Effects of *Turnera ulmifolia* (Linn.) Leaves on Blood Glucose Level in Normal and Alloxan-Induced Diabetic Rats

D. PRABU, M. NAPPINNAI, K. PONNUDURAI, A. THIRUGNANASAMBANTHAN, S. SRINIVASAN and M. RAMVIKAS

*For author affiliations, see end of text.*

Received July 23, 2008; Revised February 21, 2009; Accepted May 17, 2009

**ABSTRACT**

The methanolic extract of leaves of *Turnera ulmifolia* L was evaluated for its effect on blood glucose in alloxan-induced diabetic and euglycemic rats. The extract were administered at three doses of 100, 200 and 400 mg/kg, p.o. Glibenclamide (10 mg/kg, p.o.) was used as standard for control group. In euglycemic rat, extract were administered at three doses of 100, 200 and 400 mg/kg, p.o. Extract at 400 mg/kg and glibenclamide significantly reduced blood glucose level in normal and alloxan-induced diabetic rats and raised the liver glycogen content significantly. This indicates that the leaves extract of *Turnera ulmifolia* L posses anti-hyperglycemic activity.

**Keywords:** *Turnera ulmifolia*, Euglycemic, Antihyperglycemic, Alloxan-induced diabetes, Rats

Diabetes mellitus is abnormal carbohydrate metabolism and mainly characterized by hyperglycemia. According to world health organization (WHO), the prevalence of diabetes is likely to increase by 35% [1]. Currently, there are over 150 million diabetics patients worldwide and this is likely to increase to 300 million or more by the year 2025 [2]. Though different types of oral hypoglycemic agents are available along with insulin for the treatment of diabetes mellitus, there is a growing interest in herbal remedies because of perceived effectiveness and minimal side effects. Cell damage caused by free radicals appears to be a major contributor to aging and to degenerative disease of aging such as cancer, diabetes, cataract, and brain dysfunction [3]. Free radical formation is controlled naturally by various beneficial antioxidant compounds. Many plant derived substances are becoming increasingly known for their antioxidant activity. The plants containing nutrients serve as protectors against a wide variety of environmental stresses[4].

The plant source of the *Turnera ulmifolia* L. (Turneraceae) can grow to a height of about 2 – 3 feet tall. The leaf is more like an ovate shape. It is commonly-found in India, Brazil, Japan, China and many countries. The margin of leaf is dentate. The leaves branch out alternately. It is traditionally used for treatment of chest ailments, biliousness, indigestion and rheumatism, wound, diabetic disorder and hepatitis [5]. The leaves contain sterol, flavonoids and terpenes and seed contain the unusual fatty acids 9, 10-epoxy-octadec-cis-12-enoic acid [6]. Anti-oxidant capacity, peroxidation suppression and thiobarbituric acid reactive substance inhibition in concentration–dependent assays show that the anti-oxidant activities are strongly correlated with phenolic compound [7]. The leaves extract showed anti-inflammatory activity in rat colitis [8]. Aerial part of the plants showed anti-inflammatory and an anti-ulcerogenic activity [9]. The present study report the preliminary phytochemical screening and anti-hyperglycemic activity of methanolic extract of *Turnera ulmifolia* leaves in euglycemic and alloxan induced diabetic rats.
Preparation of the extract

The dried leaves powder (500 g) was extracted with methanol (90% w/v) for 24 h using a Soxhlet extractor. This methanol extract was concentrated to dryness under reduced pressure and controlled temperature (50-60°C) to yield solid masses (18.7%) that were completely free from solvents and subjected to preliminary phytochemical tests [10].

Chemical, drug and instruments

Alloxan (Sigma, USA), Tween 80 (Lab Chemicals, Pasle) and glibenclamide (Euglucan, Nicholas Piramal, Mumbai) were used for the study. Blood glucose levels of rats were determined using Glucometer (mg/dL) and UV-visible spectrophotometer 1601 model (Shimdzu).

Animals

Inbred colony of adult wistar albino rats (150-200g) of either sex were used for the pharmacological activities. They were kept in polypropylene cages at 25±2°C, with relative humidity 45-55% under 12h:12h light and dark cycles. All the animals were acclimatized to the laboratory conditions for a week before use. They were fed with standard animal feed (Hidustan Lever Ltd., Bangalore, India.) and water ad libitum. The test extracts and the standard drugs were administered in the form of a suspension in water using 1% Tween 80 as suspending agent. The study has got the clearance from the Institutional Animal Ethical Committee (IAEC) as per the directions of the CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals).

Experimental methods

Wistar albino rats were randomly divided into six groups six rats each. Group I (non diabetic control) and Group II (Diabetic control) were given 2 ml/kg, p.o. of 1% Tween 80. Group III, IV and V were administered methanolic extract at 100 mg, 200mg and 400 mg/kg, p.o., respectively. Group VI were treated with glibenclamide (10mg/kg, p.o).

Induction of diabetic

Hyperglycemia was induced by intra-peritoneal administration of alloxan monohydrate (150 mg/kg, i.p.). Blood samples (0.2 ml) were collected from the tail vein of each rat by venous puncture using hypodermic needle, every time for blood glucose determination using Glucometer (mg/dL). The data were subjected to statistical analysis using SPSS 11.0 for Windows. The values are represented as the mean ± SEM for six rats. Statistical significance was determined by one-way ANOVA, followed by Dunnet’s test. Values with p<0.05 were considered statistically significant.

RESULTS

The phytochemical studies of Turnera ulmifolia L showed presence of alkaloids, saponins, tannins, flavonoids, sterol and phenols. Effects of Turnera ulmifolia L extract on euglycemic rats at 100 mg was not significant, while it was significant at 200 mg on 3rd hour (p<0.05) and 5th hour (p<0.01). At 400mg of extract and glibenclamide at all hours significantly (p<0.01) reduced the blood glucose when compared to control (Table 1). The diabetic rats showed significant elevation in blood glucose levels at various intervals, where as extract treatment at 400mg and standard drug significantly (p<0.01) reduced the glucose level in blood at 4th, 8th and 7th day, when compared to the hypoglycemic control group. Treatment of 400 mg at 2nd hour and dose 200mg at all hours significantly (p<0.05) reduced the glucose level in blood. The diabetic rats in the study also showed a marked reduction in hepatic glycogen synthesis. This was regulated to normal range following the administration of 200mg, 400mg and standard group, when compared to hypoglycemic control group (Table 2).
**Effects of T. ulmifolia Leaves on Blood Glucose Level**

**Table 1. Effect of Turnera ulmifolia L. on blood glucose level in euglycemic rats**

<table>
<thead>
<tr>
<th>Group</th>
<th>Fasting</th>
<th>Blood Glucose level (mg/ dL) Mean±SEM</th>
<th>1h</th>
<th>3h</th>
<th>5h</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>96.72±6.03</td>
<td>94.81±7.21</td>
<td>94.02±4.21</td>
<td>92.42±7.40</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>94.86±7.72</td>
<td>91.08±6.78NS</td>
<td>89.78±3.24NS</td>
<td>88.63±2.82NS</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>96.78±4.96</td>
<td>86.38±4.22NS</td>
<td>75.42±4.88*</td>
<td>73.68±6.72**</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>93.41±6.78</td>
<td>80.42±3.75**</td>
<td>66.82±3.42**</td>
<td>57.23±4.03**</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>94.73±5.43</td>
<td>78.42±6.08**</td>
<td>63.42±5.06**</td>
<td>55.42±4.56**</td>
<td></td>
</tr>
</tbody>
</table>

Group I: Normal control  
Group II: 100mg/kg bw, p.o. Glibenclamide administered  
Group III: 200mg/kg bw, p.o. METU administered  
Group IV: 400mg/kg bw, p.o. METU administered  
Group V: 10mg/kg bw, p.o. glibenclamide administered  
Group VI: 400mg/kg bw, p.o. glibenclamide administered

*n = 6, NS: Not Significant, *p<0.05, **p<0.01 when compared with control Group.

**Table 2. Effect of Turnera ulmifolia L. extract on blood glucose level of alloxan-induced diabetic rats**

<table>
<thead>
<tr>
<th>Group</th>
<th>Blood Glucose level (mg/ dL) (Mean±SEM)</th>
<th>Content of Glycogen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial 1h 2h 4h 8h 7th day</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>101.82±6.03 103.31±4.31 102.42±3.47 105.38±4.43 103.4±6.72 102.84±8.44</td>
<td>754.25±20.84</td>
</tr>
<tr>
<td>II</td>
<td>186.48±2.47 190.92±1.02 184.93±3.43 197.42±3.33 208.82±4.31 225.48±3.78</td>
<td>596.53±26.43</td>
</tr>
<tr>
<td>III</td>
<td>188.14±6.03 181.41±2.04NS 176.43±3.24NS 175.48±2.42NS 170.99±0.42NS 164.14±4.78NS</td>
<td>632.43±31.12NS</td>
</tr>
<tr>
<td>IV</td>
<td>185.54±1.06 178.48±2.08NS 170.42±4.03 154.48±2.78* 146.6±0.68* 120.72±2.12*</td>
<td>730.27±43.73*</td>
</tr>
<tr>
<td>V</td>
<td>187.42±1.82 172.19±0.67NS 154.02±2.18* 130.18±1.82** 122.47±3.44** 118.5±6.23**</td>
<td>798.51±27.34**</td>
</tr>
<tr>
<td>VI</td>
<td>184.78±1.83 173.48±0.78NS 149.41±1.03* 124.43±0.83** 112.2±1.48** 101.4±6.83*</td>
<td>830.67±34.52**</td>
</tr>
</tbody>
</table>

Group I: Normal control  
Group II: Diabetic control  
Group III: Alloxan-induced diabetic rats + 100mg/kg bw, p.o. METU administered  
Group IV: Alloxan-induced diabetic rats + 200mg/kg bw, p.o. METU administered  
Group V: Alloxan-induced diabetic rats + 400mg/kg bw, p.o. glibenclamide administered  
Group VI: Alloxan-induced diabetic rats + 10mg/kg bw, p.o. glibenclamide administered

*n = 6, NS: Not Significant, *p<0.05, **p<0.01 when compared with diabetic control group.

**DISCUSSION**

The present study is a preliminary assessment of the antihyperglycemic and euglycemic effect of methanolic extract of *Turnera ulmifolia* L in alloxan-induced diabetic rat. Methanolic extract showed antihyperglycemic and euglycemic effect at different doses. The extract at 100mg/kg, body weight produced mild effect. Dose of 200mg/kg body weight produced reasonably good effect in diabetic rats and higher dose (400mg/kg body weight) showed maximum effect. Hyperglycemia is associated with the generation of reactive oxygen species (ROS) causing oxidative damage particularly to heart, kidney, eyes, nerves, liver, pancreas, small and large vessels and gastrointestinal system [11]. The increased levels of plasma glucose in alloxan-induced diabetic rats were lowered by *Turnera ulmifolia* L administration. Flavonoids, sterols, triterpenoids, alkaloids and phenolics are known to be bioactive antidiabetic principles [14, 15]. Flavonoids are known to regenerate the damaged beta cells in the alloxan-induced diabetic rats [16]. Phenolics are found to be effective antihyperglycemic agents [17]. Various phyto-nutrients and anti-oxidant may possess scavenging activity of free radicals.

Alloxan, a beta-cytotoxin induces chemical diabetes in a wide variety of animal species through damage of insulin secreting cell [18]. It is well established that sulphonylureas produce hypoglycemia by increasing the secretion of insulin from the pancreas [19, 20]. These compounds are active in mild alloxan-induced diabetes whereas they are inactive in intense alloxan diabetes (nearly all beta-cells have been destroyed). No histological studies were carried out to prove this and it is not possible to explain the detailed mechanism of antidiabetic action of *Turnera ulmifolia*. However, since our results showed that glibenclamide reduced the blood glucose levels in hyperglycemic animals, the state of diabetes is not severe. Alloxan-treated animals receiving the leaves extract of *Turnera ulmifolia* L showed rapid normalization of blood glucose levels in comparison to the control and this could be due to the possibility that some beta-cells are still surviving to exert their insulin-releasing effect by *Turnera ulmifolia*. Moreover, like sulphonylureas, oral administration of *Turnera ulmifolia* leaves extract produced hypoglycemia in normal animals. This suggests that the mode of action of the active constituents of *Turnera ulmifolia* is probably mediated by an enhanced secretion of insulin, like sulphonylureas. However, the possibility of enhanced tissue uptake by *Turnera ulmifolia* cannot be ruled out.

Insulin is a stimulator of glycogen synthase system. On the other hand, insulin inhibits glycogenolysis and in lack of insulin, glycogenolysis is not under inhibition of insulin and, therefore, glycogen content of the liver decreases [21]. Glycogen is the primary intracellular storable form of glucose and its levels in various tissues especially skeletal muscle are a direct reflection of insulin activity as insulin promotes intracellular
glycogen deposition by stimulating glycogen synthase and inhibiting glycogen phosphorylase. Since alloxan causes selective destruction of beta-cells of islets of Langerhans resulting in marked decrease in insulin levels, it is rational that glycogen levels in tissues (skeletal muscle and liver) decrease as they depend on insulin for influx of glucose [22, 23]. Moreover, this alteration in muscle and hepatic glycogen content is normalized by insulin treatment [24, 25]. Results showed that hepatic and skeletal glycogen content decreased drastically in diabetic controls which have also been reported earlier [26]. Administration of *Turnera ulmifolia* significantly increases hepatic glycogen levels in diabetic rats. This focuses the one possible way of anti-diabeticogenic action of this extract by improvement of glycogenesis process in muscle and liver. Further experiments are needed to identify the active components of the leaf extract to determine its mechanism of action. Conclusively, it is evident that methanolic extract of *Turnera ulmifolia* contains antihyperglycemic agents capable of lowering blood glucose level in hyperglycemic and normal rats.

**ACKNOWLEDGMENT**

The authors are grateful to Department of Pharmacology, C.L.Baid Metha College of Pharmacy, Chennai, India, for the constant support and encouragement throughout this study.

**REFERENCES**


**CURRENT AUTHOR ADDRESSES**

D. Prabu, Department of Pharmacology, C.L.Baid Metha College of Pharmacy, Thoraipakkam, Chennai -600097, Tamilnadu, India. E-mail: prabu.pharma@gmail.com (Corresponding author)

M. Nappinnai, Department of Pharmacaceutics, C.L.Baid Metha College of Pharmacy, Thoraipakkam, Chennai -600097, Tamilnadu, India.

K. Ponnudurai, Department of Pharmacology, Nandini Nagar Mahavidyalaya College of Pharmacy, Nandini nagar, Nawabganj, Gonda, Uttarpradesh – 271303, India.

A. Thirugnanasambanthan, Department of Pharmaceutical Chemistry, K.L.E. Society’s College of Pharmacy, Rajajinagar, Bangalore-560010, Karnataka, India.

S. Srinivasan, 5, Department of Statistics, Madras Christian College, Chennai-600 045, Tamilnadu, India.

M. Ramvikas, Department of Pharmacaceutics, C.L.Baid Metha College of Pharmacy, Thoraipakkam, Chennai -600097, Tamilnadu, India.