A study of the antidiabetic activity of *Barleria prionitis* Linn

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Introduction

Diabetes mellitus is the most important non-infective epidemic to hit the globe in the present millennium. By the year 2025, India shall have the maximum number of diabetics in the world making it, the "Diabetic capital of the world."[1] Despite the great strides, made in understanding and management of diabetes, the disease and disease-related complications are increasing unabated due to multiple defects, in its pathophysiology.[2] Parallel, to this, the holistic approach of herbs has accelerated the global efforts to harness and harvest medicinal plants having multiple beneficial effects.[3] Some of them have been evaluated and active principles isolated; however, the search for novel antidiabetic drugs continues.[4]

*Barleria prionitis* Linn (Acanthaceae) is a well-known plant in Ayurveda. It is distributed throughout India, Ceylon, and South Asia.[5] The plant is said to be rich in potassium and valued as diuretic.[6] Flavonoids, iridoid glucosides, and fatty acids have also been reported.[7-9] The extract of plant rich in iridoid glycosides is a potent hepatoprotective agent[8] and useful in respiratory infections,[10] whooping cough, and tuberculosis.[11] The juice of leaves is useful in fungal infections,[12] wound healing, bleeding teeth, toothache, and joint pain.[13,14] The roots are used in fever and glandular swelling and have been shown to 100% antifertility activity.[15] The plant has many uses but the antidiabetic potential of the plant is yet to be explored, so *B. prionitis* was selected for the present study.

Materials and Methods

Plant Material and Extract Preparation

Fresh leaves and roots of healthy mature plants of *B. prionitis* after authentification and verification (RUBL20108) were collected from the medicinal garden of Lal Bahadur Shastri College of Pharmacy, Jaipur, where it grows. The leaves and roots were dried under shade, coarsely powdered and were packed separately in airtight containers.

Alcoholic Extract

The dried plant material was coarsely powdered. The powdered mass of each part was defatted with petroleum ether (60-80°C) followed by extraction with alcohol (95% v/v) and water. The yield was found 2.16% in roots and 16.64% in leaves.
The dried alcoholic extract was formulated as suspension using distilled water and the strength of the suspension adjusted according to the dose administered (i.e., 200 mg/kg).

Both the alcoholic extract of roots and leaves drug were administered orally twice a day, for 2 weeks, in a dose of 200 mg/kg body weight, with the help of a gastric catheter.

**Preliminary Phytochemical Screening**

The chromatographic analysis of the root and leaf extract did not show the presence of the alkaloids as per monograph in the 3rd volume of Ayurvedic pharmacopoeia. Beta-sitosterol, saponins, tannins, and flavonoids were found present in both the root and the leaf alcoholic extract. The animals described as “fasted” were deprived of food for 18 h, but had free access to water. The study was carried out in the Toxicology Lab of Zoology Department, University of Rajasthan, and the study protocol was approved by the Institutional Ethics Committee.

**Toxicity Studies**

Adult albino rats of either sex weighing between 180 and 200 g were acclimatized for a period of 7 days at room temperature (25±2°C) and 50±15% relative humidity. They were housed in a standard cage and maintained on standard pellets and water ad libitum. The animals described as “fasted” were deprived of food for 18 h, but had free access to water. No death was observed up to the end of the study. The test samples were found safe up to 2.5 g/kg.

**Induction of Diabetes**

A single dose (150 mg/kg b.w., i.p.) of alloxan monohydrate (Sigma Ltd, USA) dissolved in normal saline was used for induction of Type II diabetes in rats after overnight fasting. After 1 h of alloxan administration, the animals were fed standard pellets and water ad libitum. The animals were stabilized for a week and animals showing blood glucose level (estimated by GOD-POD method) more than 200 mg/dl were selected for the study.

**Experimental Design**

The fasted rats were divided into six groups of six animals each (three group of normal animals and three groups for induction of diabetes). No standard of comparison was used.

- **Group I:** Served as normal control rats and received distilled water.
- **Group II:** Diabetic rats served as diabetic control and received distilled water.
- **Group III:** Diabetic rats received alcoholic extract of leaves (200 mg/kg b.w.) using an intragastric tube for 2 weeks.
- **Group IV:** Normal rats received alcoholic extract of leaves (200 mg/kg b.w.) using an intragastric tube for 2 weeks.
- **Group V:** Diabetic rats received alcoholic extract of roots (200 mg/kg b.w.) using an intragastric tube for 2 weeks.
- **Group VI:** Normal rats received alcoholic extract of roots (200 mg/kg b.w.) using an intragastric tube for 2 weeks.

The drug treatment was carried out every day morning (200 mg/kg b.w.) and evening (200 mg/kg b.w.) with the help of intragastric tube for 2 weeks.

After 2 weeks, body weights were determined and the animals were sacrificed under the influence of anesthetic ether. The blood was collected by heart puncture and the liver was excised and chilled in ice cold 0.9% sodium chloride.

**Methods**

The blood sample withdrawn from the sacrificed animals was centrifuged at 3000 rpm for 10 min. Blood glucose (glycosylated hemoglobin, and serum insulin (RIA using a kit from BARC, Mumbai, India Ltd) were estimated on the 15th day. The excised liver tissue was processed and liver glycogen was estimated.

**Statistical Analysis**

All the values were expressed as mean ± SEM. The data obtained through careful observation were analyzed using Student’s t-test. Wherever required ANOVA followed by Dunnett’s multiple ‘t’-test was used. A "P" Value of less than 0.05% was considered statistically significant.

**Results**

**Effect on Blood Glucose**

Analysis of data shows a decrease in the blood glucose level on treatment with the alcoholic extract of leaves and roots (200 mg/kg, orally for 2 weeks). The alcoholic leaf extract exhibited a statistically significant decrease (p<0.01) in the blood glucose level when comparison was done with the diabetic control group and between before and after treatment. But the decrease with the alcoholic root extract was statistically non-significant [Figures 1 and 2]. Both the test drugs i.e. alcoholic extract of leaves and roots did not affect the blood glucose in normal rats [Figure 3].

**Effect on Serum Insulin Level**

Insulin level was found to be decreased in the alloxan-induced diabetic rats. On administration of both leaf extract (p<0.01) and root extract (p<0.05), there was an increase in serum insulin level which was statistically significant [Table 1].

**Effect on Glycosylated Hemoglobin**

A statistically significant increase (p<0.01) was seen in the level of the glycosylated hemoglobin in the diabetic control group. The alcoholic leaf extract significantly decreased (p<0.01) the glycosylated hemoglobin level, but a moderate and non-significant decrease was seen with alcoholic root extract [Table 1].

**Effect on Liver Glycogen**

Depletion of liver glycogen content was seen in the diabetic control group. A significant increase (p<0.05) in the glycogen content of liver was observed after administration of alcoholic leaf extract, but increase with alcoholic root extract was statistically not significant [Table 1].

**Effect on Body Weight**

Body weight of alloxan-induced diabetic rats was found to be statistically less compared to the normal rats at basal level (before treatment) (p<0.01). Weight gain was not observed after the treatment with either of the test drugs, but the decrease in body weight in alcoholic leaf extract group was found to be very negligible, however statistically non-significant [Figure 4].
The study reports the antidiabetic activity of alcoholic extract of leaves of *B. prionitis* Linn, which is a well-known herb in Ayurveda. Phytochemical analysis of *B. prionitis* shows the presence of sterols, saponins, tannins, and flavonoids. Flavonoids, sterols/triterpenoids, tannins, and phenolics are known bioactive antidiabetic principles. Flavonoids are also known to regenerate the damaged beta cells in the alloxan diabetic rats.

In the present study, alloxan was used as a diabetogen. It induces diabetes by destroying β-cells of the pancreas partially, through production of reactive oxygen species. Alcoholic extract of leaves and roots were assessed for their antidiabetic activity. The alcoholic leaf extract exhibited a significant decrease in the blood glucose level in alloxan-induced diabetic animals. A non-significant decrease was seen with the alcoholic root extract. But both the treatments did not produce hypoglycemia in normal rats, which is a therapeutic advantage.

Insulin level was found decreased in alloxan-induced diabetic rats. Reversal of this effect was seen on treatment by the leaf extract. This may be indicative of regeneration of the islet cells more by the leaf extract, and possibly, attenuation of the alloxan initiated degenerative changes more prominently in the leaf extract-treated group as compared to the root extract-treated group. The same treatment, however, did not increase the serum insulin level in normoglycemic rats, so it can be concluded that the extract has the potential to enhance the glucose-dependent insulin release from the pancreatic beta cells and thereby decrease the blood glucose level only in alloxan-induced diabetic rats. The action of extract is very similar to biguanides, which are also termed as “Euglycemics.” Biguanides bring the elevated blood sugar level to its normal value and do not produce hypoglycemia. Biguanides promote peripheral uptake and utilization of blood glucose and they also exhibit a favorable effect on lipid profile i.e. a decrease in the TGs.

### Table 1:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Normal control</th>
<th>Diabetic control</th>
<th>Root treated</th>
<th>% Change</th>
<th>Leaf treated</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum insulin</td>
<td>43.40 ± 2.71</td>
<td>20.00 ± 1.53</td>
<td>26.00 ± 2.61*</td>
<td>↓30.00**</td>
<td>46.30 ± 4.54**</td>
<td>↑130.00**</td>
</tr>
<tr>
<td>Liver glycogen</td>
<td>4.20 ± 0.27</td>
<td>1.81 ± 0.17</td>
<td>2.65 ± 0.62</td>
<td>↑46.40**</td>
<td>3.56 ± 0.64*</td>
<td>↑96.68*</td>
</tr>
<tr>
<td>Glycosylated hemoglobin</td>
<td>6.00 ± 0.81</td>
<td>09.00 ± 0.64**</td>
<td>08.00 ± 0.89</td>
<td>↓11.00**</td>
<td>7.00 ± 0.71**</td>
<td>↓22.00**</td>
</tr>
</tbody>
</table>

Each value represents the mean ± SEM of six observations, Student’s paired T-test: *P < 0.05, **P < 0.01, ↓-Decrease; ↑- Increase; R- comparison to the diabetic control group
potent hepatoprotective, showing a highly significant decrease in TGs. This suggests that the mechanism of studied herb is similar to that of biguanides.

In diabetes, glycogen content decreases due to enhanced glycogenolysis and the normal capacity of the liver to synthesize glycogen is impaired, which is due to insulin deficiency. The liver glycogen was found depleted in the diabetic control group. A significant increase in the liver glycogen level on administration of alcoholic leaf extract was observed which may be due to an increase in the insulin level by it. Reversal of the depletion indicates attenuation of severity of diabetes and can be considered as an index of the presence of antidiabetic activity in the test drug.

Protein can universally bind non-enzymatically with glucose or other sugars present in the vicinity. The degree of glycation is directly proportional to the concentration of the sugar present in the surrounding medium. Therefore, estimation of glycosylated hemoglobin (HbA1c) gives an accurate reflection of mean plasma glucose concentration over this period and correlates best with the degree of the glycemia. A change in HbA1c of 1% would reflect a blood glucose alteration of about 30 mg%. A significant decrease with leaf extract (P<0.01) was observed in the treated rats as compared to alloxan-induced diabetic rats. On treatment with roots, the decrease was moderate. This is indicative of a better glycemic control for a longer period by the leaf sample.

A significant reduction in the body weight was observed in the alloxan-induced diabetic rats. The decrease in the weight in diabetes is due to continuous excretion of glucose and decrease in peripheral uptake of glucose and glycogen synthesis. The decrease in weight was arrested on administration of alcoholic leaf extract to a greater extent as compared to root extract. All the above observations suggest that the test drug i.e. alcoholic leaf extract can be a promising antidiabetic.

Conclusion

Studies revealed that alcoholic leaf extract of B. prionitis can be considered as an important addition to the therapeutic armamentarium for the treatment of diabetes. Further studies can be undertaken at the cellular and molecular level, which may further elucidate its mechanism in detail.

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References


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