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HYPOGLYCEMIC AND ANTIHYPERGLYCEMIC EFFECT OF LEAVES OF *VINCA ROSEA* LINN.

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Abstract : Oral administration of water fraction of alcoholic extract of leaves of *Vinca rosea* (fam. apocynaeceae) led to marked lowering of blood glucose level in normal and streptozotocin induced diabetic rats. The hypoglycemic effect of the fraction was comparable with that of tolbutamide.

Key words : *Vinca rosea* hypoglycemia antihyperglycemic effect

INTRODUCTION

A number of crude drugs extracted from plant sources such as garlic *(Allium sativum)*, neem *(Azadirachta indica)*, Jaman *(Eugenia jambolana)* and gurmur *(Gymneme sylveste)* have been reported to possess hypoglycemic activity (1). *Vinca rosea* (fam. apocynaeceae) *(Bengali*, Nayantara), a native of West Indies, is a medicinal plant commonly grown in Indian gardens. Various parts of this plant have been reported to exert hypotensive and hypocholesteremic activity (2,3). Dhar et al (4) have reported that the plant can cause contraction in isolated guineapig ileum. Chopra et al (5) have mentioned that the plant is used as a remedy for diabetes and the infusion of leaves administered in menor and juice of leaves is applied in wasp sting. They also mentioned that leaves contain a syrupy alkaloid, a resin and essential oil. Vincristin and Vinblastin sulphate obtained from leaves of *Vinca rosea* have been known to possess antileukemic property (6). Although Chopra et al (5) have mentioned that the plant can be used as remedy for diabetes, no systematic study on the hypoglycemic activity of leaves seems to have been reported. In the present study the hypoglycemic effect of water soluble part of ethanolic extract of leaves of *Vinca rosea* has been investigated in experimental animals and compared with the effect of a standard hypoglycemic drug.

METHODS

Alcoholic extract of matured leaves of *Vinca rosea* was dissolved in distilled water and filtered. The filtrate was evaporated to dryness. The dried mass was purified by extracting serially with petroleum ether, chloroform and ethanol in Soxhlet apparatus. Each fraction was concentrated on distillation. For studying biological activity the extracts were dissolved in normal saline. 500 mg/ml solution was used in experiments.

Albino rats of Wistar strain of either sex weighing 100-150g were used. Six animals were used for each group of study. Animals were kept on a standardised diet and water ad *libitum*. For experimental purpose animals were kept fasting overnight but were allowed free access to water.

PRELIMINARY STUDIES WITH DIFFERENT FRACTIONS

Each fraction (petroleum ether, chloroform and ethanol) was given orally with the help of a gastric tube to conscious rats in a dose of 1000 mg/kg after taking the control blood samples. Further samples of blood were collected at 2 h, 4 h and 6 h after administering the fractions. Control animals received equal volume of saline. Tolbutamide (250 mg/kg,

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po) served as the reference standard in all the animals. Blood samples were collected from orbital sinus and blood glucose was estimated by the glucose oxidase method (7).

STUDIES WITH ETHANOLIC EXTRACT

(a) *Effect on normal rats:* Ethanolic extract in graded doses (100, 250, 500 and 1000 mg/kg, po) was given to normal rats after taking control blood samples. Further samples of blood were collected 2 h, 4 h and 6 h after treatment.

(b) *Effect on oral glucose tolerance:* Glucose tolerance curve was obtained by feeding glucose orally at a dose of 10 g/kg and blood samples were collected at 0 h, 0.5 h, 1 h and 2 h of administration of glucose. The study was repeated in rats in which 500 mg/kg of the extract was given orally 3½ h before eliciting the glucose tolerance curve.

(c) *Interaction with exogenous insulin:* Soluble insulin (1 IU/kg) was injected intraperitoneally to fasting rats and blood samples were collected at 0 h and at the end of 1 h, 2 h and 3 h of treatment. A similar study was repeated with the extract (500 mg/kg, po) given 2 h prior to insulin.

(d) *Effect on streptozotocin induced diabetic rats:* In this group of rats blood samples were collected 24, 48 and 72 h after an intraperitoneal injection of streptozotocin at a single dose of 50 mg/kg body weight. Stable hyperglycemia was produced after 72 h and the effect of the extract was tested. Extract (500 mg/kg) was given orally 72 h after streptozotocin injection after drawing the first blood sample. Further samples of blood were collected 2, 4 and 6 h after addministration of the extract.

RESULTS

Amongst the fractions tested, maximum activity was obtained with water soluble ethanolic extract which led to 26.22, 31.39, 35.57 and 33.37 per cent reduction in blood sugar at the end of 4 h at the doses of 100, 250, 500 and 1000 mg/kg, per orally (po) respectively. It was also noted that 500 mg/kg, po dose of the extract decreased the blood sugar level to the maximum extent (35.57 per cent) at the end of 4 h (Fig.1). In order to check whether there was a statistically significant difference in hypoglycemia acheived by the four doses at 4 h, Scheffe's procedure (9) for multiple comparison of all the four groups of doses along with control group was applied. The estimated F-value at 5 per cent level was higher than the tabulated figures indicating a statistically significant difference in the hypoglycemic effects elicited by the four doses.

EFFECT ON ORAL GLUCOSE TOLERANCE

In glucose fed rats the extract increased the tolerance for glucose significantly ($P<0.001$) 1/2 h after glucose administration. After 1 hour the extract-induced glucose level maintained a steady value almost overlapping with tolbutamide-induced level (Fig. 2).

Interaction with exogenous insulin: The extract was found to potentiate the hypoglycemic effect of exogenous insulin. Insulin 1 IU/kg, ip produced 35.48 per cent fall in blood sugar at the end of 2 h without causing any convulsions. 500 mg/kg of the extract was found to produce 35.57 per cent fall in blood sugar at the end of 4 h. To coincide the peak effects of extract and insulin, extract (500 mg/kg, po) was administered 2 h before insulin injection. It was observed that all the rats developed convulsions without any mortality at the end of 1 h of insulin injection and the reduction in blood sugar was 72.62 per cent. However, maximum reduction was attained 2 h after insulin injection (75.62 per cent) i.e. 4 h after extract administration which is more or less same as observed after 3 h (76.71 per cent) of insulin injection (Fig. 3). This can be compared with the suppression of glucose level when the drug alone was used (Fig. 1).

Effect on streptozotocin induced diabetic rats: In streptozotocin induced diabetic rats the average fasting blood sugar was 280-290 mg/dl which can be considered as mild diabetes and the fall in blood

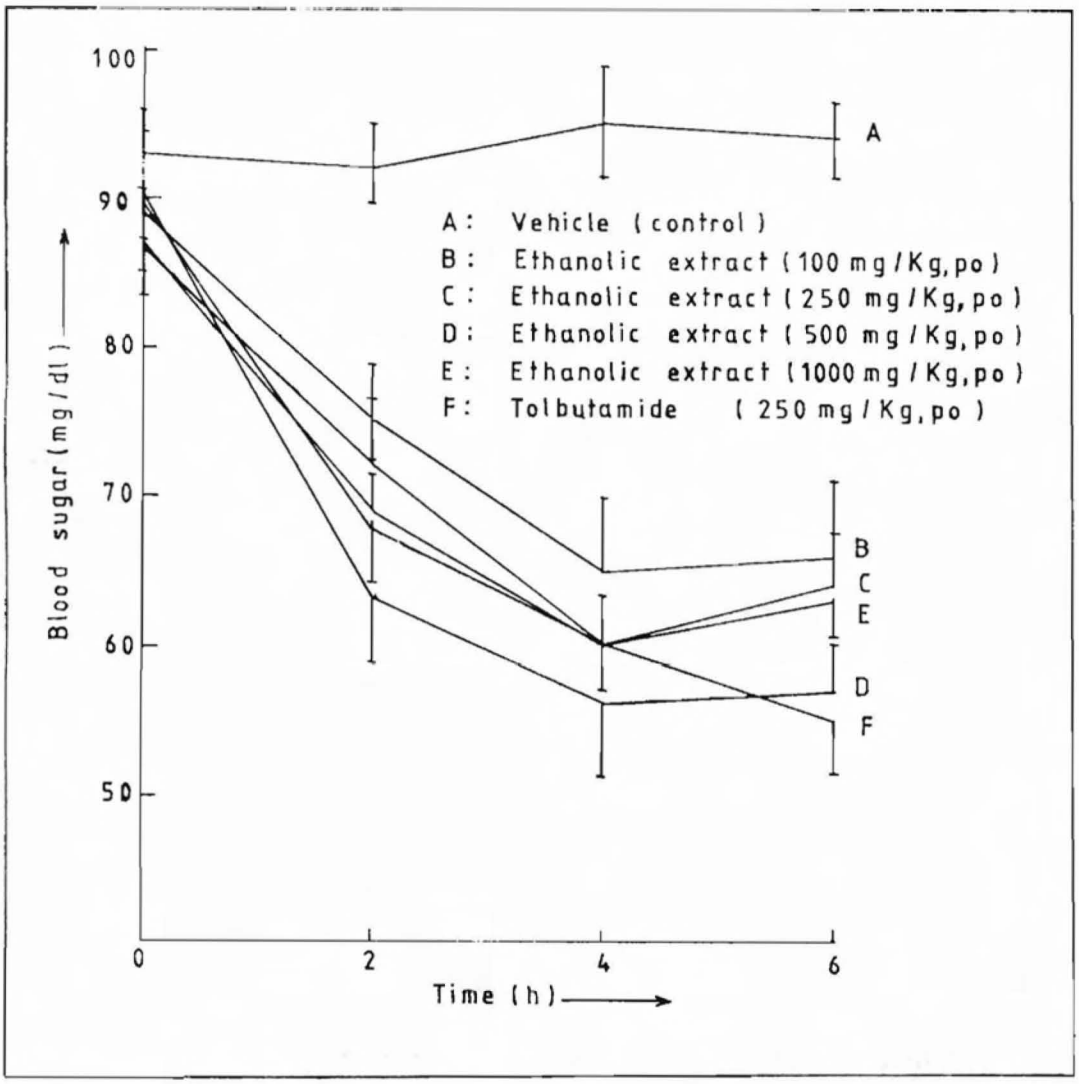

Fig. 1 : Dose response curve of ethanolic extract of leaves of *Vinca rosea*. Each point represents the mean of six observations, and the bars represent the standard error.

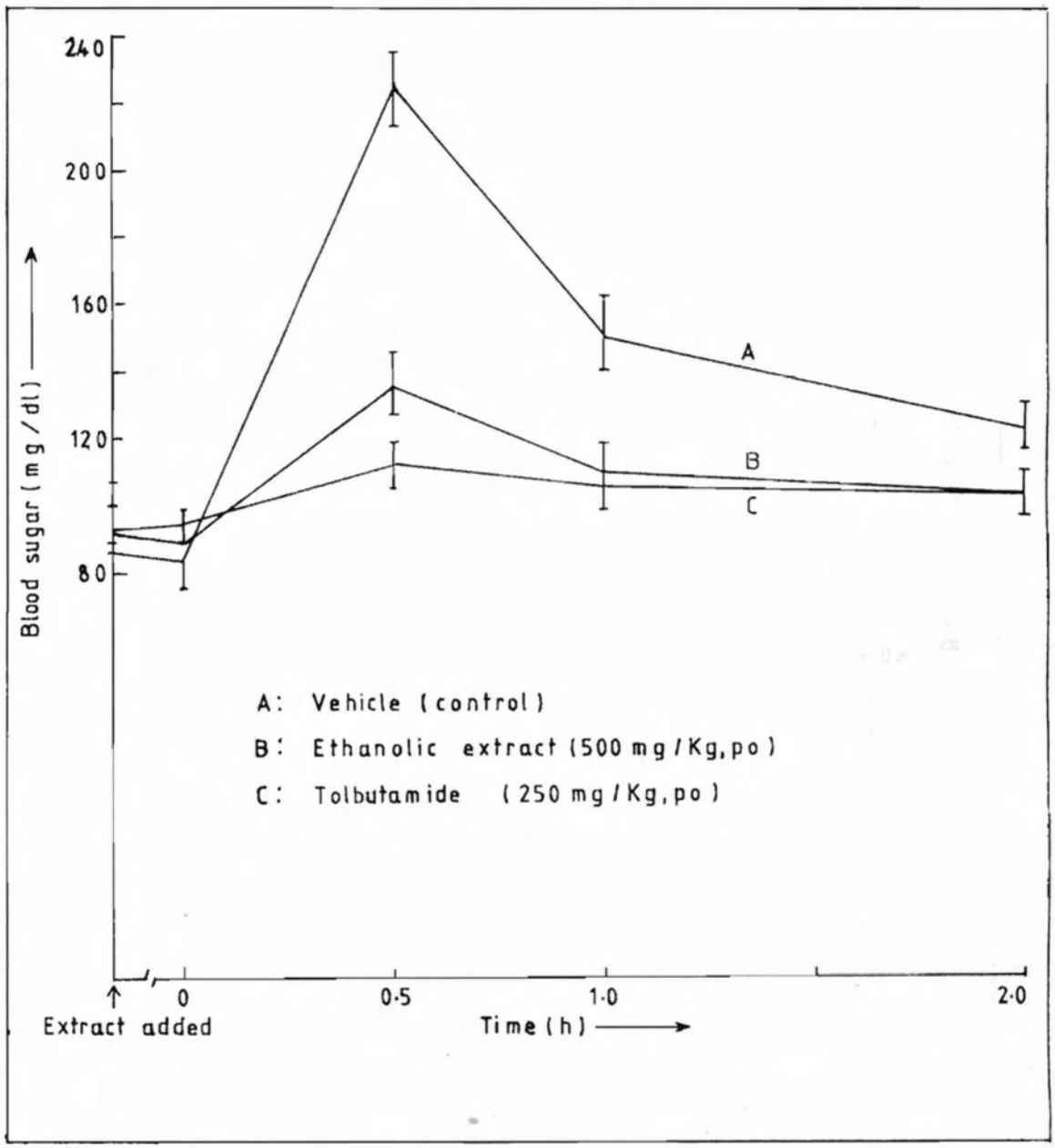

Fig. 2 : Effect of ethanolic extract of leaves of *Vinca rosea* on oral glucose tolerance in rats. Each point represents the mean of six observations, and the bars represent the standard error.

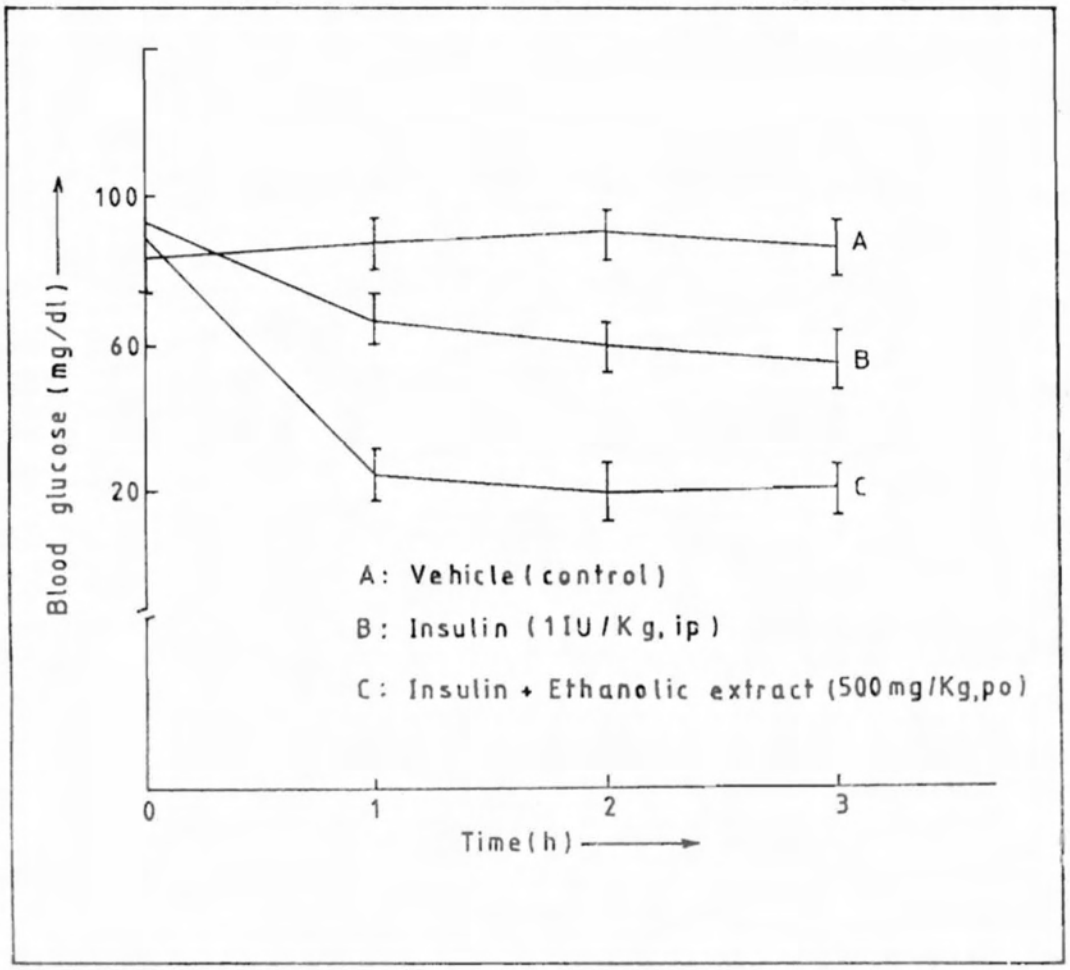

Fig. 3: Interaction of ethanolic extract of leaves of *Vinca rosea* with exogenous insulin in normal rats. Each point represents the mean of six observations, and the bars represent the standard error.

sugar at the end of 4 h was 20.67 per cent with the extrct (500 mg/kg, po) and 33.27 per cent with tolubtamide (250 mg/kg, po) respectively ($P < 0.01$; Fig. 4). At the end of 2 h and 6 h the fall in blood sugar level was 15.47 and 19.92 per cent for the extract and 10.12 and 32.16 per cent respectively for tolbutamide.

The hypoglycemic potentiality of the extract was comparable to that of tolbutamide in normal and diabetic rats. It was observed that the extract (500 mg/kg, po) is equipotent in normal rats (Fig. 1) and in diabetic rats the activity of the extract was about 60 per cent that of tolbutamide (Fig. 4).

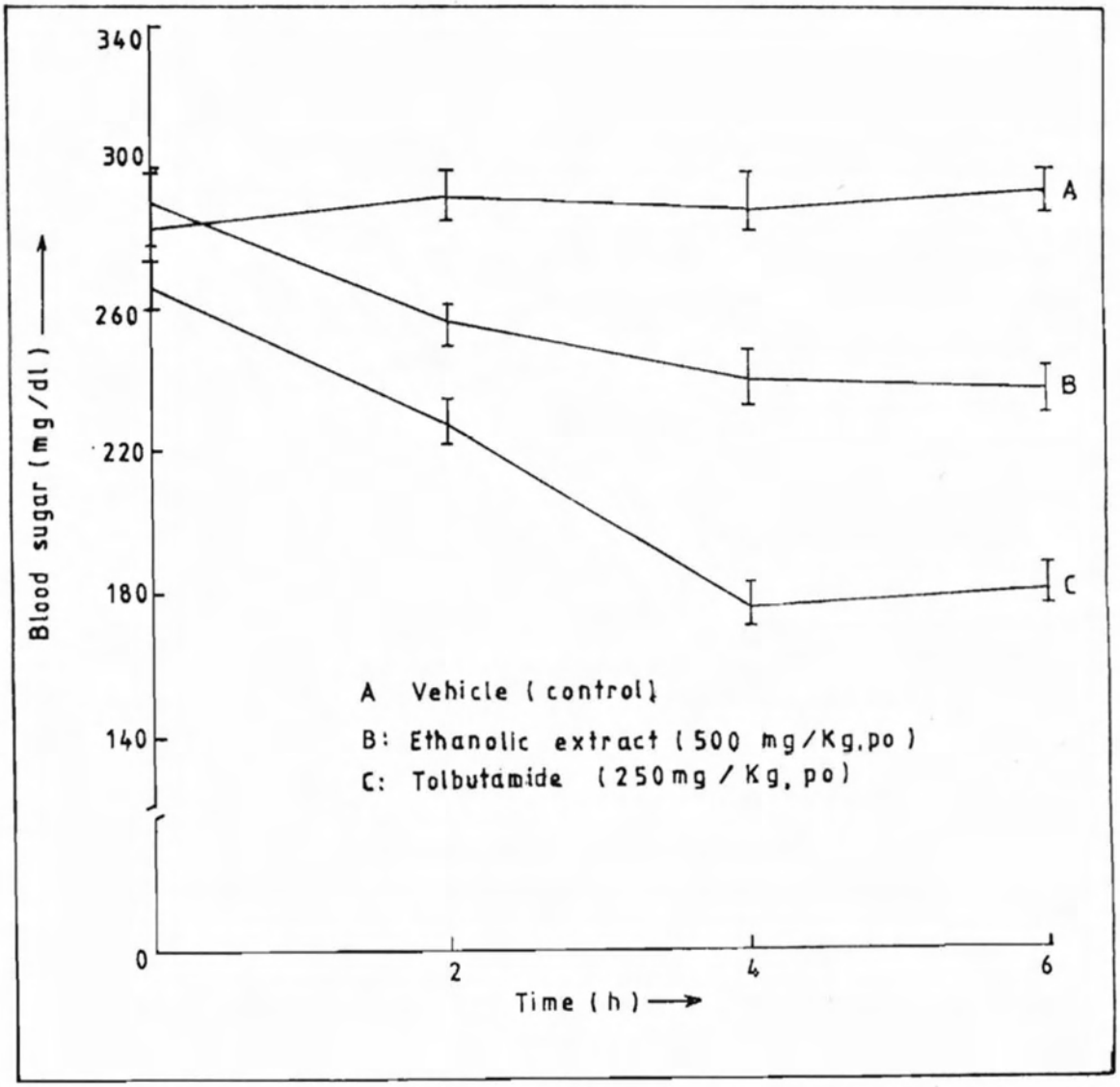

Fig. 4 : Effect of ethanolic extract of leaves of *Vinca rosea* in diabetic rats. Each point represents the mean of six observations, and the bars represent the standard error.

DISCUSSION

The results revealed that a water soluble alcoholic extract of *Vinca rosea* leaves suppresses the glucose level in normal fasting, glucose-fed and diabetic rats when compared to the placebo-treated animals (Fig. 3). The efficacy of the comparatively low dose of the extract (500 mg/kg, po) vs 250 mg/kg, po of tolbutamide indicates its lower toxicity. This is supported by the fact that even with the 4000 mg/kg, ip dose, no gross behavioural changes were observed in mice. Also the results show that the water soluble ethanolic extract may potentiate the hypoglycaemic effect of insulin. The syrupy alkaloid,

resin and essential oil reported by Chopra et al (5) might be either totally or partially responsible for the effects observed by us. Vincristin and vinblastin sulphate obtained from the leaves can not be ruled out to have antihyperglycemic properties although they have been marked as antileukemic agents (6).

The results reveal that the maximal glucose suppression occured after 4 h of treatment by the effective dose of 500 mg/kg of the water soluble ethanolic extract. The hypoglycemic responses induced by different doses have been found to be distinctly and significantly different at 4 h period. Thus the choice of 500 mg/kg as effective oral dose is not arbitary. This is in conformity with an earlier observation by Chakraborty et al (8) where the same dose was found to be most suitable for reducing blood glucose level in diabetic rats. Thereafter the glucose level rose again even by the treatment of a higher dose of the extract. The possible implication of these results seems to be a 'switching on' of some 'recovery mechanism' inside the system and/or the system becomes resistant to the extract as far as its hypoglycaemic effect is concerned.

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