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ORIGINAL ARTICLE

Effect of *Psoralea corylifolia* on dexamethasone-induced insulin resistance in mice

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Abstract The whole plant of *Psoralea corylifolia* (PC) is traditionally used in the treatment of diabetes. Mice were treated with prestandardised dose of dexamethasone for 22 days and effect of PC at the doses of 100, 200 and 300 mg/kg, p.o. on plasma blood glucose level, serum triglyceride level, glucose uptake in skeletal muscle, levels of hepatic antioxidant enzymes (GSH, SOD, catalase and LPO), and body weight were observed. PC showed significant decrease in plasma glucose and serum triglyceride levels ($p < 0.01$) at the dose of 100 and 200 mg/kg, p.o. and also stimulated glucose uptake in skeletal muscle. The levels of antioxidant enzymes GSH, SOD, and catalase were significantly increased ($p < 0.01$) and there was significant decrease ($p < 0.01$) in level of LPO.

Hence it can be concluded that *Psoralea carylifolia* may prove to be effective in the treatment of Type-II Diabetes mellitus owing to its ability to decrease insulin resistance.

1. Introduction

Diabetes mellitus (DM) is the most common endocrine disorder. More than 150 million peoples are suffering from it worldwide and this is likely to be increase to 300 million by the year 2025. More than one-fifth of them are Indians. According to the International Diabetes Federation, India has been declared as "Diabetic Capital of the World" at the recent conference in Paris. Plants have been used as sources of drugs for the treatment of diabetes in developing countries, where the costs of conventional medicines are a burden to the population.

Despite the introduction of hypoglycemic agents from natural and synthetic sources, diabetes and its secondary complications continue to be a major medical problem. Many indigenous Indian medicinal plants have found to be useful to successfully manage diabetes. One of the greatest advantages of traditional medicinal plants is that these are readily available and have no side effects. Even WHO has suggested the evaluation of the potential of plants as effective therapeutic agents, especially in areas in which we lack safe modern drugs.

Glucocorticoids in excess inhibit insulin secretion from pancreatic beta-cells, decrease glucose utilization and stimulate glucagons secretion, lipolysis, proteolysis and hepatic glucose

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production. Glucocorticoids can modulate the insulin action at both binding sites and post binding sites and cause decreased glucose utilization in muscles. Glucocorticoids also cause insulin resistance by decreasing hepatic glucose utilization and decreasing glycogen synthesis. Free fatty acids may be elevated in insulin resistance because of impaired insulin-dependant down-regulation of lipolysis, hence leading to increase in triglyceride levels in muscles as well as in other tissues presumably because of excess of circulating free fatty acids, which are then deposited in these organs. The triglycerides are reported to be potent inhibitor of insulin signaling and result in acquired insulin resistance state (Andrews and Walker, 1999).

Traditionally, *Psoralea corylifolia* is used in the treatment of diabetes, lipid disorders, inflammation, ulcer and bronchitis (Kirtikar and Basu, 2005). *P. corylifolia* is reported to have antifungal (Xingyong et al., 2006), antidepressant (Chen et al., 2007), antioxidant, and antibacterial activity (Naznin and Khatunea, 2004). Taking into consideration the traditional claims and reported activities, PC has been studied for its anti-diabetic activity in diabetic animals. Hence the present study was planned to investigate the effect of *P. corylifolia* on dexamethasone-induced insulin resistance in mice.

2. Materials and methods

2.1. Plant material and preparation of extract

Fresh plant of *P. corylifolia* was collected from Aurangabad, Maharashtra, India. The specimen was authenticated at Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, with voucher specimen No. 08–12 and cataloged. The Plant was washed with distilled water and shade dried and latter powdered. This powder was then defatted with petroleum ether and then macerated with methanol for 72 h with occasional shaking. It was then filtered and the solvent was evaporated under vacuum. The yield of methanolic extract of *P. corylifolia* (PC) was 3.4% (w/w). PC when subjected for phytochemical study showed the presence of beta-sitosterol, terpenoids, phenolic compounds, saponins, glycosides and tannins.

2.2. Animals

Albino mice weighing 25–30 g were used for study and were kept in an animal house at 26 ± 2 °C with relative humidity 44–56% along with light and dark cycles of 12 h. Institution Animal Ethics Committee has approved the experimental protocol. Animals were provided with standard diet and water *ad libitum*. The food was withdrawn 18–24 h before the start of the experiment.

2.3. Experimental design

2.3.1. Acute toxicity study (OECD, 425)

The acute toxicity study for methanolic extract of *P. corylifolia* was performed using albino mice. The animals were fasted overnight prior to the experiment and maintained under standard conditions. PC was found safe up to dose of 3000 mg/kg, orally.

2.3.2. Dexamethasone-induced insulin resistance in mice

All the mice were weighed before treatment, group I (normal control) received equivalent amount of 1% gum acacia (1 ml/kg, p.o.), and 30 mice were rendered hyperglycemic by daily administration of a prestandardised dose of dexamethasone (1 mg/kg, intramuscular) for consecutive 7 days and then divided into five groups of six animals each. Group II (DEXA-control) continued to receive only dexamethasone and 1%gumacacia (1 ml/kg, p.o.) for next 15 days, III received Pioglitazone (2 mg/kg, p.o.) along with dexamethasone respectively for 15 days. Groups IV–VI were treated with dexamethasone along with three different doses of PC100, 200, 300 mg/kg, p.o. respectively for 15 days. Simultaneously four other groups (groups VII–X), each with six normoglycemic animals, were administered equivalent amount of Pioglitazone and three different doses of PC100, 200, 300 mg/kg, p.o. respectively (Table 1). On the last day, after overnight fasting, all the animals were weighed and later sacrificed by cervical dislocation. Blood samples were collected and used for estimation of glucose and triglyceride (Gholap and Kar, 2005). Biochemical estimation of plasma glucose and serum triglyceride was done by GOD/POD and GPO/POD method respectively using standard diagnostic kits from Rajesh Chemical Ltd., India.

2.3.3. Hepatic antioxidant enzymes assay (estimation of MDA, GSH, SOD, and CAT)

Liver samples were dissected out and washed immediately with ice cold saline to remove as much blood as possible. Liver homogenates (5%, w/v) were prepared in cold 50 mM Tris buffer (pH 7.4) using Remi homogenizer. The unbroken cells and cell debris were removed by centrifugation at 5000 rpm for 10 min using a Remi refrigerated centrifuge. The supernatant was used for the estimation of GSH (Ellaman, 1959), malondialdehyde (MDA) (Slater and Sawyer, 1971), superoxide dismutase (SOD) (Mishra and Fridovich, 1972) and catalase (Aebi and Bergmeyer, 1974; Colowick et al., 1984) levels (Table 2).

2.3.4. Effect on glucose uptake in isolated mice hemidiaphragm

Glucose uptake in mice hemidiaphragm was estimated by the method described by Chattopadhyay et al. (1992) with some modification. Twelve sets, containing graduated test tubes ($n = 6$) each, were used for study of non-insulin assisted and insulin assisted glucose uptake. The diaphragms were taken out quickly avoiding traumas and divided into two halves. The hemidiaphragms were rinsed in cold Tyrode solution (without glucose) to remove any blood clots. In non-insulin assisted glucose uptake study, one hemidiaphragm of each animal from groups I to VI was exposed to 2 ml Tyrode solution with glucose (2000 mg/l) in respective graduated test tubes. In insulin assisted glucose uptake study, the remaining hemidiaphragm of each animal from groups I to VI was exposed to 2 ml Tyrode solution with glucose (2000 mg/l) + insulin (0.25 IU/ml) in respective graduated test tubes. All the graduated test tubes were incubated for 30 min at 37 °C in an atmosphere of 95% O_2–5% CO_2 with shaking at 140 cycles per minute. Following incubation, the hemidiaphragm was taken out and weighed. The glucose content of the incubated medium was measured by GOD/POD, enzymatic method (Sabu and Subburaju, 2002; Ghosh et al., 2004).Glucose uptake was calculated as the difference between the initial and final glucose content in the incubation medium (Table 3).

2.4. Statistical analysis

The results were expressed as mean ± SEM and statistically analyzed by ANOVA followed by Dunnett test, with level of significance set at $p < 0.05$.