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Research Article

Protective Role of Pitcher of *Nepenthes khasiana* Hook against Dexamethazone Induced Hyperlipidemia and Insulin Resistance in Rats

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ABSTRACT

The present research was made to investigate the potential hypoglycemic and hypolipidemic effect of *Nepenthes khasiana* Hook in Dexamethazone-induced Hyperlipidemia and Insulin Resistance in Rats. Hypoglycemic and hypolipidemic effect of pitcher extract of *Nepenthes khasiana* Hook was tested at two different doses of 250 & 500 mg/kg p.o. On day 11 of treatment, blood was collected for the estimation of serum glucose and lipid parameters. Pitcher extract was compared with standard Glibenclamide at a dose of 500 mcg/kg p.o. pitcher extract and Glibenclamide significantly decreased (P<0.05) dexamethazone induced elevation of serum glucose when compared to disease control group. Pitcher extract at a dose of 500 mg/kg showed better activity than standard. The present study indicates that pitcher extract of *Nepenthes khasiana* Hook show significant glucose and lipid lowering activity.

Keywords: *Nepenthes khasiana* Hook; Dexamethazone; Insulin Resistance; Hypolipidemic effect.

INTRODUCTION

Diabetes is a global disease with a huge adverse impact on health and mortality, particularly from cardiovascular disorders. It occurs at any time of life from infancy to old age. Type-2 diabetes is primarily a lifestyle disorder. This accounts for around 90% of diabetes cases and increasing at an astonishing rate. Particularly in developing countries like India. In 1995, it has been estimated that around 135 million people had this condition, and this may increase to as many as 300 million by the year 2025 (King et al., 1998).

Liver is an insulin dependent tissue, which plays a pivotal role in glucose and lipid homeostasis and is severely affected during diabetes (Seifter & England, 1982). During diabetes a profound alteration in the concentration and composition of lipid occurs (Sochar et al., 1995). Decreased glycolysis, impeded glycogenesis and increased gluconeogenesis are some of the changes of glucose metabolism in the diabetic liver. Diabetes mellitus is known to cause hyperlipidemia through various metabolic derangements. Among several metabolic derangements, insulin deficiency has been known to stimulate lipolysis in the adipose tissue and give rise to hyperlipidemia and fatty liver. Thus, in diabetes hypercholesterolemia and hypertriglyceridemia often occur (Hardman & Limberd, 2001).

Dexamethasone, a very potent and highly selective glucocorticoid. People are taken as steroidal supplement but Corticosteroids profoundly affect carbohydrate and protein metabolism. Teleologically, these effects of glucocorticoids on intermediary metabolism can be viewed as protecting glucose-dependent tissues (e.g., the brain and heart) from starvation. They stimulate the liver to form glucose from amino acids and glycerol and to store glucose as liver glycogen. In the periphery, glucocorticoids diminish glucose utilization, increase protein breakdown and the synthesis of glutamine, and activate lipolysis, thereby providing amino acids and glycerol for gluconeogenesis. The net result is to increase blood glucose levels. Because of their effects on glucose metabolism, glucocorticoids can worsen glycemic control in patients with overt diabetes and can precipitate the onset of hyperglycemia in patients who are otherwise predispose (Bernard et al. 2006).

The Genus *Nepenthes* is a scandent or rarely erect insectivorous herbs, subshrubs or shrubs distributed from Southern china to north eastern Australia and New Caledonia, and extending westwards to Seychelles and Malagasy (Madascar). One Species *Nepenthes Khasiana* has been found in North East India (in the Garo Hills and Khasi Jantia Hills of Meghalaya and some part of Assam upto 1200 m). This is also called Pitcher plant. The stem of pitcher plants are climbing herbs or

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undershrubs which often climb by means of the tendrillar stalk of the pitcher. The pitcher itself is a modification of the leaf blade (Dutta, 2000). The pitcher contains juice also. Traditionally it is reported that juice from the unopened pitcher of *Nepenthes khasiana* Hook. used for the treatment of diabetes (Kumar, 2002). So, The present research was made to investigate the potential hypoglycemic and hypolipidemic effect of *Nepenthes khasiana* Hook in Dexamethazone-induced Hyperlipidemia and Insulin Resistance in Rats.

MATERIAL AND METHODS

The plant *Nepenthes Khasiana* collected in the month of June-August from the Jarain area of Jaintia Hills of Mehghalaya. The plant was identified from the standard literature (Wealth of India, 2001) then confirmed and authenticated by Botanical Survey of India, Shilong. The collected plant material was washed thoroughly with the help of water to remove the earthy matter or adherent impurity and then shade dried. The dried material was powdered by means of mechanical grinder. The resulting powdered material was stored in air tight glass container for further studies.

Extraction of Crude Drugs (Harborne, 1998)

About 150gm of powdered drug of pither of *Nepenthes khasiana* was taken in a 5000ml of round bottom flask and extracted for 72 hrs by continuous hot percolation process using different solvent according to the increasing polarity; likewise petroleum ether, benzene, chloroform, acetone, ethyl acetate, methanol, ethanol, water. The extracts were filtered through whatmann filter paper to remove impurities present. The extracts were then concentrated by vacuum distillation, cooled and placed in desiccators to remove the excessive moisture.

Phytochemical analysis (Kokate, 2002; Harborne, 1998)

The concentrated extracts were subjected to chemical test as per the methods mentioned in the reference book for the identification of the various constituents.

Acute toxicity study

Healthy Wister albino rats of either sex weighing 100 ± 20 g were divided into 5 groups of 6 animals each. The animals were housed under standard conditions and room temperature (25 ± 2° C) was controlled. All animals were fed with standard rat pelleted diet and had free access to tab water ad libitum. The study has got the approval from the Institutional Animal Ethical Committee (IAEC) of Committee for the Purpose of Control and supervision of Experiments on Animals (CPCSEA). Methanolic extract of pitcher was administered orally through gastric intubation in 5% T80 at doses of 500, 1000, 1500, 2000 and 3000 mg/kg bw and control group received 0.5 ml of 5% T80. The animals were observed continuously for 72 hr for any signs of behavioral changes, toxicity and mortality.

Dexamethasone-induced insulin resistance and hyperlipidemia (Mahendran & Devi, 2001)

Animals were divided in to 5 groups, each consisting of six rats. Rats in the first group received vehicle and served as control group, while the second group of rats received vehicle plus dexamethasone (10 mg/kg s.c.) and served as positive control group. Rats in experimental groups 4-5 were treated with methanolic extract of pitcher of *Nepenthes khasiana* (250 & 500 mg/kg p.o.) plus dexamethasone, whereas rats in the 3

Rd group were treated with standard drug Glibenclamide (500 µg/mg p.o.). All the animals received their respective assigned treatment daily for a period of 10 days. Rats of group 2-5 were daily fasted over night before dexamethasone treatment. On day 11, the animals were anesthetized with ether, and blood was collected from retero-orbital plexus. Serum was then separated for the estimation of glucose, cholesterol, triglyceride, high density lipoprotein (HDL) and low density lipoprotein (LDL) by using respective kits.

Statistics

All the results were expressed as Mean ± SEM, and the data were analysed using one- way ANOVA followed by Student-newman-keuls post-test using GraphPad Prism software. $P<0.05$ was considered significant.

RESULTS

Phytochemical screening

Phytochemical screening of plant extracts revealed

Table 1: Effect of Methanolic Extract of Pitcher in Biochemical Parameters

Group	Serum Glucose mg/dl	Serum Cholesterol mg/dl	Triglyceride mg/dl	HDL mg/dl	LDL mg/dl
Control	41.5 ± 4.12	85.33 ± 4.45	88.83 ± 5.79	45.5 ± 1.72	27.66 ± 3.27
Diabetic control	155.5 ± 1.91[a]	152 ± 7.38[a]	186.6 ± 4.35[a]	26 ± 0.85[a]	88.5 ± 5.48[a]
Standard	50 ± 3.02[¥]	108.16 ± 3.62[¥]	121.83 ± 3.81[¥]	35 ± 0.81[*]	56.33 ± 2.65[¥]
P250	70.33 ± 1.99[¥]	105 ± 2.80[¥]	113.16 ± 3.03[¥]	40.5 ± 2.43[¥]	47.66 ± 2.17[¥]
P500	84.16 ± 4.23[¥]	90.38 ± 9.01[¥]	131 ± 7.43[¥]	44.33 ± 2.92[¥]	78.83 ± 6.39[ns]

All value expressed in Mean ± SEM, One-way ANOVA followed by Student-Newman-Keuls Method. a P<0.001 when compared with Control, ¥ P<0.001 when compared with Diabetic control, * P<0.01 when compared with Diabetic control, b P<0.05 when compared with Diabetic control, ns Non significant

that the presence of flavonoids, alkaloids, glycoside, tannins, saponins, phytosterols.

Acute toxicity study

There was no mortality or any signs of behavioral changes or toxicity observed after oral administration of methanolic extract of pitcher up to the dose level of 3000 mg/kg bw in rats.

Dexamethasone induced insulin resistance and hyperlipidemia

The entire group significantly (P<0.001) decreased dexamethasone-induced elevation of serum glucose, cholesterol, triglyceride and LDL. Methanolic extract of pitcher at a dose level of 500 mg/kg shows no significant effect in the reduction of LDL level when compared with positive control group (Diabetic control). The standard and extracts treated group significantly (P<0.001) increase the level of HDL when compared with positive control group (Diabetic control). The result was present in Table 1.

DISCUSSION

Acute toxicity study revealed that the methanolic extract of pitcher does'nt shows any toxicity and mortality at dose level of 3000 mg/kg bw.

Insulin resistance in type2 diabetes is not only associated with hyperglycemia but also with hyperlipdemia and atherosclerosis (DeFronzo et al., 1992; Reaven 1988). Insulin resistance in humans has been shown to be present in conditions like NIDDM, obesity and dyslipidemia. Thus interventions to decrease insulin resistance may postpone the development of NIDDM and its complications. Treatment with natural herbs is likely to be fraught with lesser side effects compared to the presently used synthetic oral antidiabetic agents.

In the present study it has been found that the elevation of serum glucose and abnormal changes in the lipid profile in dexamethasone treated rats indicating the hyperglycemia and hyperlipidemia caused by this drug. Previous reports also show the same findings in this model [Nanjan et al., 2007; Shalam et al., 2006]. Dexamethasone increases triglyceride levels, causing an imbalance in lipid metabolism leading to hyperlipidemia [Wiesenberg et al., 1998] and an increase in glucose levels leading to hyperglycemia [Mahendran & Devi, 2001]. Pharmacological doses of glucocorticoids induce ob gene expression in rat adipocyte tissue with in 24 h. This is followed by complex metabolic changes resulting in decrease in food consumption; reduction in body weight, profound obesity often accompanied by diabetes and development of insulin resistance with enhanced blood glucose and triglyceride levels. Methanolic extract of pitcher at the dose level of 250 & 500 mg/kg prevented the rise in triglyceride, glucose, cholesterol and LDL caused by dexamethasone. Further, this also prevented the progressive decrease in HDL and body weight caused by dexamethasone. The phytochemical screening shows the presence of flavonoids in the extract might be a responsible active principle for these effects.

CONCLUSION

In conclusion, oral administration of methanolic extract of pitcher lowers serum glucose, triglyceride, cholesterol and LDL concentrations and improve the level of HDL in dexamethasone-administered rats. The methanolic extract showed significant anti-diabetic effect in rats after oral administration. Thus the claim made by the traditional Indian systems of medicine regarding the use of this plant in the treatment of diabetes stands confirms. The results suggest the presence of biologically active principle flavonoids which may be worth further investigation, elucidation.

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