamurugan and Muthusamy, 2008), *Cocculus hirsutus* (Thakare et al., 2009), *Carica papaya* (Sadeque and Begum, 2010), *Carissa spinarum* (Hegde and Joshi, 2010), *Dodonaea viscosa* (Ahmad et al., 2012), *Pinus roxburghii* (Khan et al., 2012), *Trichodesma sedgwickianum* (Saboo et al., 2013), *Oflpomoea staphylina* (Bag and Mumtaz, 2013) and Khamira Gaozaban Ambri Jadwar Ood Saleeb Wala (Akhtar et al., 2013). The current study was conducted to determine hepatoprotective activity of *C. arvensis*.

Materials and Methods

Collection of plant

C. arvensis was collected from the wheat fields of Nia Lahore, Jhang Road, Faisalabad and was verified by the Dr. Mansoor Hameed, Associate professor, Botany Department at University of Agriculture, Faisalabad. The plant was kept in the college herbarium for future reference.

Preparation of plant extract

The plant was washed to remove the dust and then shade dried for almost one week and grounded in to powder with the help of commercial grinder. The powdered plant was soaked in ethanol for 3-4 days with occasional shaking at certain time intervals. After 3 -4 days, the solution was filtered with the help of muslin cloth and the marc was pressed and filtrate was collected in volumetric flask. The filtrate was evaporated with the help of rotary evaporator at 70°C. After evaporation the solution was allowed to dry for some days, and stored in amber color bottle.

Experimental animals

Swiss albino mice of either sex weighing between 22-35 g were used and were kept at animal house in College of Pharmacy, GC University Faisalabad, Pakistan, in 12/12 hours cycle of day and night. These were feed with standardized pellet diet and water *ad libitum* (Shanmugasundaram and Venkataraman, 2005).

Protocol for hepatotoxicity induced by paracetamol

All animals were divided into 5 groups containing 5 animals each. Group 1 served as a control group receiving distilled water only (p.o). Group II served as paracetamol control group and received water and paracetamol 250 mg/kg (p.o) dissolved in water daily for 7 days (Sabir and Rocha, 2008). Group III was treated with silymarin as reference drug 50 mg/kg (p.o) daily for 7 days and received paracetamol 3 hours after silymarin (Girish et al., 2009). Group IV was treated with *C. arvensis* extract at doses of 250 mg/kg (p.o) for 7 days and received paracetamol 250 mg/kg (p.o) for 7 days 3 hours after the extract dose. Group V was treated with *C. arvensis* extract at doses of 500 mg/kg (p.o) for 7 days and received paracetamol 250 mg/kg (p.o) for seven days 3 hours after the extract dose (Sabir and Rocha, 2008).

Biochemical investigations

All animals were decapitated 24 hours after the last treatment by cervical decapitation. B

Blood was allowed to clot and serum was separated with the help of centrifuge at 4,000 rpm for 20 min. Biochemical serum investigations were done by evaluating the activities of liver marker enzymes AST, ALT, ALP and total bilirubin (Shanmugasundaram and Venkataraman, 2005).

Histopathological studies

The liver was removed from the animals and was placed in 10% buffered formalin (4% formaldehyde in phosphate buffered solution). The staining procedure for histology was done by hematoxy-lin, a basic dye stains nuclei blue and eosin, an acidic die, stains pink color to cytoplasm.

Identification of active constituent by HPLC

C. arvensis contains an important flavonoid, quercetin which has proved to exhibit the hepatoprotective activity (Pavanato et al., 2003). High performance liquid chromatographic method was adopted to identify the presence of the quercetin in ethanolic extract of *C. arvensis*. The sample was prepared by using the methanol. The mobile phase used in this experiment was a mixture of acetonitrile, methanol and acetic acid with the flow rate of 0.5 mL/min. The ODS 250 mm x 4.6 mm column was used and chromatogram obtained by using UV detector at 288 nm (Khadeem, 2007).

Statistical analysis

One-way ANOVA (analysis of variance) was used for statistical analysis. Results were represented by Mean ± SE.

Results

The normal mean value of alkaline phosphatase was 267.2 ± 11.6 IU/L. Paracetamol administration raised the alkaline phosphatase level up to 450.6 ± 71.9 IU/L. The administration of 250 mg/kg of *C. arvensis* extract brought the enzyme value to the 329.6 ± 34.7 IU/L which was comparable ($p<0.001$) to the standard silymarin 269.8 ± 18.6 IU/L. The administration of 500 mg/kg of the extract brought the enzyme value to the 309.4 ± 29.8 IU/L which was comparable ($p<0.001$) to the standard silymarin 269.8 ± 18.6. IU/L. The normal

Table I

Effect of ethanolic extract of *Convolvulus arvensis* on liver enzymes and total bilirubin

	Alkaline phosphatase (IU/L)	ALT (IU/L)	AST (IU/L)	Total bilirubin (g/dL)
Normal (D/W)	267.2 ± 11.6	61.0 ± 13.1	68.2 ± 9.3	0.7 ± 0.1
Paracetamol control 250 mg/kg	450.6 ± 71.9	159.8 ± 81.8	198.6 ± 75.5	2.1 ± 0.2
Silymarin 50 + Paracetamol 250 mg/kg	269.8 ± 18.6^c	66.4 ± 24.4^c	69.2 ± 14.1^c	0.7 ± 0.1^c
Extract 250 + Paracetamol 250 mg/kg	329.6 ± 34.7^c	86.2 ± 19.6^a	98.6 ± 27.7^c	0.8 ± 0.1^c
Extract 500 + Paracetamol 250 mg/kg	309.4 ± 29.8^c	80.2± 18.1^b	84.4 ± 13.2^c	0.8 ± 0.1^c

Data are mean ± SE; Significant $^a p<0.05$; $^b p<0.01$; $^c p<0.001$

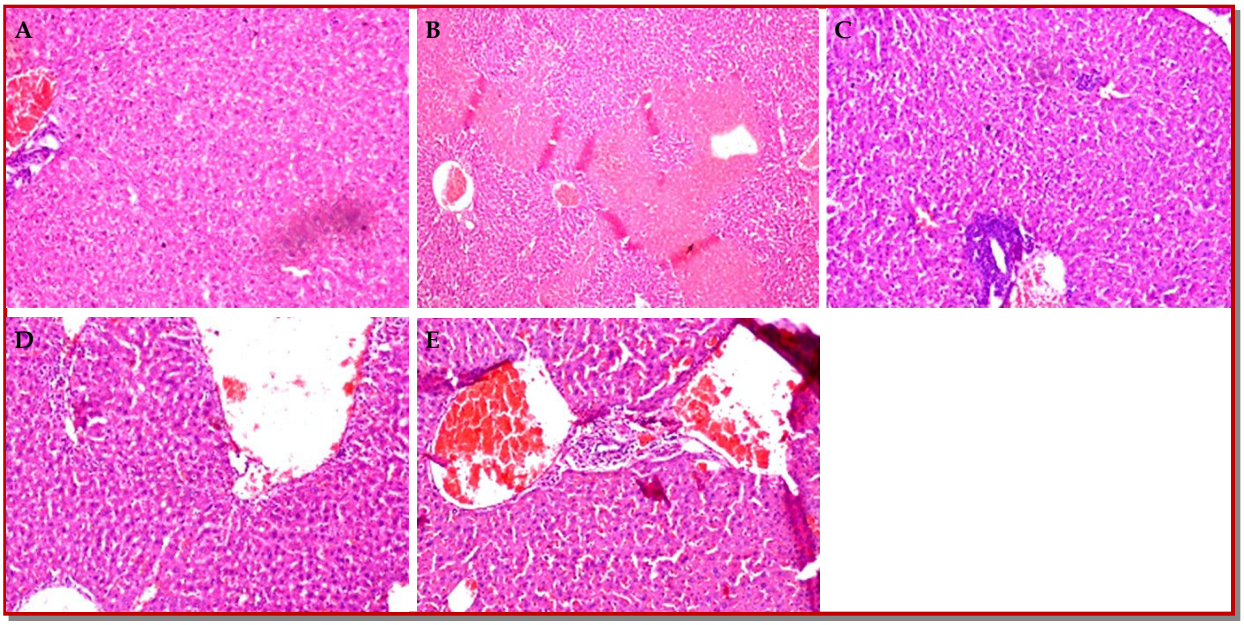

Figure 1: Histological picture of liver parenchyma of normal group (A) paracetamol-treated group (B) Showing extensive necrosis, moderate inflammation and ballooning; silymarin-treated group (C) showing mild portal inflammation with no balooning and necrosis; extract 250 mg/kg treated group (D) showing moderate inflammation and mild ballooning; and extract 500 mg/kg treated group (E) showing mild degree of sinusoid dilatation and inflammation with no necrosis and ballooning

mean value of ALT was 61.0 ± 13.1 IU/L. Paracetamol administration raised the ALT level up to 159.8 ± 81.8 IU/L. The administration of 250 mg/kg of the extract brought the enzyme value to the 86.2 ± 19.6 IU/L which was comparable ($p<0.05$) to the standard silymarin 66.4 ± 24.4 IU/L. The administration of 500 mg/kg of the extract brought the enzyme value to the 80.2 ± 18.1 IU/L which was comparable ($p<0.01$) to the standard silymarin 66.4 ± 24.4 IU/L. The normal mean value of AST was 68.2 ± 9.3 IU/L. Paracetamol administration raised the AST level up to 198.6 ± 75.5 IU/L. The administration of 250 mg/kg of the extract brought the enzyme value to the 98.6 ± 27.7 IU/L which was compa-rable ($p<0.001$) to the standard silymarin 69.2 ± 14.1 IU/L. The administration of 500 mg/kg of the extract brought the enzyme value to the 84.4 ± 13.2 IU/L which was comparable ($p<0.001$) to the standard silymarin 69.2 ± 14.1 IU/L. The total bilirubin normal value was 0.7 ± 0.1 g/dL. After treatment with paracetamol, total bilirubin level was raised to 2.1 ± 0.2 g/dL. The administration of 250 mg/kg of the extract brought the bilirubin value to the 0.8 ± 0.1 g/dL which was comparable ($p<0.001$) to the standard silymarin 0.7 ± 0.1 g/dL. The administration of 500 mg/kg of the extract brought the bilirubin value to the 0.8 ± 0.1 g/dL which was comparable ($p<0.001$) to the standard silymarin 0.7 ± 0.1 g/dL.

From the histopathological results of normal, paracetamol-treated and extracts-treated mice, it was noted that healthy cells were observed with normal shape, nuclei and parenchyma in normal group (Figure 1). However, paracetamol-treated mice liver showed extensive area of cell necrosis, moderate chronic inflammatory cells and some ballooning of cells. While the silymarin treated group showed mild portal inflammation with no ballooning and necrosis. The experimental group treated with 250 mg/kg of the extract showed moderate degree of inflammation and mild hepatitis and ballooning, while mild dilatation of sinusoid and mild inflammation with no necrosis and no ballooning were seen in group treated with 500 mg/kg of the extract. So, the results showed less damage to the liver parenchyma in pretreated groups with extracts as compared to the paracetamol-treated groups.

Chromatogram of ethanolic extract of *Convolvulus arvensis* was shown in Figure 2.

Discussion

The plant *C. arvesis* is traditionally for the treatment of jaundice (Thakral et al., 2010). Many other plants of Convolvulaceae are used as hepatoprotective. Mungole et al. (2010) determined the hepatoprotective activity of *Ipomoea obscura* (L) (Convolvulaceae) consisting of alkaloids, phenolics, flavonoids and saponins. Another plant of Convolvulaceae family *C. fatmensis* Ktze. possess hepatoprotective activity (Atta et al., 2007). Aqueous extract of seeds of *Cuscutae semen* Lam. (Convolvulaceae) showed hepatoprotective activity (Adewusi and Afolayan, 2010). Aqueous and ethanolic extracts of *Cuscuta chinensis* (Convolvulaceae) also showed hepatoprotective effect in paracetamol-induced toxicity (Kumar et al., 2011). Main constituents of the *C.*

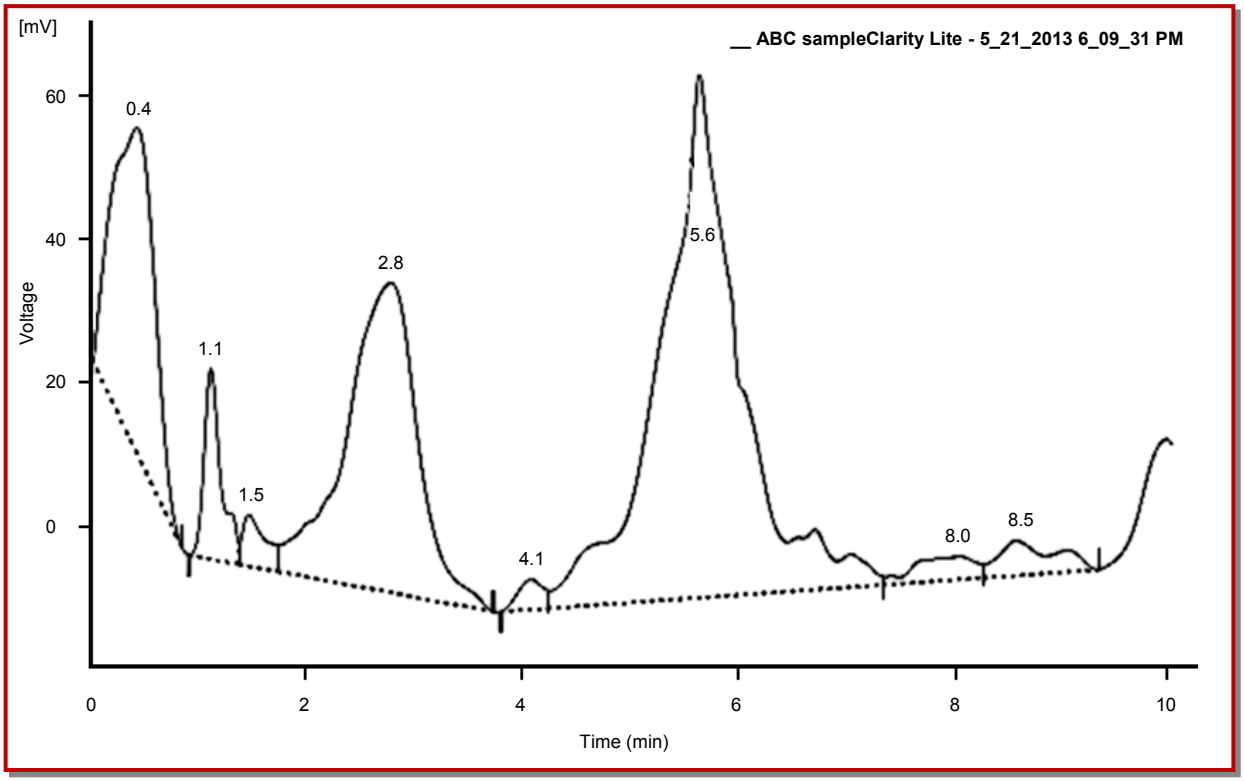

Figure 2: Chromatogram of ethanolic extract of *Convolvulus arvensis*

arvensis are Quercetin, Kaempferol (Kaur and Kalia, 2012). Quercetin is flavonoid and it is reported to be hepatoprotective (Pavanato et al., 2003). Therefore the hepatoprotective action of the *C. arvensis* might be due to the hepatoprotective constituents present in it.

C. arvensis extract 250 and 500 mg/kg showed almost same results. The groups treated with extract and paracetamol showed less increase in level of enzymes (ALP and AST) values and total bilirubin as compared to the paracetamol treated group ($p<0.01$). While for ALT, extract 250 and 500 mg/kg showed ($p<0.05$) and ($p<0.01$) respectively. The results indicated that group treated with extract showed remarkable recovery ($p<0.01$). The silymarin which was used as a standard bought the enzymes values to the normal values.

Additionally, histopathological examinations were also done to support the biochemical investigations. Paracetamol-treated group showed extensive necrosis, inflammation and ballooning showing hepatotoxicity. While histopathology of the mice of groups treated with the both extracts showed mild damage to the liver as compared to paracetamol. However silymarin treated group showed only mild inflammation with no ballooning and necrosis.

Furthermore, the presence of important active constituent, quercetin in ethanolic extract of *C. arvensis* was confirmed by using the HPLC because it gave the peak at same retention time as appeared for the standard.

It is also worth noted that the plant showed almost similar results at both concentrations. As the plant contains certain tropane alkaloids which may be hepatotoxic at higher doses. So, there is need to determine the dose for its hepatoprotective action.

Conclusion

Ethanolic extract of *C. arvensis* possess hepatoprotective activity due to quercitin.

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