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Research Article

EFFECT OF MORINGA OLEIFERA ON HYPERGLYCAEMIC RESPONSE INDUCED BY SUB-CHRONIC FRUCTOSE FEEDING IN SUSCEPTIBILITY RATS

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Abstract: The effect of *Moringaoleifera*on fructose-induced hyperglycaemia was investigated in rats in-view of the increasing incidence of fructose induced metabolic syndrome usually characterized by insulin resistance among other features. When compared to the control, fructose-fed rats showed higher glycaemic response in the rats. *Moringaoleifera*however, reached the glucose-induced hyperglycaemia when administered in combination with glucose orally into the animals for oral glucose tolerance test (OGTT). Glucose tolerance analysis revealed that the blood glucose level of fructose-fed rats reached a higher peak level of 9.0±0.7mmol/l compared with the peak plasma glucose concentration of 6.5±0.6 mmol/ml in animals not given a combination of glucose with the extract (P<0.05). However, when *Moringaoleifera* was administered simultaneously with glucose for OGTT, it caused lower glycaemic response judging from the lower GRI or glycaemic response index of 260.0± 11.60mmol.min/l compared to the GRI (463.3±20.1mmol.min/l) of fructose-fed rats not given the extract (P<0.05), thus *M. oleifera* improved glucose tolerance as indicated by the higher glucose tolerance index (GTI) of fructose-fed rats treated with *M. oleifera* compared to their counterparts that were not given the extract (P<0.05). Thus, *M. oleifera* improved glucose handling in fructose-induced glucose intolerance in the rats. The call for restriction of intake of fructose diets and the possible therapeutic significance of *M. oleifera* in diabetes, particularly in type-2 diabetes was therefore upheld.
Key words: Fructose, Oral Glucose Tolerance, Glucose Tolerance Index, Glycaemic Response Index, Insulin Resistance.

INTRODUCTION

*Moringaoleifera*commonly known as "The Miracle tree" or "Ben oil tree" is the best known and most widely distributed species of Moringaceae family, having an impressive range of medicinal uses with high nutritional value throughout the world. The leaves of *M. oleifera* have been reported to be a valuable source of both macro and micronutrients, rich source of B-carotene, protein, vitamin C, Calcium and potassium and act as a good source of natural antioxidants; and thus enhance the shelf life of fat containing foods, fruit(pod)/drum sticks and leaves have been used to combat malnutrition, especially among infants and nursing mothers for enhancing milk production and also regulate thyroid hormone imbalance.[1] A number of medicinal properties attributed to different parts of Moringa have been recognized by Ayurvedic inmedicines.[2] The plant finds its wide applicability in the treatment of cardiovascular diseases as the roots, leaves, gum, flowers and thiocarbamate glycosides as their chemical constituents which are suggested to be responsible for the diuretic, cholesterol lowering, antiulcer, hepatoprotective and cardiovascular protective properties of the tree. The roots have been reported to possess antispasmodic activity through calcium channel blockade which forms the basis for its traditional use in diarrhea. It also possesses antimicrobial activity due to its principle component pterygospermin.[3]

Of interest is the potential use of *M. oleifera*for the treatment of diabetes mellitus.[4] More than 20 years, Gill had observed that the prevalence of diabetes, especially type-2 diabetes was increasing particularly in developing countries.[5] This has been attributed, in part, to dietary and other life style changes from the traditional to those of more westernized societies.[6] In many of these countries, attention is being turned to indigineous plants as herbal remedies for many diseases including diabetes. Several years ago, demonstrated the hypoglcamic effect of *M. oleifera*reduced alloxan-induced diabetes rats. More recently, Kolawole et al. [7] showed that *M. oleifera* reduced plasma glucose in normaglycaemic and glucose-induced hyperglycemic rats. In a recently concluded investigation, evidence indicated that *M. oleifera*may play beneficial role in pregnancy-induced diabetes. An extension search on the literature revealed little or no information on the possible therapeutic effects of *M. oleifera*on
Fructose-induced diabetes in rats.

The present study was therefore carried out to see possible effects of *M. oleifera* on fructose-induced glucose intolerance in view to further assessing its potential as a herbal remedy for human diabetes. This is necessary in view of the increasing cases of fructose-induced metabolic syndrome which has type-2 diabetes as one of its main features. [7-8]

MATERIAL AND METHODS

Experimental Animals

Albino rats of both sexes weighting 180-200g, were obtained from the laboratory animal centre of the animal care unit of the Biological Garden, Yaba College of

Technologyyaba, for a 2 week acclimatization period before commencing the actual experiments. They cages were thoroughly cleaned, and the rats were weighted daily. They were allowed free access to rat feed and tap water. On this regime, the animals remained healthy and active throughout the period of acclimatization and experiments.

Collection Of Plants And Extraction

The plants were collected from Ota in Ogun State. For the extraction, the leaves were removed, washed free of sand and cut into pieces. The leaves were air-dried before being ground into powder using pestle and mortar. Fifty grams (50g) of the powder was extracted with. 250 ml of distilled water using the Soxhlet method. The extract was slowly evaporated in vacuole to obtain a total yield of 2.8g. Weighed sample of the dried extract was used to prepare solution of extract for oral glucose tolerance test (OGTT). Freshly prepared leaf extract was always used for the experiments.

Experimental Design And Administration Of Materials

The rats were randomly selected and assigned to 3 groups of 1 rats per cage. One group (Normal Control) was given, the normal feed and ordinary tap water while the animals in the other 2 groups were given fructose for 21 days as 10% solution in drinking water. One of the fructose treated groups, designated as Fructose-Treated, was given only glucose for! oral glucose tolerance test (OGTT) while the other group received glucose combined with extract as a single solution for the test. The procedure for OGTT was as described in earlier reports[9] Briefly, a glucose load of 3.0g/kg with was delivered into the stomach of 18-Hour fasted animals by oro-gastric intubation as 30% glucose fructose-control) or as glucose-extract solution (fructose-.Brideliaza). The glucose-extract solution was constituted such that the dose of the extract was 250.0 mg/kg while the glucose load was 3.0 g/kg with an administration volume b.wt. Blood samples were then obtained from the tail for the determination of blood glucose concentration; using an electronic digital blood glucose analyzer (Accu-Check Advantage, Roche, USA) just before oral glucose infusion (0 minute) and at 30, 60, and 120 minutes of OGTT.

Data Analysis

Results of blood glucose determinations are given as mean +SEM. The glucose tolerance index (GTI) for each rat was taken as the incremental area under its glucose tolerance curve. It is calculated by summation of the areas of the trapezoids defined by individual points on the curve. Statistical analysis was done using IBM SPSS (Version 19) software package. Statistical differences between means was determined by Student's it-test. When comparison of means involved more than two.groups, analysis of variance (ANOVA) followed by Turkey's post-hoc test was employed and Differences were considered significant when $P<0.05$.

RESULTS

The glucose tolerance curves in Fig. 1 shows the plasma glucose profiles of the three groups of rats after the administering the glucose load. It could be observed that the fasting blood glucose concentration of rats given ordinary tap water (Normal Control) was 4.7± 0.3 mmol/l, a value that was comparable to that of the animals fed with fructose (Fructose-Control) which was 4.8+ 0.4 mml/l ($P>0.05$). At the 60th minute time point of OGTT, the blood glucose concentration reached a peak level of 6.8+0.4 mmol/1 in the normal control group while the peak (8.2+0.7mmol/|| was attained at the same time point in the fructose-Control rats. At120-minute time point, the blood glucose level of the Fructose-Control group dropped to 6.8±0.5mmol/l; however the corresponding value was lower ($P<0.05$) in the Normal Control (5.2+0.3 mmol/l). The pattern of glycaemic response of animals in Fructose Moringa group revealed that *M. oleifera*reduced blood glucose levels during OGTT. Table 1 shows the results of analysis of glycaemic response index (GRO and glucose tolerance index (GT1). The extract of *M. oleifera* caused lower glycaemic response judging from the lower glycaemic response index (GR1) of 250.0+26.0 mmol.min/1 compared to the GRI of rats similarly treated with fructose but not given the plant extract for OGTT (GRl=483.3+30.Immol.mni/l-, $P<0.05$), The response was not found to be associated with body weight as evidenced by the considerable scatter of scatter points in the scatter plot shown in Fig. 2. Thus, *M. oleifera*improved glucose tolerance as indicated by the higher glucose tolerance index (GT!) body weight of fructose fed rats treated with *M. oleifera*or OGTT (GTI - 4.0+0.3 mmof'.min"1!} and those that were similarly treated but not given the plant extract (2.7±0.2 mmor1^{-1}.min-1!; PO.05).

Effects of Molinga*Oleifera*Beath (Euphorbraccae) on HyperglycaemicResponse Induced by sub–Chronic Fructose Feeding In Suscepitable Rats

Table 1: Glycaemic Response Index Or GRI (Mmol.Min/L;) And Glucose Tolerance Index (GTI) In Different Groups Of Rats

	GRI In Mmol.Min/L	GTI X 10^{-3} IN $MMOL^{-1}.MIN^{-1}$
Normal Control	175.5 ± 20.1	5.7 ± 03
Fructose Control	483.3 ± 30.1	2.7 ±0.2
Fructose *MoringaOleifera*	250.0 ± 26.0	4.0 ±0.3

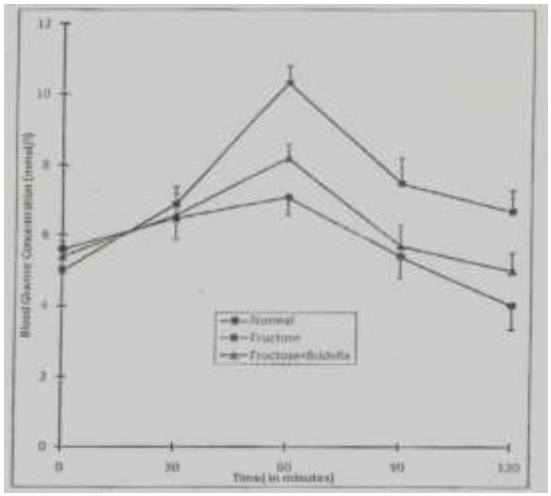
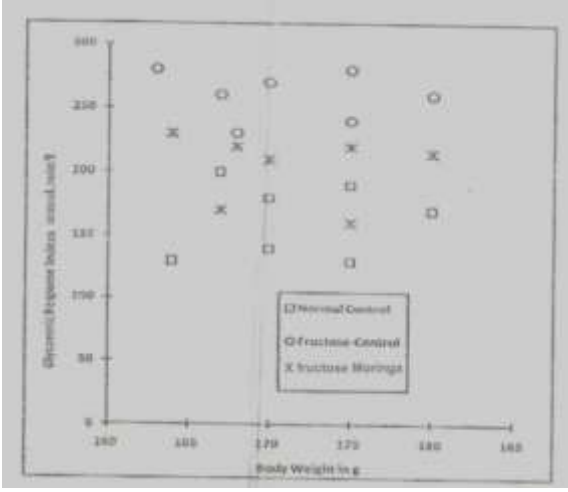


Fig-1: The Blood glucose concentration of different groups of rats in glucose tolerance test.



Fig, 2r Scatter Plot Showing Lack of Association between Body Weight and Glycaemic Response

DISCUSSION

It is now -well established that fructose feeding causes insulin resistance in experimental animals.[8] There is therefore little or no doubt that the glucose intolerance observed in this study is a consequence of insulin resistance induced by excess fructose feeding in the rats. However, Concomitant measurement of insulin would have been more elucidating. Previous studies carried out in rats and other rodents indicated similar effect of excess fructose intake on carbohydrate metabolism.[2] Thus an adverse effect of fructose on insulin sensitivity is now well established. Several mechanisms have been suggested for the phenomenon of fructose-induced insulin resistance. One proposed mechanism involves the hypertriglycemic' effect of fructose. Fructose is readily metabolized to fat in the liver and can lead to nonalcoholic fatty liver disease and insulin resistance. A more recently proposed mechanism by Catena et al (2003) indicated that feeding rats with 66% fructose for two weeks caused a decrease in insulin receptor mRNA and subsequent insulin receptor numbers in skeletal muscle and liver, In another recent report, Litherland et al, suggested a mechanism involving GLUTS, a fructose transporter that has high expression in young obese Zuckerrats.The results of this study support the call urging the general population particularly the diabetics to reduce their fructose consumption.

It is of interest that *M. oleifera*, a common medicinal plant, reduced glycaemic response to glucose challenge in fructose-induced glucose intolerance in this study. This is more so considering the inadequacy of western medical facilities in many poor countries. When such facilities arc available, several problems including treatment complications and compliance problems are usually associated with conventional drug and insulin therapy. Oral hypoglycaeniic drug therapy for controlling insulin resistance and hyperglycaemia in type-2 duabetes often fails, and glucose metabolism deteriorates progressively due to. Worsening insulin sensitivity and associated complications. Most patients may later require insulin therapy, but several side effects may accompany insulin use. The use of herbal remedies constituted with medicinal plants such as *M. oleifera* agrees with socioeconomic realities of many rural dwellers in poor developing countries like Nigeria.

The exact mechanism involved in the glycaemic action of *M. oleifera* is not yet clear; studies are in progress to clarify the effect of *M. oleifera* on carbohydrate metabolism. The plant may act like an insulin secretagogue by stimulating insulin secretion by the pancreas or/and enhance insulin sensitivity in various organs especially the muscle and the liver in a manner similar to insulin sensitizers. In this study, glucose and the plant extract were administered simultaneously into the rats to determine the pattern of oral glucose tolerance; it is therefore not possible to rule out the possibility that *M. oleifera* affects intestinal glucose absorption in the rats in a manner similar to alpha-glucosidase inhibitors.

The present paper is the report of a recently concluded short-term study on the glycaemic effect of *M. oleifera* on glucose intolerance induced by sub-chronic fructose loading in rats. We hope that the result of this short term investigation will stimulate more discussions about the adverse effects of chronic ingestion of fructose diets and the potential role of *M. oleifera* in controlling increased glycaemic response associated with type-2 diabetes and other insulin resistant states in man.

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