Antidiabetic activity of Zizyphus xylopyrus Fruits

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ABSTRACT
Ziziphus xylopyrus is known for its medicinal properties for sore throats, dysentery, inflammation of the uterus and as an anti-convulsant, Anti-Depressant, anti-inflammatory in all over world. This research was undertaken to test the effect of Ziziphus xylopyrus fruits extract on the diabetes of Rat. Ziziphus xylopyrus fruits extract (100 mg/kg, 200 mg/kg) was administered orally to Rat with the help of oral feeding needle. A total of 84 rats divided in 14 groups were employed in this study. Alloxan induced diabetes model was used in whole study. Serum total cholesterol, serum triglyceride, total protein, was also estimated before and after administration of fruits extract. Fruits extract was significantly (P < 0.001) reduce blood glucose level in alloxan induced diabetic rats. Fruits extract was significantly (P < 0.001) reduce total cholesterol level it also decrease (P < 0.001) triglyceride level. This drug was also increase (P < 0.001) total protein level.

Keyword: Diabetes, Blood glucose, Zizyphus xylopyrus, Kat-ber

1. Introduction
Ziziphus xylopyrus is spiny shrubs and small trees in the buckthorn family, Rhamnaceae, distributed in the warm-temperate and subtropical regions throughout the world[1]. The fruit is an edible drupe, yellow brown, red, or black, globose or oblong, 1–5 cm (0.39–2.0 in) long, often very sweet and sugary, reminiscent of a date in texture and flavour. Zizyphus xylopyrus Fruits is also called as Kat-ber in hindi.This plant is widely used in Turkish as a potent sedative. The root bark of this plant is reported to have antinociceptive, anti-convulsant, Anti-Depressant and anti-inflammatory activity[2]. The major chemical composition of Ziziphus xylopyrus are rich in flavonoids in particular quercetin, quercitrin, kaempferol-4’-methylether and kaempferol, tannins (7.2%), d-7, 3’, 4’-trihydroxyflavan-3, 4-diol and oleanolic acid[3,4,5]. It also contains cyclopeptide alkaloid. flavonoid compounds are reported to have antidiabetic activity. Diabetes mellitus is a chronic metabolic disorder, mainly characterized by disruption in
carbohydrates, protein, and fat metabolism caused by the complete or relative insufficiency of insulin action\(^6\)\(^7\). Diabetes mellitus is a global health problem and the diabetic was constantly increasing. Present investigation was designed to investigate *Ziziphus xylopyrus* fruits for antidiabetic activity using alloxan induced diabetes model.

2. Materials and Methods

**Plant material**

Fresh Fruit of *Ziziphus xylopyrus* were collected from area adjoining forests of Bhopal in the month of March and got authenticated from Department of Botany Dr. H. S. Gour University, Sagar (M.P.), India (Refer no. 294, Herbarium no. bot/her/2013). Extract of *Ziziphus xylopyrus* Fruits was administered in different concentration (100 mg and 200 mg per kg b.wt.) daily for duration of 15 days to rats with the help of an oral feeding needle.

**Animal**

Wistar rats (150–200 g) were group housed (n= 6) under a standard 12 h light/dark cycle and controlled conditions of temperature and humidity (25±2 °C)\(^8\). Rats received standard rodent chow and water ad libitum. Rats were acclimatized to laboratory conditions for 7 days before carrying out the experiments. All the experiments were carried in a noise-free room between 08.00 to 15.00 h. Separate group (n=6) of rats was used for each set of experiments. The animal studies were approved by the Institutional Animal Ethics Committee (IAEC), constituted for the purpose of control and supervision of experimental animals by Ministry of Environment and Forests, Government of India, New Delhi, India.

**Chemicals:** Alloxan monohydrate, Glibenclamide, Normalsaline and *Ziziphus xylopyrus*.

**Hypoglycemic Activity in Rats**

Animals were divided into three groups of 6 rats each.

**Group I:** Rats served as normal-control and received the vehicle (0.5 ml normal saline/day/rat)

**Group II:** Rats (normal) were administered *Ziziphus xylopyrus* (100 mg/kg b.wt./day) in normal saline orally for 7 days.

**Group III:** Rats (diabetic) were administered *Ziziphus xylopyrus* (200 mg/kg b.wt./day) in normal saline orally for 7 days.

**Induction of Experimental Diabetes in Rats**

After fasting, diabetes was induced by a single i.p. injection of 120 mg/kg body weight of 'Alloxan monohydrate' in normal saline. The animals were allowed to drink 5% glucose solution overnight to overcome the drug-induced hypoglycemia. These animals were tested for diabetes after 15 days and animals with blood glucose (fasting) were selected for experimentation.

**Experimental Protocol**

Animals were divided into five groups of 6 rats each.

**Group I:** Rats served as normal-control and received the vehicle (0.5 ml normal saline/day/rat)

**Group II:** Rats served as diabetic-control and received the vehicle (0.5 ml normal saline/day/rat)

**Group III:** Rats (diabetic) were administered *Ziziphus xylopyrus* (100 mg/kg b.wt./day) in normal saline orally for 15 days.

**Group IV:** Rats (diabetic) were administered *Ziziphus xylopyrus* (200 mg/kg b.wt./day) in normal saline orally for 15 days.

**Group V:** Rats (diabetic) were administered Glibenclamide (600µg/kg) in normal saline orally for 15 days.

**Biochemical Determinations**

After 15th day of treatment, blood was collected from the retro orbital sinus of overnight fasted rats. The serum was separated and triglycerides and cholesterol level were determined by using, triglycerides test kit and cholesterol test kit (Span diagnostic Ltd., Surat) respectively. Thereseum total protein was determined by Biuret method\(^9\).

**Statistical Analysis**

The data were expressed as mean ± SEM. The data of hypoglycemic activity and antidiabetic activity were analyzed by one way analysis of variance (ANOVA) followed by “Tukey’s post hoc test.” p value less than 0.05 was considered as statistically significant.

3. Results and Discussion

**Table 1:** Effect of *Zizyphus xylopyrus* on hypoglycemic activity in normal rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Hypoglycemic (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td>96.11±1.88</td>
</tr>
<tr>
<td>II</td>
<td><em>Ziziphus xylopyrus</em> (100 mg/kg)</td>
<td>97.14±2.98</td>
</tr>
<tr>
<td>III</td>
<td><em>Ziziphus xylopyrus</em> (200 mg/kg)</td>
<td>100.32±1.65</td>
</tr>
</tbody>
</table>

**Table 2:** Effect of *Zizyphus xylopyrus* treatment on blood glucose (mg/dl) in normal and diabetic rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Blood glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td>101.16 ± 3.36</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic Control</td>
<td>249.81 ± 2.0</td>
</tr>
<tr>
<td>III</td>
<td><em>Ziziphus xylopyrus</em> (100 mg/kg)</td>
<td>243.03 ± 2.5</td>
</tr>
<tr>
<td>IV</td>
<td><em>Ziziphus xylopyrus</em> (200 mg/kg)</td>
<td>251.07 ± 2.7</td>
</tr>
<tr>
<td>V</td>
<td>Glibenclamide (600µg/kg)</td>
<td>249.10 ± 1.8</td>
</tr>
</tbody>
</table>

Values are expressed as mean±S.E.M (n = 6). Values are statistically significant at * **P<0.001 vs. normal group; * ***P < 0.001 vs. diabetic control group (One-way ANOVA followed by Tukey’s post hoc test).
Table 3: Effect of Zizyphus xylopyrus treatment on biochemical Parameters in normal and diabetic rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>TC (mg/dL)</th>
<th>TG (mg/dL)</th>
<th>Total protein (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td>91.12 ± 3.12</td>
<td>78.16 ± 6.12</td>
<td>8.60 ± 0.10</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic Control</td>
<td>189.11 ± 9.00</td>
<td>121.01 ± 10.5</td>
<td>6.02 ± 0.10</td>
</tr>
<tr>
<td>III</td>
<td>Zizyphus xylopyrus (100 mg/kg)</td>
<td>116.14 ± 5.12***</td>
<td>91.23 ± 5.19***</td>
<td>7.00 ± 0.19***</td>
</tr>
<tr>
<td>IV</td>
<td>Zizyphus xylopyrus (200 mg/kg)</td>
<td>106.5 ± 6.10***</td>
<td>88.53 ± 8.15***</td>
<td>7.70 ± 1.10***</td>
</tr>
<tr>
<td>V</td>
<td>Glibenclamide (600µg/kg)</td>
<td>101.23 ± 7.43***</td>
<td>82.04 ± 7.20***</td>
<td>8.04 ± 1.00***</td>
</tr>
</tbody>
</table>

TC: Total Cholesterol, TG: Total Triglycerides
Values are expressed as mean±S.E.M (n = 6). Values are statistically significant at * ***P<0.001 vs. normal group; * ***P < 0.001 vs. diabetic control group (One-way ANOVA followed by Tukey’s post hoc test).

4. Conclusion
The current research concludes that the extract of fruits of Ziziphus xylopyrus, based on acute toxicity studies are safe at the decided dose level of 100 and 200 mg/kg of body weight. Ziziphus xylopyrus has hypoglycemic effect in diabetic rats and it does not have hypoglycemic action in normal rats. Our study provides a way to study the antidiabetic activity of the Extract of fruits of Ziziphus xylopyrus for the development of anti-diabetic formulation.

Conflict of Interest: We declare no conflict of interest.

5. References