Abstract

Background: Liver diseases cause serious health issues. Plant based drugs play vital role for management of liver diseases. *Ficus carica* is traditionally used for treatment of liver diseases. In the previous study we determined *in vivo* hepatoprotective activity of methanolic extract of leaves and its derived fractions. Ethyl acetate fraction exhibited excellent activity. The purpose of present study was Isolation and identification of active components from *F.carica* leaves which are responsible for hepatoprotective activity.

Methods: The study was designed to identify most active hepatoprotective sub - fraction from ethyl acetate fraction of *Ficus carica* by *in vitro* study *and* evaluation of its *in vivo* hepatoprotective effect in animal model. Ethyl acetate fraction was subjected to column and total eight sub-fractions were obtained. *In vitro* hepatoprotective effect of all sub-fractions was determined on HepG2 cell lines. Toxicity was induced by CCl_4 (Carbon tetrachloride) and silymarin was used as positive control. On the basis of results the most active sub-fraction was subjected to LC-MS and FT-IR analysis for identification of bioactive compounds. *In vivo* hepatoprotective effect was determined in mice. Toxicity was induced by CCl_4, at the end of the experiment, biochemical parameters such as ALT, AST, ALP, bilirubin and total protein were estimated in serum. Histopathology of liver tissues was also done.

Results: Sub-fraction $\mathbf{F_{VI}}$ exhibited significant ($P<0.05$) hepatoprotective activity as compared to other sub-fractions which was almost similar to the standard drug silymarin. Six known bioactive compounds were identified from this sub-fraction after LC-MS analysis. *In vivo* hepatoprotective activity of sub- fraction $\mathbf{F_{VI}}$ was evaluated in CCl_4 induced toxicated mice. Administration of CCl4 significantly increased level of ALT (Alanine transaminase), AST (Aspartate aminotransferase), ALP (Alkaline phosphatase)

and bilirubin and decreased the total protein. Treatment with sub-fraction **F_{VI}** significantly ($p<0.05$) reversed the level of these biomarkers toward normal at both doses of 25 mg/kg and 50 mg/kg.

Conclusion: Our findings confirmed the hepatoprotective effect of ethyl acetate fraction of *F.carica*. It could be a good candidate for development of natural hepatoprotective drug, pre-clinical investigation on ethyl acetate fraction is recommended.