# EFFECT OF FICUS RELEGIOSA ON BLOOD GLUCOSE AND TOTAL LIPID LEVELS OF NORMAL AND ALLOXAN DIABETIC RABBITS

**Noreen Wadood, Abdul Wadood, Mohammed Nisar***

**Department of Pharmacology & Therapeutics, Khyber Medical College, Peshawar and *Pharmacy Department, University of Peshawar**

Background:The present study was planned to observe the hypoglycemic effect of the 'Ficus relegiosa', a traditional medicinal plant. This study was performed to study the possible role of indigenous medicinal plants in the treatment of Diabetes mellitus (type-2) Methods: Normal rabbits were divided into 5 groups (1-5) of six animals each. Group 1 served as control and received 15 ml of water only. Group 2 received tolbutamide 500-mg/Kg body weight. Group 3-5 received the extract of Ficus relegiosa dissolved in 15ml of water in doses of 200 mg/Kg, 250 mg/Kg and 300mg/Kg body weight respectively. The diabetic rabbits were also divided in 5 groups on the same pattern. The blood glucose and total lipid levels were estimated before and 1,2, 3 and 4 hours after the administration of the extract. Results: The extract exerted a significant ($P< 0.05$) hypoglycemic effect in normal rabbits, which was however short lived. The hypoglycemic effect was not significant ($P> 0.05$) in alloxan treated rabbits. The extract had no significant effect ($P> 0.05$) on total lipid levels in normal as well as in alloxan-treated diabetic rabbits. The doses used did not show acute toxicity or result in behavioral changes. Conclusion: From this study it may be concluded that the extract acts by initiating the release of insulin by pancreatic beta cells of normal rabbits.

## INTRODUCTION

A number of indigenous plants are claimed to be useful in the treatment of diabetes mellitus based on folk medicine[1]. Several such plants show hypoglycemic activity when taken orally, for example, Allium cepa[2], Momordica foetida[3], Coccinia indica[4], Momordica charantia[5] and Cuminum nigrum[6]

Ficus relegiosa is a large tree belonging to the family Urticaeae. This tree is given the name of Budhidhidru or tee of wisdom by Buddhists. The leaves of tree are long, petioled, ovate, cordate, narrow acuminate and entire or partially undulated towards the apex. It is commonly known as Pipal and its leaves are used by practitioners of the Unani system of medicine as a gargle in salivation, as a wash for ulcers and as an astringent injection in leucorrhoea.[7] Its roots and leaves have been used for the treatment of diabetes mellitus and to treat infertility in women.[8]

The present work was undertaken with the aim to study the effect of the alcoholic extract of the leaves of Ficus relegiosa on the blood glucose levels and total lipid levels of normal and alloxan-diabetic rabbits. Acute toxicity and behavioral changes were also studied to check the safety of these doses.

## MATERIALS AND METHODS

Experiments were performed on male, adult rabbits of local strain weighing 0.58-1.98 Kg. They were fed on green vegetables and grains and allowed tap water ad libitum.

O-touluidine, glacial acetic acid, thiourea and trichloroacetic acid were obtained from E.Merck, Darmstadt, Germany. Tolbutamide was provided by Hoechst, Germany.

The alcoholic extract was prepared by the method described by Qayum at al [9]. The fresh leaves were obtained from local trees, were dried in the shade and the completely dried leaves were powdered with an electric grinder. The powder was extracted for 8 hours with petroleum ether to give a brown residue. Continued extraction with 95 % alcohol gave a clear solution. Subsequently, this solution was evaporated, then partitioned between water and alcohol and then again evaporated under reduced pressure to obtain the desired material.

The animals were made diabetic by the method described by Akhtar et al[5] was adopted. A group of rabbits was made artificially diabetic by injecting 10% solution of alloxan monohydrate in distilled water into each animal into one of the marginal veins of their ear at dosage rate of 150 mg /Kg body weight. The diabetes mellitus usually develops within a week in the rabbits. Eight days after injection, the blood glucose levels of the surviving rabbits were estimate. Rabbits with blood glucose above 200 mg/100ml were considered as diabetic.

The procedure for collection of blood was adopted as described by Akhtar et al[5]. The blood glucose estimation was done by the method of Winkers and Jacob[10] using the O-toludine reagent. Blood total lipids estimation was done using a total lipid kit (Merckotest ® 3321).

The possible toxic effects of the extract were studied on rabbits of a local strain weighing between 0.9-1.8 kg. The rabbits were divided into 5 groups of ten each. Group I, served as control and received 15 ml of water only. Groups 2-5 received the alcoholic extract of Ficus relegiosa dissolved in 15ml of water in doses of 200, 250 and 300-mg/kg body weight respectively. They were kept under observation for 7 days. The animals were also

closely examined for signs of restlessness, excitement, intoxication and behavioral changes [10].

### Statistical analysis

Mean percent blood glucose were expressed as mg/100 ml $\pm$ standard error in all experiments and Student's 't' test was used to check their significance.

## RESULTS

The effects of different doses of the extract of Ficus relegiosa and tolbutamide on blood glucose levels of normoglycaemic rabbits are shown in Table 1and 11.

The observations show that water used as control in these experiments did not show any significant change ($P>0.05$) on blood glucose levels of normal rabbits.

The mean percent decreases in blood glucose levels produced by 200 mg/Kg of Ficus relegiosa extract at 1,2,3 and 4 hours were $26.72 \pm 0.68$, $27.86 \pm 0.93$, $35.91 \pm 0.69$ and $4.62 \pm 2.41$ respectively. The mean percent decreases are significant ($P>0.05$) at 1,2 and 3 hours, while non significant ($P>0.05$) at 4 hours.

The mean percent decreases in blood glucose levels produced by 250 mg/Kg of Ficus relegiosa extract at 1,2,3 and 4 hours were $31.51 \pm 0.81$, $35.91 \pm 0.90$, $49.26 \pm 0.73$ and $5.36 \pm 0.79$ respectively. The mean percent decreases are significant ($P>0.05$) at 1,2 and 3 hours, while non significant ($P>0.05$) at 4 hours.

The mean percent decreases in blood glucose levels produced by 350 mg/Kg of Ficus relegiosa extract at 1,2,3 and 4 hours were $38.57 \pm 0.81$, $49.51 \pm 0.74$, $61.50 \pm 0.73$ and $5.51 \pm 0.74$ respectively. The mean percent decreases are significant ($P>0.05$) at 1,2 and 3 hours, while non significant ($P>0.05$) at 4 hours.

The mean percent decreases in blood glucose levels produced by 500mg/Kg of tolbutamide at 1,2,3 and 4 hours were 10.2 ± 0.83, 16.8 ± 0.92, 18.3 ± 0.83 and 22.3 ± 0.86 respectively which are significant (P< 0.05) at 2,3 and 4 hours.

The alcoholic extract of the leaves of Ficus relegiosa in various doses had no significant effect on blood glucose levels in alloxan diabetic rabbits (data not shown).

The tolbutamide used in a dose of 500 mg/kg had no significant effect on blood glucose levels in alloxan diabetic rabbits (data not shown).

The alcoholic extract of the leaves of Ficus relegiosa in various doses had no significant effect on total lipid levels in normoglycaemic as well as in alloxan diabetic rabbits (data not shown).

*Table-1: Effect of tolbutamide and Ficus relegiosa extract on blood glucose levels of normal rabbits*

| **Time interval (Hours)** | **Blood glucose in mg/ 100ml** | | | | |
|---|---|---|---|---|---|
| ——— | Control | Tolbutamide | Ficus relegiosa | | |
| ——— | ——— | (500mg/Kg) | (200mg/Kg) | (250mg/Kg) | (350mg/Kg) |
| 0 | 93.6±1.42 (6) | 91.7±2.14 (6) | 89.7±5.7 (6) | 92.8±5.46 (6) | 98.5±4.7 (6) |
| 1 | 93.3±1.43 (6) | 83.0±1.72 (6) | 66.8±4.3* (6) | 64.6±2.6* (6) | 61.62±3.1* (6) |
| 2 | 94.1±1.52 (6) | 77.3±1.61* (6) | 64.9±3.6* (6) | 60.8±2.7* (6) | 51.2±1.65* (6) |
| 3 | 93.2±1.54 (6) | 76.5±1.48* (6) | 58.6±3.26* (6) | 48.3±2.14* (6) | 39.3±1.22* (6) |
| 4 | 93.2±1.45 (6) | 72.5±1.31 (6) | 86.3±4.7* (6) | 88.7±4.6 (6) | 93.8±3.65 (6) |

Figures in parenthesis indicate number of animals, Each value represents the mean ± standard error

* indicates significant change

*Table-2: Mean percent decreases in blood glucose by tolbutamide and Ficus relegiosa extract in normal rabbits*

| **Time interval (Hours)** | **Control** | **Tolbutamide** | **Ficus relegiosa** | | |
|---|---|---|---|---|---|
| ——— | ——— | (500mg/Kg) | (200mg/Kg) | (250mg/Kg) | (350mg/Kg) |
| 1 | 0.39 ± 0.11 (6) | 10.2 ± 0.83 (6) | 26.72 ± 0.68 (6) | 31.51± 0.81 (6) | 38.57 ± 0.81 (6) |
| 2 | 0.51± 0.13 (6) | 16.8 ± 0.92 (6) | 27.86 ± 0.93 (6) | 3591 ± 0.90 (6) | 49.51± 0.74 (6) |
| 3 | 0.43± 0.08 (6) | 18.3 ± 0.83 (6) | 35.91± 0.69 (6) | 49.26± 0.73 | 61.50± 0.73 (6) |
| 4 | 0.45± 0.12 (6) | 22.3± 0.86 (6) | 4.62± 2.41 (6) | 5.36± 0.79 (6) | 5.51± 0.74 (6) |

Figures in parenthesis indicate number of animals, Each value represents the mean ± standard error

## DISCUSSION

The present study revealed that the alcoholic extract of the Ficus relegiosa produced a significant ($P< 0.05$) hypoglycaemic effect when administered orally to normal rabbits. This effect is short lived and lasts only for 3 hours after which the blood glucose is back to normal. The extract of Ficus relegiosa, however, did not show any significant ($P>0.05$) effect on blood glucose levels of alloxan-treated rabbits. For comparison, the effect of the standard hypoglycaemic drug tolbutamide (500 mg/kg) was observed on the blood glucose levels off normal and alloxan treated diabetic rabbits. Tolbutamide produced significant ($P<0.05$) hypoglycaemic effect in normal rabbits but not in alloxan treated rabbits. This finding is in accordance with the observations of Augusti and Benaim[2] and Akhtar et al[11].

Sulphonylureas, including tolbutamide, have been reported to produce hypoglycaemia by stimulating the pancreatic β cells to release more insulin in to the blood stream, thus increasing glycogen deposition in the liver, causing a reduction of glycogen levels, and having an extra pancreatic effect to possibly increase the number of insulin receptors [12].

In view of the similarity between the effects of tolbutamide and Ficus relegiosa, it may be likely that the hypoglycaemic effect of Ficus relegiosa also be medicated through the release of insulin from the pancreatic β cells. A similar mechanism has been proposed to explain the hypoglycaemic effect in normal rabbits of other indigenous plants such as Momordica foetida [3], Momordica charantia [5], Eriobotrya japonica[13]and Acacia arabica [14].

Diabetes mellitus is often associated with hyperlipidaemia[15]. Thus, blood total lipids were also estimated in normal and alloxan diabetic rabbits after oral administration of alcoholic extract of the leaves of Ficus relegiosa, which significantly reduce the blood glucose levels but not blood total lipid levels in normal rabbits. The total blood lipids were markedly increased in alloxan diabetic rabbits, but were not lowered by the extract of Ficus relegiosa. Similarly tolbutamide had no significant effect in lowering the total lipids in normal as normal as well as in alloxan diabetic rabbits.

However, the reason for the short duration of action of the extract remains to be established.

Acute toxicity studies did not reveal visible signs and symptoms of toxicity.

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**Address for correspondence**

**Dr Noreen Wadood,** Department of Pharmacology & Therapeutics, Khyber Medical College, Peshawar, Pakistan