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Oral hypoglycaemic activity of a commercially available herbal preparation

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Summary

The aim of this study was to establish the oral hypoglycaemic activity of a commercially available herbal powder (mixture of equal parts of *Salacia reticulata* Wight, *Strychnos potatorum, L.F. Cardiospermum microcarpum, H. B. K. and Santalum album,* L) used in the treatment of diabetes mellitus.

This was shown by demonstrating the ability of the herbal mixture given orally, at a dosage of 2mg/100g body weight, to lower the fasting blood glucose levels and to improve glucose tolerance in healthy male Sprague – Dawley rats.

The results indicate that the extract significantly lowered the fasting blood glucose levels in the treatment group 1 h., 2 h., and 3h. after oral administration of the extract, when compared with those of the control group which received distilled water ($p<0.05$, <0.01, <0.01 respectively). Maximum hypoglycaemic activity (12.2% reduction of fasting blood glucose) was observed 2 hours after administration of the extract. When the glucose tolerance test was performed, the control group of animals given distilled water, followed one hour later by an oral dose of 50% w/v glucose solution, showed the maximum increase (51.1%) in blood glucose concentration, after one hour. In contrast, the animals treated with the extract showed a significant improvement in their ability to utilise an external glucose load (maximum increase was only 28.8%) ($p<0.001$). The area under the curve of percentage increase in blood glucose was also significantly less in the treatment group than in the control group ($p<0.001$).

Introduction

Despite the progress of conventional chemistry and pharmacology in producing effective drugs, several thousands of medicinal plants are still used throughout the world in therapeutics, including the treatment of diabetes mellitus. The aqueous extracts of plants are orally administered to control diabetes mellitus (1, 2, 3). Different parts such as bark, roots, leaves and stems either singly or in combination are prescribed by Ayurvedic physicians in the treatment of diabetes. Though more than 400 such plants are reputed to have hypoglycaemic activity, only a few of them have received adequate medical or scientific evaluation (4).

In Sri Lanka, approximately 40 plants are reputed to have oral hypoglycaemic activity (1). Among these, the most widely used are *Momordica charantia*, L, *Ficus benghalensis*, L, *Aegle marmelos*, (L.) Corr, *Salacia reticulata*, Wight and *Gymnema sylvestre*, R. Br. ex Schult.

The herbal mixture with the claimed oral hypoglycaemic activity, used in this study consists of S. *reticulata* (family Hippocrateaceae; Sinhala – Kothalahimbutu), *Strychnos potatorum*. L.F. (family – Loganiaceae; Sinhala – Ingini), *Cardiospermum microcarpum* H.B.K. (family – Sapindaceae; Sinhala – Welpenala) and *Santalum album* L. (family-Santalaceae; Sinhala – Sudu – Handun) (5). Though the aqueous extract of *S. reticulata* root bark has been shown to possess oral hypoglycaemic activity (6) no precious study has been done to determine the hypoglycaemic activity of the particular combination of herbs in the mixture under investigation.

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The present study was undertaken because of the widespread use of the herbal mixture by diabetics in Sri Lanka. Its popularity is evidenced by the production of the preparation in commercial quantities by a company in Colombo. Hence there is both a need as well as a justification for a close scrutiny of the reported efficacy of this preparation in the treatment of diabetes mellitus.

Materials and Methods

All experiments were carried out at room temperature (30°C±3°C).

Experimental animals

Healthy adult male Sprague – Dawley rats (body weight 200g ± 50g) were maintained on a standard laboratory diet purchased from the Oils and Fats Corporation of Sri Lanka. The animals were fasted overnight (16-18 hours) before the commencement of all experiments.

Preparation of the herbal extract

Each of the herbs in the mixture was purchased in a powdered form from William Grinding Mills, Dehiwela. The products did not carry an expiry date and were tested within two weeks of purchase. The herbal powders were mixed in equal quantities and an extract was prepared as follows: 10g of the mixture was boiled with 1000 mL of distilled water for about 1 h until the final volume was 500 mL. This was centrifuged for 5 min. at 3000 rpm and the supernatant was used. The method of preparation recommended by the manufacturers is to add 1000 mL of boiling water to 20g of the herbal mixture and keep for 10 minutes. After this period the mixture was centrifuged at 3000 rpm for 5 min. and the supernatant used. As the supernatant prepared by this method did not have any effect on the fasting blood glucose levels, the modified method described above was used.

Administration and dosage of herbal extract

The drug was administered by oral intubation while the animals were under light diethyl ether anaesthesia. The dosage (20 mg/mL/100g body weight) corresponded to the normal therapeutic dose (2 tea spoons = 10g) of the plant extract administered to human adults.

Blood glucose estimation

Blood samples (50 µL) were obtained using a microcap (Drummond Scientific company, U.S.A.) by tail puncture when the animals were under light anaesthesia, and blood glucose was determined by the glucose oxidase method (7).

Effect of the herbal extract on fasting blood glucose level

Rats were fasted overnight (n=28). The animals were randomly divided into two groups after taking blood samples for the determination of fasting blood glucose levels. The control group received distilled water (1mL/100g body wt.), while the treatment group received the herbal extract. After the administration. blood samples were collected at 1 h intervals for 3 h and the glucose levels estimated.

Effect of the extract on the glucose tolerance test

Rats were fasted overnight (n=26). After taking blood samples for the determination of fasting blood glucose levels, they were divided into two groups. The control group received distilled water, while the treatment group received the herbal extract. One hour after the administration, all received an oral dose (1 mL/100g body wt.) of glucose solution (50% w/v). Blood samples were collected at 1 h intervals for 3 h and glucose levels estimated. The area under the curve of percentage increase of blood glucose concentrations for each animal was calculated as follows: (8)

$$\text{Total area} = \text{time interval} \times \frac{\text{first} + \text{last concentrations}}{2} + \text{sum of all other concentrations}$$

Results and Discussion

The effect of the herbal extract on fasting blood glucose is given in Figure 1. It is clear that in the treatment group, there was a decrease in the fasting blood glucose values expressed as a percentage of the zero time blood glucose values at 1, 2 and 3h after the administration of the extract. The maximum effect (12.2% reduction, $p<0.001$) was seen at 2 h. In contrast, the corresponding curve for the control group showed little deviation from the zero time level.

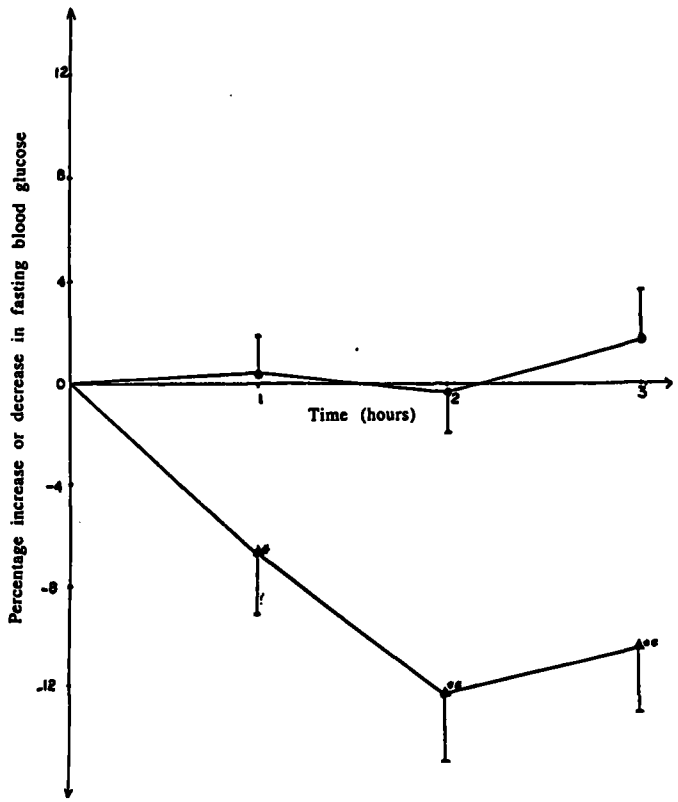

Figure 1

Effect of the herbal mixture on fasting blood glucose levels. Two groups of fasted rats (n=28) were orally administered either the extract of the herbal mixture or distilled water (1 mL/100 g body wt.) Blood samples (50 µL) were collected at zero time and at 1 h intervals for glucose assay. Results are expressed as percentage increase/decrease of blood glucose with respect to the zero time blood glucose values. Results of 3 experiments were pooled. Mean ± SEM values are given.

●——● distilled water. ▲——▲ herbal mixture.

*$p < 0.05$ **$p < 0.01$

The effect of the herbal extract on oral glucose tolerance is illustrated in Figure 2. The results are given as a percentage increase of the zero time fasting blood glucose level. The control group that received distilled water, followed 1 h. later by an oral dose of glucose, showed the maximum increase (51.1%) in blood glucose concentration after 1 h. In contrast, the animals treated with the herbal extract showed a significant improvement in their ability to utilize an external glucose load. The maximum increase in this group, also after 1 h was only 28.8% ($p<0.001$). The area under the curve of percentage increase in blood glucose after administration of the oral glucose load was also significantly less in the treatment group (55.9) than in the control group (105.8) ($p<0.001$) [see Fig. 3].

Hence, the orally administered herbal extract significantly reduced not only the fasting blood

glucose level in healthy rats but also significantly improved their tolerance of an external glucose load.

The root bark of *S. reticulata* has been shown by Karunanayake *et al*(6) to have hypoglycaemic activity when administered orally to healthy laboratory rats. In the above study, 250g of dried powdered root bark of the plant was boiled in 1000mL distilled water for 3 hours and the final volume was reduced to 100 mL in vacuo. This 250/dL extract caused a 30% reduction in fasting blood glucose levels at a dosage of 1 mL/100g body wt. The concentrations used in the above study (6) are much higher than those used by us.

In the present study, a 2g/dL extract of the herbal mixture produced a 12.2% reduction in fasting blood glucose levels.Therefore, 40% of the hypoglycaemic effect of S. *reticulata* shown in the study of Karunanayake et al. was shown in this study by an extract of a mixture almost 125 times less concentrated.

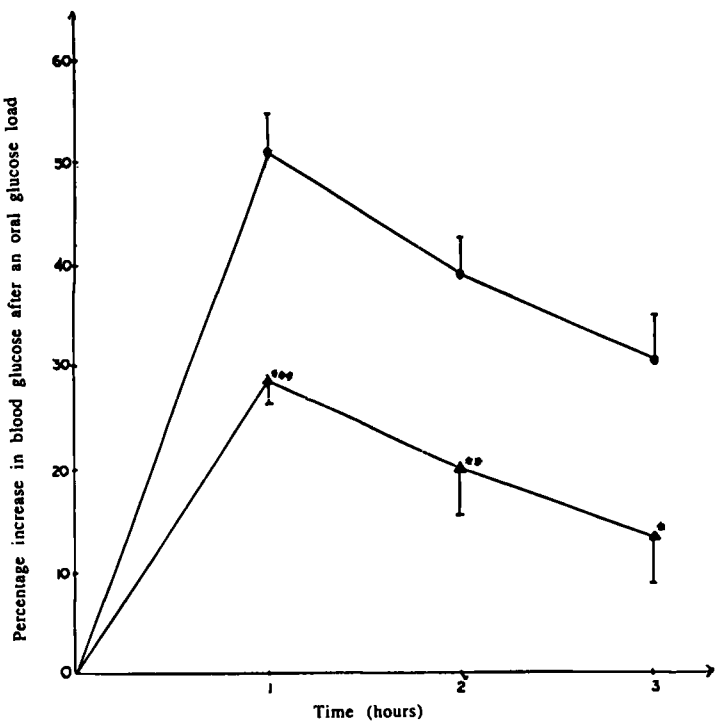

Figure 2

Effect of the herbal preparation on the oral glucose tolerance of rats. Fasted rats (n=26) were administered distilled water/herbal mixture (1 mL/100g body wt.) 1 h prior to an oral glucose load (1 mL of 50% w/v solution/100g body wt.). Blood samples (50 µL) were collected at zero time and at 1 h, 2 h and 3 h after the glucose load for assay of blood glucose. Results are expressed as percentage increase of blood glucose with respect to fasting blood glucose values. Results of 3 experiments were pooled. Mean ± SEM values are given.

●——● distilled water. ▲——▲ herbal mixture.

*$p < 0.02$ **$p < 0.01$ *** $p < 0.001$

It is likely that more than one of the herbs contributed to the hypoglycaemic activity. Further work should therefore be directed towards investigating the hypoglycaemic activity of each of the four herbs singly and in various combinations to identify those herbs in the preparation contributing to the hypoglycaemic activity and those which may have a potentiating effect or which, possibly, are included to counteract any toxic effects.

Further, evidence of chronic toxic effects should also be sought. Evidence of hepatic toxicity, if any, can be studied by the assay of serum levels of hepatic enzymes which include alkaline phosphatase, gamma-glutamyl transpepatidase and the aminotransferases and by histopathological studies. Renal toxicity, if any, can be investigated by assay of N-acetyl β-D-glucosaminidase and by histopathological studies.

In addition, the effect of this preparation on rats rendered diabetic by streptozotocin or alloxan treatment should be studied before studies on diabetic patients are undertaken.

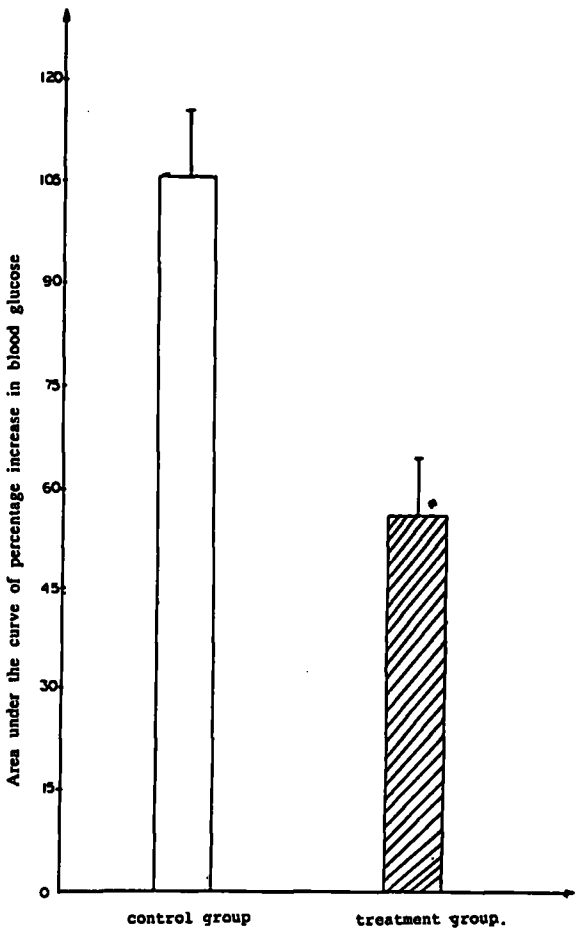

Figure 3

Mean and S.E.M. of areas under the curves of percentage increase of blood glucose concentrations, shown in Fig 2. The bar charts represent the glucose tolerance curve areas of animals treated with distilled water and with herbal mixture.

□ – control group ▨ – test group * $p < 0.001$.

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