The roots of *Rhus mysorensis* of Anacardiaceae family is used by the tribes of Andhra Pradesh, India, for the treatment of various hepatic disorders. In this study, the root of *Rhus mysorensis* was selected for the investigation of its hepatoprotective activity against CCl4 induced hepatotoxicity. The rats were given a daily pre-treatment with ethyl acetate *Rhus mysorensis* root 200, 400 and 800 mg/kg and silymarin (25 mg/kg) followed by CCl4 at a dose of 1.25 ml/kg orally for seven days. On the eighth day, blood was collected from the reto orbital plexus of all the rats. Serum was separated by centrifugation and analyzed for serum glutamic pyruvate transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), alkaline phosphatase (ALKP), cholesterol (CHL), total protein (TPTN) and albumin (ALB). The result of the present study suggests that ethyl acetate extract of *Rhus mysorensis* root showed better hepatoprotective activity due to the presence of phytoconstituents such as steroids, triterpenoids and flavonoids. Thus, the present study provides a scientific and rational for the traditional use of this plant on the management of liver diseases.