SUMMARY AND CONCLUSION

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Traditional systems of medicine have become a topic of global importance. Current estimates suggest that, in many developing countries, a large proportion of the population relies heavily on traditional practitioners and medicinal plants to meet primary health care needs. Although modern medicine may be available in these countries, herbal medicines (phytomedicines) have often gained popularity for historical and cultural reasons. Concurrently, many people in developed countries have begun to turn to alternative or complementary therapies, including medicinal herbs. A few plant species have been scientifically evaluated for their possible medical application. Safety and efficacy data are available for even fewer plants, their extracts and active ingredients, and the preparations containing them. The present study emphasizes the use of the fruit (HF) and the bark (HB) extracts of *Helicteres isora* in the maintenance of normoglycemia in diabetes and in the prevention of complications associated with it.

The fruit and the bark of *Helicteres isora* were collected from the hills near Sultanpatri, Kerala. They were shade dried and powdered. Then the *Helicteres isora* was characterized by analyzing the biochemical parameters (carbohydrate, protein, fibre, calcium, phosphorus, total iron, sodium, potassium, chromium), enzymic (catalase, superoxide dismutase, glutathione peroxidae, glutathione -S- transferase) and non-enzymic antioxidants (vitamin C, vitamin E, flavonoids, tannins, total carotenoids, reduced glutathione, thiamine and riboflavin). The free radical scavenging activity of the methanol extract of the fruit and the bark extracts of *Helicteres isora* were also determined. Ames test was done to test the mutagenicity. Toxicity studies in the selected plant were carried out as a requirement for Ethical

Committee clearance. The fruit and the bark extracts of *Helicteres isora* were administered in two different doses of the extracts (150 mg and 200 mg/kg body weight) to rats and the body weight, hematological parameters, selected biochemical parameters and the levels of blood glucose were analysed. The antidiabetic effects of the fruit and the bark extracts of *Helicteres isora* individually and in selected combinations were determined and compared with the effects of selected oral antidiabetic drugs - glibenclamide and metformin. The blood glucose, liver glycogen, plasma insulin, serum fructosamine, carbohydrate metabolizing enzymes, serum and liver lipid profile, oxidative stress markers, total protein and histopathological analyses were carried out to determine the antidiabetic effect of *Helicteres isora.* The phytochemicals in *H.isora* were screened qualitatively and by thin layer chromatography. The extracts were subjected to HPLC to find out the active constituents present in it.

The findings of the present study are

- Both the HF and the HB extracts were found to contain reasonably good amounts of nutrients, carbohydrates, protein, fibre and minerals namely calcium, phosphorus, potassium, sodium, iron and chromium.
- Enzymic antioxidants namely catalase, superoxide dismutase, glutathione peroxidase, glutathione-S-transferase and non-enzymic antioxidants, vitamin E, vitamin C, flavonoids, tannins and glutathione were found in rich amounts in both the fruit (HF) and the bark (HB) powders of *Helicteres isora.*
- Both the fruit and the bark extracts of *Helicteres isora* were found to be effective in inhibition of *in vitro* lipid peroxidation, superoxide generation, nitric oxide generation, scavenging DPPH free radicals and hydroxyl radicals.

- Ames *Salmonella* microsome assay indicated that both the HF and the HB are antimutagenic at the dose level tested (100 μg / plate).
- The results of the acute toxicity study indicated that both the HF and the HB were devoid of any acute toxicity at the dose levels of 150 mg/ kg body weight and 200 mg / kg body weight.
- No adverse effect of both the fruit and the bark extracts of *Helicteres isora* were observed on the body weight. Also the hematological parameters, RBC, WBC and platelet counts and hemoglobin value proved that the HF and the HB caused no chronic toxicity.
- All the biochemical parameters assessed viz., total bilirubin, AST, ALT, ALP and creatinine in serum and blood urea did not deviate from those of the controls and those rats treated with either 150 mg or 200 mg of HF and HB. This indicated that the HF and the HB administration did not cause any hepatic or renal toxicity in the control rats. Restoration of the levels of these parameters in diabetic rats treated with HF and HB revealed the possible reversal of the damage caused by streptozotocin.
- The results of the dose relationship study indicated that the selected doses of the fruit and the bark extracts of *Helicteres isora* reduced the blood glucose level in streptozotocin-induced diabetic rats. Among the two dosages of HF and HB tested, 200 mg / kg body weight was found to be more effective than the 150 mg / kg body weight.
- Oral administration of HF and HB individually and in selected combinations significantly lowered the blood glucose level in streptozotocin-induced diabetic rats. It showed that the hypoglycemic

activity of these extracts was on par with that of the allopathic drugs glibenclamide and metformin.

- Individual and coadministration of HF and HB restored the normal liver glycogen levels. This effect is similar to that of glibenclamide and metformin.
- Plasma insulin concentrations were not significantly different in the rats treated with HF and HB individually and in combinations as compared to the untreated control rats. Administration of HF and HB did not produce any significant increase in plasma insulin level of normoglycemic rats, whereas the HF and HB treated diabetic rats have shown increased levels of plasma insulin when compared to the diabetic control rats. From the results of the present study, it appears that still insulin producing cells are functioning and stimulation of the insulin release could be possible by the treatment of the extracts of HF and HB. The increased plasma insulin may be due to the activation of beta cells of islets of langerhans.
- A significant reduction of serum fructosamine (glycosylated plasma proteins) in the diabetic rats treated with HF, HB, glibenclamide and metformin treatment confirmed the effect of these in controlling the level of blood glucose. Both HF and HB extracts decreased the activity of gluconeogenic enzymes, glucose-6-phosphatase and fructose-1,6-bisphosphatase and enhanced the glucose oxidation by the pentose phosphate shunt through activation of its principle enzyme glucose-6-phosphate dehydrogenase in streptozotocin-induced diabetic rats and increased the glycogen synthesis by activating its key enzyme glucokinase. The enhanced activities of the enzymes and increased level of serum insulin in HF and HB treated groups may lead to

increased utilization of glucose. Insulin enhances the hepatic carbohydrate metabolism by increasing the biosynthesis of enzymes of glycolysis, glycogenesis, and pentose oxidative pathway and by inhibiting gluconeogenesis.

- The reversal of hyperlipidemia in the streptozotocin-induced diabetic rats by HF and HB proved these to be hypolipidemic. The highly significant hypolipidemic effect of HF and HB on the diabetic rats shows that it can delay, if not, prevent the lipid mediated secondary complications of diabetes.
- Studies on antioxidant action demonstrated that the concentrations of malondialdehyde and hydroperoxides in liver of HF and HB treated diabetic rats showed significant reduction indicating the increased scavenging of lipid peroxides or decreased rate of lipid peroxidation. Thus both HF and HB exhibit highly significant inhibitory effects of lipid oxidation and hence the disease caused due to lipid peroxidation can be prevented by both HF and HB administration.
- A concomitant decrease in the antiperoxidative enzymes namely catalase, glutathione peroxidase, superoxide dismutase and glutathione transferase and an increase in the non-enzymic antioxidants, vitamin E, vitamin C, vitamin A and reduced glutathione were observed in the liver of both the HF and the HB treated diabetic rats. This indicates that these herbal extracts play an important role in scavenging toxic intermediates of incomplete oxidation in the body.
- Assay of protein status in serum revealed that the HF and the HB treatment restored the total protein levels to normalcy.

- The histopathological study revealed that the histological changes occurred due to diabetes were reverted back to normal which inturn indicates the protective effect of *Helicteres isora.*
- The phytochemical analysis of the extracts of *Helicteres isora* shows the presence of two active components, rosmarinic acid and scutellarein, which may be responsible for the antioxidant and antidiabetic activity.

The findings of the present study clearly demonstrates that the fruit and the bark extracts of *Helicteres isora* have a pronounced and remarkable blood glucose lowering potential in streptozotocin - induced diabetic rats comparable to those produced by glibenclamide and metformin. Therefore, *Helicteres isora* can be used as an effective antihyperglycemic dietary adjunct for the treatment of diabetes and a potential source for the discovery of new orally active agents for future diabetes therapy. It could be concluded that the fruit and the bark extracts of *Helicteres isora* are hypoglycemic, hypolipidemic, antiperoxidative and antidiabetic.

Recommendations

- Further comprehensive chemical and pharmacological investigations are required for the elucidation of the mechanism of action of active constituents in the fruit and the bark extracts of *Helicteres isora.*
- The *in vitro* antidiabetic activity of rosmarinic acid and scutellarein can be done to validate its hypoglycemic effect.
- A placebo- controlled trial is needed to properly assess the safety and efficacy before the plant extracts can be routinely recommended as therapy.
- Future research to refine the extraction of *Helicteres isora* could lead to improved pharmaceutical products.