

ON THE PRESENCE OF AN ANTIDIABETIC PRINCIPLE IN
MOMORDICA CHARANTIA

By

K. P. CHATTERJEE

The Research Division, East India Pharmaceutical Works Ltd., Calcutta

(Received March 30, 1963)

The fruit of the Indian plant *Momordica Charantia*, was found to contain antidiabetic principle. Of the two varieties of the fruit, the bigger one was found to be more active than the smaller one. No activity was found in the seeds. The centrifuged juice was more active than the alcoholic extract. Its hypoglycemic property was observed in alloxan diabetes with mild ketosis where tolbutamide failed to respond.

Many indigenous plants of India are known to be used for the treatment of diabetes. The treatment had always been attempted by the oral route and many claims of cure are on record. A proper evaluation of these claims on modern scientific lines had not been systematically attempted before. It was, therefore, felt that it would be worthwhile to study them, mainly on experimentally produced diabetes-like condition in laboratory bred rabbits.

Recently it is reported (Vad, B G, unpublished data) that the juice of *Momordica Charantia*, common bitter gourd, has been used with significant success in the oral treatment of diabetes. The treatment is to give 4 oz. of fresh bitter gourd juice, preferably divided into two or three doses, before each meal. Sharma, Sogani and Aurora (1960), using only the crude extract of the fruit, observed the hypoglycemic effect both in normal and in alloxan diabetic animals. But it was not reported if the alloxan diabetes was a mild or a severe one.

The fruits are of two varieties. One is long, oblong and pale green in colour and the other is small, oval and dark green. The present paper reports on the studies of hypoglycemic activity of the two varieties of the fruit and of the different preparations made from it, in normal and in alloxan diabetic rabbits with mild and high ketosis.

METHODS

The different preparations studied, were as follows :—

(a) *Pressed extract of the whole fruit.*—The fruits, both varieties, were cut into pieces, wrapped in a small piece of pressure resistant cloth and pressed under a screw press. Generally the volume of the extract was 65 per cent of the weight of fruit.

It was found that the smaller variety possessed very little activity (Table 1) and hence subsequent investigations were carried on with the bigger variety only.

(b) *Aqueous extract of seeds.*—The seeds were crushed and suspended in a known volume of water. The volume, made up, was 10 per cent of the volume of the extract obtainable from the same weight of the whole fruit.

(c) *Pressed extract of the fruit without seeds.*—This was prepared as described in (a).

(d) *Alcoholic extract.*—The fruit, without seed, was crushed and alcohol was added to make it 75 per cent with respect to the pressed extract obtainable. The slurry was stirred for six hrs and left overnight. The extract was filtered and distilled under partial vacuum (71 mm) at 35°—45°C. Few drops of silicone emulsion (Dow Chemical) were added near the end of distillation to prevent frothing. The residue, a green coloured thick paste, was diluted with water and the volume, made up, was 65 per cent of the weight of the fruit.

(e) *Centrifuged extract.*—The extract, as under (c), was centrifuged (3000 r. p. m.) at 5°—10°C for 20 min and a moderately clear supernatant liquid was obtained.

Each of these preparations was made, the day before the experiment and preserved at 10° (ca). Doses of administrations of the preparations and tolbutamide were 3 ml/kg body weight and 0.5 g/kg body weight respectively.

Healthy rabbits having normal glucose tolerance, of weights varying between 1.5 kg and 2.0 kg were divided into 7 groups of 6. The preparations (a), (b), (c), (d), (e) and tolbutamide were separately administered to each group. Another 3 dozens of normal rabbits were given intravenous injections of alloxan (Hoffman-LaRoche), 100 mg/kg body weight. All of them developed permanent diabetes. Some of them had high urinary excretion of ketone bodies. Several animals died after few days. However those, that survived, were kept under close observation for one month during which

occasional injections of insulin were given to check the severity of the disease. Among these alloxan-diabetic rabbits, some 18 were selected and divided into 3 groups of 6. Two groups with mild ketosis were orally treated with the preparation (e) and tolbutamide. The third group with high ketosis was treated with the preparation (e) only.

The rabbits were all kept on starvation overnight and allowed to take water only. Blood samples were withdrawn from the ear vein before and at intervals after the administration of the preparations and tolbutamide for the estimation of blood sugar.

Blood sugar and urine ketone bodies were estimated by the methods of Hagedorn and Jensen (1923) and Behre (1940) respectively. Urine ketone bodies were estimated on 24 hrs' collection of urine. The potency of the fruit is expressed as percentages of the standard substance, tolbutamide, according to the procedure laid down by Mark (1926) for the biological assay of insulin.

RESULTS

In this study of hypoglycemic activity of the fruit, *Momordica Charantia*, it was observed that the bigger variety was more effective than the smaller one. The active principle was entirely confined in the flesh (Table I). While

TABLE I

Bio-assay of hypoglycemic activity of different preparations of Momordica Charantia in normal rabbits.

(6 rabbits were used in each experiment. Doses of administration of the preparations from the fruit and of tolbutamide were. 3 ml/kg. and 0.5 g/kg respectively)

Substance administered	Blood sugar response mg/100 ml		Mean reduction per cent \pm S.E.	Mean hypoglycemic potency as per cent of tolbutamide.*
	Initial mean values	4 hrs pool mean values		
1. Tolbutamide	98.2	69.5	29.0 \pm 1.95	—
2. Preparation (a) (bigger)	109.0	90.2	17.2 \pm 0.76	59.4
3. Preparation (a) (smaller)	97.3	91.8	5.5 \pm 1.01	19.1
4. Preparation (b)	90.7	90.3	0.0	0.0
5. Preparation (c)	105.5	84.3	20.0 \pm 1.03	69.4
6. Preparation (d)	108.2	86.3	20.0 \pm 1.17	69.3
7. Preparation (e)	105.7	82.8	22.0 \pm 1.35	76.2

*The calculations were based on the doses mentioned.

preparing the alcoholic extract, it was noticed that if the temperature of distillation was allowed to increase above 45°C, the hypoglycemic activity deteriorated. The preparation (e) possessed the maximum activity (Table I) and could reduce the blood sugar level in alloxan diabetic rabbits with mild ketosis, where tolbutamide failed (Table II). In animals with high ketosis the preparation was found to be ineffective (Table II).

TABLE II

Comparative study of hypoglycemic activity of the Preparation (e) and Tolbutamide in alloxan diabetic rabbits.

(6 rabbits were used in each experiment. Doses of administration of the preparation (e) and of tolbutamide were 3 ml/kg and 0.5g/kg respectively)

Substance administered	Blood sugar response mg./100 ml.		Mean of urinary excretion of ketone bodies*	Mean reduction per cent \pm S. E.
	Initial mean values	4 hrs. pool mean values		
1. Preparation (e)	422.0	351.3	0.843	17.3 \pm 2.65
2. Tolbutamide	335.8	335.8	0.874	0.0
3. Preparation (e) —*mg. 24 hours collection of urine	347.3	345.5	36.97	0.53 \pm 0.01

DISCUSSION

It was observed that tolbutamide had no hypoglycemic activity in alloxan diabetes. This observation was in conformity with the reports of earlier workers (Dulin and Johnston, 1957; Mirsky, Perisutti and Jinks, 1956; Schambye, 1957 and Houssay *et al* 1957). But the fruit, as has been found, could exert its hypoglycemic activity in certain types of alloxan diabetes and appeared to be superior to tolbutamide in this respect. Sharma *et al* (1960), however, using 6 ml of the crude extract of the fruit/kg body weight, observed a greater amount of fall in blood sugar level in alloxan diabetes. But he did mention neither about the two varieties of the fruit nor about the nature of the alloxan diabetes. The activity of the different preparations from the fruit was found to deplete gradually, even in the cold, with time. The various symptoms of diabetes, other than mild ketosis, in which the fruit was effective, are now under investigation.

It appears that the mode of action of the fruit is different from that of tolbutamide. The principal action of tolbutamide as believed by many investigators, is a stimulation to greater release of insulin by the beta-cells of

the pancreas. However, there is some evidence that points to inhibition of those factors which either impede the action of insulin peripherally or cause its destruction. At any rate, it can be assumed that the hypoglycemic effect of tolbutamide is accomplished through insulin itself. Considering all these suggestions about the mechanism of action of tolbutamide, it appears that *Momordica charantia* can execute its hypoglycemic action in those cases where insulin secretion from pancreas is almost stopped. But it can not prevent the increased fatty acid oxidation in liver as observed by its ineffectiveness in high ketosis.

However the results so far obtained are encouraging and further work on the insolation and purification of hypoglycemic principle from the fruit is in progress.

The author is grateful to Mr. P. Bagchi, Research Director, for his helpful suggestions.

REFERENCES

- Behre, J. A. (1940). *J. Biol. Chem.*, **136**, 25.
- Dulin, W. E. and Johnston, R. L. (1957). *Ann. N. Y. Acad. Sci.*, **71**, 177.
- Hagedorn, H. C. and Jensen, B. N. (1923). *Biochem. Z.*, **137**, 92.
- Houssay, B. A., Pehos, J. C., Tiodosio N.; Bowkett, J. and Aplabaum, J. (1957). *Ann. N. Y. Acad. Sci.*, **71**, 12.
- Mark, H. P. (1926). League of Nations Report on Insulin Standardisation. p. 56. Geneva. Publication of the League of Nations.
- Mirsky, I. A., Perisutti, G. and Jinks, R. (1956). *Proc. Soc. Exptl. Biol. & Med.*, **91**, 475.
- Schambye, P. (1957). *Diabetes*, **6**, 146.
- Sharma, V. N.; Sogani, R. K. and Aurora, R. B. (1960). *Ind. J. Med. Res.*, **48**, 471.
-