Abstract
1.0 Abstract

The present study was selected to examine the uses of *Helicteres isora* fruit with the context of the modern scientific framework with an aim to substantiate the claims made in the traditional system of medicine.

The whole work of present study was divided broadly into phytochemical and pharmacological studies. Phytochemical studies involved authentication, extraction and characterization of possible compounds in the active extract of *Helicteres isora* fruit. While pharmacological studies involved screening of various pharmacological activities of *H. isora* in different experimental animal models.

The collected sample of *Helicteres isora* fruit authenticated on the basis of morphological characters mentioned in different texts and floras. For standardization of *H. isora*, different quantitative limit tests like ash value and extractive values were determined. The fruit was found to contain 7.0 % total ash, 1.03 % acid insoluble ash, and 3.94 % water soluble ash.

After authentication, the dried powder of *H. isora* fruit was extracted in two sets. In first set, the powder was extracted with 50 % alcohol, which was found to yield 17% w/w dried extract. In another set of extraction, dried powder was extracted with pet-ether, ethyl acetate and N-butanol successively. They were found to yield 10.01 %, 20.03 %, and 8.60 % w/w dried extracts respectively. All these extracts were studied for their pharmacological activities in different animal models.

During pharmacological study, different extracts of *H. isora* fruit were studied to evaluate their antiulcer, hepatoprotective, antihyperlipidemic, and antidiabetic activities in animal models.

In the present study, the antiulcer activity of *H. isora* fruit was studied in ethanol induced gastric ulcers in rats. Except pet-ether extract, all other extracts (alcoholic, ethyl acetate, and N-butanol extracts) were found to reduce gastric ulcers in ethanol-treated rats. Gastric wall mucus content (GWMC) was found to increase significantly by treatment with pet-ether, ethyl acetate, and N-butanolic extracts. However, the alcoholic extract failed to do so. Lipid peroxidation was found to be lowered in rats treated with alcoholic (AE), ethyl acetate (EA), and N-butanol (NB) extracts while pet-ether extract (PE) failed to show this effect. Superoxide dismutase and catalase activities were increased by alcoholic extract, pet-ether, ethyl acetate, and
N-butanol extracts in ethanol induced gastric ulcers in rats. N-butanol extract was found to be most effective compared other extracts. Therefore this extract was selected for detailed study of antiulcer activity in alcohol induced gastric ulcers in rats. Similarly, alcoholic extract was studied in various gastric ulcer models along with N-butanolic extract. In ethanol induced gastric ulcer model, N-butanolic extract was found to reduce the ulcer index in a dose dependent manner.

To evaluate the probable mechanism of action for antiulcer activity, we studied the effect of alcoholic and N-butanolic extracts in ethanol induced gastric ulcers in rats pretreated with either $N^G$-nitro-L-arginine methyl ester (L-NAME) or indomethacin, or N-ethylmaleimide, and in pylorus ligated rats. The antiulcer activity of alcoholic and N-butanolic extracts was inhibited by pretreatment with either L-NAME, indomethacin and N-ethylmaleimide. This inhibition suggests the possible role of NO, sulphhydryl compounds, and prostaglandins in antiulcer activity of $H. \text{isoro}$ fruit in ethanol induced gastric ulcers in rats.

In pylorus-ligated rats, ethanol significantly increased the ulcer index and total acid output. However, pepsin activity was not altered by ethanol. Administration of alcoholic and N-butanolic extracts significantly reduced the ulcer index, total acid output, and pepsin activity as compared to ethanol treated and pylorus ligated rats. Total carbohydrate (TC) was significantly reduced while protein content (PR) was unaffected by ethanol in pylorus-ligated rats. Alcoholic and N-butanolic extracts significantly increased the total carbohydrate content in gastric juice. Treatment with N-butanolic extract significantly increased the mucin activity that was reflected from TC/PR ratio (total carbohydrate/protein ratio) in alcohol-treated and pylorus-ligated rats. However, alcoholic extract failed to increase the mucin activity.

In hepatoprotective study, CCl$_4$ induced liver damage was reflected from significant rise in serum Serum glutamate oxaloacetate transaminase (SGOT), Serum glutamate pyruvate transaminase (SGPT), and Alkaline phosphatase (ALP). Alcoholic, pet-ether, ethyl acetate and N-butanolic extracts were found to significantly reduce the SGOT, SGPT, and ALP levels except the alcoholic extract that failed to reduce SGOT levels when compared with CCl$_4$-treated rats. In CCl$_4$-treated rats, lipid peroxidation measured as thiobarbituric acid reacting substances (TBA-RS) was significantly elevated in liver homogenates along with significant decrease in activity of superoxide dismutase and catalase enzymes and depleted levels of reduced glutathione. Reduced levels of TBA-RS in liver homogenates of alcoholic,
pet-ether, ethyl acetate, and N-butanolic extracts treated animals reflected decreased lipid peroxidation in \( \text{CCl}_4 \)-treated rats. Rats treated with alcoholic, pet-ether, ethyl acetate, and N-butanolic extracts showed significant increase in superoxide dismutase and catalase activities and also raised the reduced glutathione levels as compared to \( \text{CCl}_4 \) treated rats.

In antihyperlipidemic study, elevated levels of serum cholesterol, and triglycerides reflected the hyperlipidemia induced by high cholesterol diet (HCD) in rats. HCD-induced hyperlipidemic rats also showed increased serum LDL and VLDL levels along with significant decrease in HDL levels as compared to control rats. Alcoholic, pet-ether, ethyl acetate, and N-butanol extracts were found to decrease the serum cholesterol, triglycerides, LDL and VLDL levels in HCD hyperlipidemic rats, except ethyl acetate and N-butanol which failed to affect VLDL level significantly. Alcoholic, pet-ether, ethyl acetate, and N-butanol extracts treated hyperlipidemic rats showed significant increase in HDL level. All extracts were found to increase HDL/LDL ratio along with significant decrease in atherogenic index. Among all extracts, pet-ether extract was found to be most effective in HCD-induced hyperlipidemia.

The antihyperglycemic activity of \( \text{H. isora} \) fruit was studied in alloxan-induced diabetic rats. Alloxan-induced diabetic rats showed decrease in body weight, polyphagia, and polydypsia. Alcoholic, pet-ether, ethyl acetate, and N-butanol extracts failed to prevent the loss in body weight compared to diabetic rats. Food intake and water intake were reduced by all the extracts except the ethyl acetate extract which failed to affect the water intake in the diabetic rats.

Alloxan-induced diabetic rats showed severe hyperglycemia compared to control rats. Treatment of diabetic rats with alcoholic, pet-ether, ethyl acetate, and N-butanol extracts reduced the blood sugar level to the extent of severe hypoglycemia.

Diabetes is associated with hyperlipidemia. In the present study, this was reflected by increase in serum cholesterol, triglycerides, LDL, and VLDL levels in alloxan-induced diabetic rats as compared to control animals. Serum cholesterol and triglycerides levels were found to be lowered in alcoholic, pet-ether, ethyl acetate, and N-butanol treated diabetic rats. Treatment with alcoholic, pet-ether, ethyl acetate, and N-butanol extracts significantly lowered the serum LDL, and VLDL levels as compared to diabetic rats. Serum HDL level was found to be lower in alloxan-induced diabetic rats. Treatment with alcoholic, pet-ether, ethyl acetate, and N-butanol extracts
failed to affect the serum HDL level. However, HDL/LDL ratio was significantly higher in alcoholic, pet-ether, and N-butanol treated diabetic rats. The ethyl extract failed to affect this parameter.

In the present study, serum, SGOT and SGPT levels were found to be raised in diabetic rats. Treatment with alcoholic, pet-ether, ethyl acetate, and N-butanol extracts showed significant decrease in serum SGOT and SGPT levels as compared to diabetic rats. This suggests the beneficial effects of *H. isora* fruit on hepatic damage.

Serum urea level was significantly higher in alloxan-induced diabetic rats as compared to control rats. None of the extracts significantly affected the serum urea level. On the contrary, alcoholic, ethyl acetate, and N-butanol extracts-treated rats showed the increased level of serum urea as compared to diabetic rats. Statistically insignificant rise was observed in serum creatinine levels.

Alloxan-induced diabetic rats showed lower levels of liver glycogen as compared to control rats. In the present study, liver glycogen content was found to be increased in diabetic rats treated with alcoholic, pet-ether, ethyl acetate, and N-butanol extracts as compared to diabetic rats.

In conclusion, we can say that *H. isora* fruit possesses antiulcer, hepatoprotective, antihyperlipidemic and antidiabetic activity in rats. The antiulcer activity in ethanol-induced gastric ulcer model may be through either strengthening of the gastric mucosal barrier, free radical scavenging activity, release of nitric oxide and/or prostaglandins. Hepatoprotection against CCl₄-induced hepatic damage may be attributed to its free radical scavenging activity. The antihyperlipidemic activity observed in HCD-induced hyperlipidemic rats indicated that the presence of β-sitosterol in *H.isora* fruit may be responsible for its antihyperlipidemic activity. The antihyperglycemic activity observed in alloxan-induced diabetic rats suggests that *H. isora* fruit possesses potent antidiabetic activity that may be mediated through its insulin releasing and/or insulin sensitizing activity.