HYPOGLYCEMIC EFFECTS OF LEUCODELPHINIDIN DERIVATIVE ISOLATED FROM FICUS BENGALENSIS (LINN.)

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Abstract: A Leucodelphinidin derivative isolated from the bark of Ficus bengalensis Linn demonstrated hypoglycemic action at a dosage of 250 mg/kg given both in normal and alloxan diabetic rats. It’s action is closely similar to that of an effective dose of glibenclamide (2 mg/kg) tested under the same conditions. However, after a glucose load the plant product is only just significantly active but not as effective as the sulphonylurea. This efficacy of the plant product as a hypoglycemic agent adds to its other therapeutic effects, as it belongs to the class of flavonoids.

Key words: Ficus bengalensis Linn
alloxan diabetes
leucodelphinidin glibenclamide glucose flavonoids

INTRODUCTION

The therapeutic use of Ficus bengalensis Linn (Banyan tree) in the treatment of diabetes mellitus has been reported (1, 2). Both the water soluble and ethyl acetate soluble fractions of the bark were shown to be active. A glycoside of leucopelargonidin derivative from the former and two separate derivatives of leucocyanidin and leucodelphinidin from the latter were isolated (3). The first two compounds and a water insoluble trisaccharide of leucocyanidin derivative also isolated from the same bark (3) were found to possess antidiabetic effect (2, 4, 5). The aim of the present study is to test and compare it with glibenclamide the remaining compound viz leucodelphinidin derivative. It had shown peak hypoglycemtic action at two hours after its administration in a pilot study on normal rats (about 20% blood glucose reduction).

METHODS

Fresh bark of Banyan tree was collected locally and the middle saffron coloured part of it, was separated and dried under the sun. It was ground well and defatted by extraction with petroleum ether (B.P. 40-60°C) and solvent ether exhaustively (24 hr each) in a soxhlet apparatus. These extracts were discarded. The bark powder was taken out of the soxhlet and dried again to remove the solvents. It was put into the soxhlet and extracted exhaustively with double distilled alcohol (8 hr). The alcoholic extract was collected and the solvent removed under reduced pressure. The tarry residue left behind was stirred with enough water to dissolve all the water soluble fraction. The mixture was allowed to stand overnight when a red precipitate and a red solution were separated. The precipitate was filtered out and allowed to dry in the funnel. This water insoluble residue was dissolved in methanol: chloroform (30: 2.5V/V)
mixture and chromatographed over silica gel-G of 60 to 120 mesh (3). Elution of column with methanol-chloroform (1 : 11 V/V) gave the red coloured compound 5,7,3' trimethylether of leucodelphinidin 3-0-α-L rhamnoside (Fig. 1) with a yield of 200 mg/kg bark. It was crystallised from ethylacetate-petroleum ether mixture. The compound with a melting point of 171°C is soluble in ethyl alcohol, methyl alcohol and ethyl acetate. With alcoholic hydrochloric acid, it developed a purple colour, which deepened on warming. With FeCl₃ it gave a blue colour which is characteristic of flavonoids.

![Chemical structure](image)

**Fig. 1 : Leucodelphinidin derivative.**

R = Rhamnose

### Animal experiments:

Studies were conducted on normal albino rats as well as those which were made diabetic by a subcutaneous injection of Alloxan monohydrate (160 mg/kg). After one month when the condition of diabetes was stabilized, rats with a blood glucose range of 200-250 mg/100 ml were selected.

Rats were fed on a laboratory diet (Gold Mohar, Lipton India Ltd., Bangalore). Blood was collected from the venous pool of the eyes of 18 hr fasting rats for glucose estimation by the method of glucose oxidase.

Six rats each were grouped in (3 + 3) groups of normal and diabetic and each group was tested as listed below:

Drugs were administered with a stomach tube after the determination of their fasting blood glucose levels (FBG).

1. Normal control: Given normal saline (10 ml/kg).
2. Normal: Administered trimethyl ether of leucodelphinidin 3-0-α-L rhamnoside (250 mg/kg).
3. Normal: Administered glibenclamide (2 mg/kg).
4. Diabetic: Given normal saline (10 ml/kg).
5. Diabetic: Administered leucodelphinidin as the above derivative and hereafter called leucodelphinidin (250 mg/kg).
6. Diabetic: Administered glibenclamide (2 mg/kg).

After administrations as shown above, blood glucose was again estimated after two hrs in each animal and the glucose statistically analysed by student’s t-test.

### Effects of glucose tolerance:

Three groups of diabetic rats belonging to groups 4-6 were also given a solution of A.R. glucose (100 mg/ml) at a dosage of 3 g/kg after 30 min of administration of the drugs. Blood glucose was determined every 30 min for 2.5 hours. The mean percentage rise in each group was calculated and the values statistically analysed.

### RESULTS AND DISCUSSION

Both leucodelphinidin and glibenclamide decreased significantly the FBG of normal and diabetic rats by 20 to 24% at two hours (see Table I). In GTT the maximum percentage rises of blood glucose in leucodelphinidin and glibenclamide treated groups were 48 and 33 respectively which are far below that of a control maximum rise of 71% (Table II).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Blood glucose mg/100 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 hr</td>
</tr>
<tr>
<td><strong>Normal rats</strong></td>
<td></td>
</tr>
<tr>
<td>Saline</td>
<td>77±0.02±7.7</td>
</tr>
<tr>
<td>Leucodelphinidin</td>
<td>82±8</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>81±2.7</td>
</tr>
<tr>
<td><strong>Diabetic rats</strong></td>
<td></td>
</tr>
<tr>
<td>Saline</td>
<td>295±0.01±11.0</td>
</tr>
<tr>
<td>Leucodelphinidin</td>
<td>300±0.01±14</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>298±0.01±12</td>
</tr>
</tbody>
</table>

*P < 0.01; **P < 0.001 as compared to 0 hr.
TABLE II: Effect of leucodelphinidin and glibenclamide treatment on glucose tolerance of diabetic rats (values are mean±S.D.).

<table>
<thead>
<tr>
<th>Group</th>
<th>0</th>
<th>0.5</th>
<th>1</th>
<th>1.5</th>
<th>2</th>
<th>2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic control</td>
<td>207±10·35</td>
<td>257±12·85**</td>
<td>336±15**</td>
<td>342±13·2**</td>
<td>355±12·9**</td>
<td>340±13·2**</td>
</tr>
<tr>
<td>(250 mg/kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leucodelphinidin</td>
<td>220±11</td>
<td>250±12*</td>
<td>310±12·3**</td>
<td>315±12**</td>
<td>325±11·5**</td>
<td>305±13·0**</td>
</tr>
<tr>
<td>(2 mg/kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>225±11</td>
<td>275±12·5</td>
<td>300±13·2**</td>
<td>285±12**</td>
<td>235±11</td>
<td>227±11·4</td>
</tr>
</tbody>
</table>

*P < 0·01; **P < 0·001

The mean percentage rise of blood glucose in the control is 57·5±17 as against the significantly low percentage rises of 37±12 and 17±9 respectively in the above treated groups (P<0·05 and 0·001). These results suggest that if glibenclamide improves the glucose tolerance in diabetic condition by 70%, the leucodelphinidin does so only by 35%. These variations may reflect the superiority of the 3rd generation sulphonylurea as a hypoglycemic agent over the plant principle.

Flavonoids have a wide spectrum of pharmacologic properties (6), the mechanism of which is largely unknown. Glibenclamide and flavonoids with structures similar to that of leucodelphinidin (Fig. 1) have shown to act as insulin secretagogues (4, 7, 8). According to report (6, 9) the presence of two hydroxyl groups in ring C and the absence of a ketogroup and a double bond in ring B of flavonoids as found in this compound, increase their therapeutic effects without toxicity. Therefore, leucodelphinidin may become useful as an antidiabetic agent and further studies are required to elucidate the mechanism of its action.

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2. Brahamchari HD, Augusti KT. Isolation of orally effective hypoglycemic compounds from Ficus bengalensis Linn. Indian J Physiol Pharmacol 1964; 8: 60-64.