ACTA SCIENTIARUM POLONORUM
Acta Sci. Pol. Technol. Aliment. 16(1) 2017, 93–99
www.food.actapol.net pISSN 1644-0730 eISSN 1889-9594 http://dx.doi.org/10.17306/J.AFS.2017.0460

ORIGINAL PAPER

Received: 21.12.2016
Accepted: 13.02.2017

DIETARY INTAKE OF BOILED BREADFRUIT (*TRECULIA AFRICANA*) SEEDS DID NOT IMPROVE HYPERGLYCEMIA IN STREPTOZOTOCIN INDUCED DIABETIC RATS: EFFECT ON THE ORAL GLUCOSE TOLERANCE OF NORMOGLYCEMIC RATS

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ABSTRACT

Background. Although African breadfruit (*Treculia africana*) is said to be useful in the dietary management of diabetes, the effect of cooking on its glycemic index has not been reported. Hence this study has investigated the effect of a dietary intake of boiled breadfruit on the serum glucose, glucose tolerance, body weights and relative organ weights of streptozotocin (STZ) induced diabetic rats.
Materials and methods. Twenty albino rats were used and were divided into four groups of five rats. Groups 1 (normal control) and 2 (diabetic control) received standard rat pellets while groups 3 (diabetic-test group) and 4 (non-diabetic) rats received breadfruit.
Results. The blood glucose of the normoglycemic rats fed standard rat feeds peaked at 30 min (149.75 ±11.12 mg/dl) following oral glucose loading (3 g/kg) but reduced to 85.25 ±21.05 mg/dl after another 90 min, while the blood glucose of the normoglycemic rats fed breadfruit peaked at 30 min (146.25 ±15.22 mg/dl) following oral glucose loading, but elevated (130.75 ±36.69 mg/dl) after another 90 min. There was significant elevation ($P < 0.05$) of the serum glucose, relative liver weight (RLW) and relative kidney weight (RKW) but a significant decrease in the body weights of the diabetic control compared with the normal control; no significant difference ($P > 0.05$) in the serum glucose, body weights, RLW and RKW of the test group compared with the diabetic control, and no significant differences ($P > 0.05$) in the serum glucose, body weights, RLW and RKW of the normal rats fed the breadfruit diet compared to the normal control.
Conclusion. The study showed that the traditional method of cooking African breadfruit negatively affects its hypoglycemic property.

Keywords: diabetes, oral glucose tolerance, diet, nutrition

INTRODUCTION

Diabetes mellitus is a global health problem that is causing problems for humans around the world and becoming increasingly prevalent at an alarming rate (Aloulou et al., 2012), including amongst the rural Nigerian population. The inability of modern treatments to control all the pathophysiological aspects of diabetes, as well as the enormous cost it imposes on the economy of the developing nations of the world,

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has underscored the need for alternative strategies (WHO, 2002). When someone suffers from diabetes, the liver has been found to increase in weight due to increased lipolysis, resulting from insulin absence or insensitivity, while the kidney has been reported to increase in weight due to glucose overutilization and the subsequent enhancement of glycogen synthesis, lipogenesis, and protein synthesis. These changes could lead to complications in renal and hepatic functions (Eleazu et al., 2013a).

Many specific interventions have been carried out in the management and prevention of diabetes and one of the integral components is medical nutrition. Dietary modification is the simplest and cheapest way to manage diabetes. Dietary management may involve diet alone, diet with oral hypoglycemic drugs, or diet with insulin (Wolever et al., 2008).

Treculia africana Decne (Moraceae), commonly known as African breadfruit, is one of several tropical African plants with ethnomedicinal and nutritive values (Olatunji et al., 2014; Oyelola et al., 2007). The plant is also reported to be an important component of some ancient anti-diabetic recipes used in the Western and Middle Belts of Nigeria (Oyelola et al., 2007).

Although the hypoglycemic actions of the roots and seeds of this plant have been reported (Ajiboye et al., 2016; Olatunji et al., 2014; Oyelola et al., 2007), the effect of processing the seed (the edible part) on its hypoglycemic action has not been reported. This is especially important as the seed is eaten after being processed, and different food processing techniques could affect the starch digestibility of foods, which in essence will affect the glycemic indices of these foods.

In view of this, the present study sought to investigate the effect of a dietary intake of boiled breadfruit on the serum glucose, body weights and relative organ weights of streptozotocin induced diabetic rats and on the oral glucose tolerance of normoglycemic rats.

MATERIAL AND METHODS

Chemicals

Streptozotocin (STZ) was purchased from Sigma and Aldrich Chemical Company, Germany. Every other chemical that was used for this study was also of analytical grade.

Plant materials

Dehulled African bread fruit (*Treculia africana Decne*) seeds were purchased from the central (meat) market, Abakaliki, Ebonyi State, Nigeria. They were washed and boiled to softness (about 2 h). Afterwards, they were drained of water, dried for 24 h, milled to flour and fed to rats in a dietary incorporation.

Animal experiments

Healthy albino rats of both sexes (about 8 weeks old) were bought from the Veterinary Department, University of Nigeria Nsukka, Nigeria. They were housed in breeding cages in the animal house of the Federal University, Ndufu-Alike Ikwo (FUNAI), Abakaliki, Nigeria and allowed to acclimatize for 14 d prior to the commencement of the experiment. The animals were handled following approval by the Board of the Biochemistry Programme, FUNAI, Abakaliki, Nigeria which was in line with the guidelines for the care and use of laboratory animals (NRC, 1985).

Induction of diabetes

Following 2 weeks of acclimatization, a freshly prepared solution of streptozotocin (0.1 g dissolved in 5 ml of freshly prepared sodium citrate buffer 0.1 M, pH 4.4) was injected intraperitoneally to rats which had been fasted overnight, at a dosage of 65 mg/kg body weight. To prevent early mortalities arising from STZ induced hypoglycemia, the STZ challenged rats were allowed to drink 3% glucose solution (in water) at 8 h post STZ induction and for 24 h thereafter, after which it was removed.

The STZ-treated rats with fasting blood glucose levels ≥200 mg/dl after 7 d of STZ induction were considered to be diabetic and used for the study.

Experimental procedure

Both normal and STZ-treated rats with stable diabetes were divided into four groups comprising of five rats per group, as follows:

- Group 1. Non-diabetic rats fed standard rat feeds (non-diabetic control)
- Group 2. Diabetic rats fed standard feeds (diabetic control)
- Group 3. Diabetic rats fed a breadfruit-incorporated diet (3 g/kg; test group)
- Group 4. Normal rats fed a breadfruit-incorporated diet (3 g/kg; breadfruit group).

The body weights of the rats were recorded on a daily basis and their diets and water were both given *ad libitum*. At the end of 14 d, the rats were fasted overnight and on the 15th day, they were euthanized by cervical dislocation. Blood was collected by cardiac puncture into plain tubes and allowed to clot. Sera were harvested from the clotted blood samples by centrifuging at 3000 × g for 20 min and used for the assay of glucose using Randox Assay Kits, following the methods described by Tietz (1995). The organs (liver and kidney) were excised and weighed.

The percentage change in the body weights of the rats was calculated as:

$$\{\text{final body weight} - \text{initial body weight}\} / \text{final body weight}\} \times 100$$

Similarly, the relative organ weights of the rats were calculated as follows:

$$\text{relative liver weight, g/100 g} = \{\text{total liver weight} / \text{final body weight}\} \times 1000$$

$$\text{relative kidney weight, g/100 g} = \{\text{total kidney weight} / \text{final body weight}\} \times 100$$

Oral Glucose Tolerance Test (OGTT)

Oral glucose tolerance tests were carried out during the last week of experimentation, following the method described by Chaturvedi et al. (2004). To perform OGTT, rats in groups 1 and 4 were fasted overnight and the next day, blood samples were collected from the tail vein of each rat just before (0 h) glucose administration and at 30 min, 60 and 120 min respectively after glucose administration (3 g/kg).

Statistical analysis

The generated data was analyzed statistically using the statistical package for social sciences (SPSS) version 17.0. One-way analysis of variance (ANOVA) was used for the comparison of means. Results were considered to be significant when $P < 0.05$.

RESULTS

The pictorial presentations of the *Treculia africana* fruits and the dehulled seeds that were used for this study are shown in Figures 1a and 1b. The result of the serum glucose levels of the rats investigated in this study is presented in Table 1. The glucose levels of the diabetic control rats were significantly increased

Fig. 1a. *Treculia africana* fruits

Fig. 1b. Dehulled *Treculia africana* seeds

Table 1. Serum glucose levels of rats, mg/dl

Groups	Serum glucose
Normal control	80.52 ±13.55[a]
Diabetic control	393.05 ±76.05[c]
Test group	317.03 ±68.60[bc]
Breadfruit alone	114.15 ±16.40[ab]

Values are means ±SD.
[a–c]Means with different superscript letters along each column are significantly different ($P < 0.05$).

($P < 0.05$) when compared with the normal control. Conversely, the glucose levels of the normal rats fed breadfruit did not differ significantly ($P > 0.05$) from that of the normal control. Intake of the breadfruit diet by the diabetic rats of group 3 did not significantly reduce ($P > 0.05$) their elevated glucose levels in comparison with the diabetic control.

The results of the oral glucose tolerance test of the normal rats fed standard rat feeds or the breadfruit diet are shown in Figure 2.

As shown in the figure, the blood glucose of the normal rats fed standard rat pellets achieved a maximum peak (149.75 mg/dl) at 30 min after oral glucose loading, but declined to 85.25 mg/dl after another 90 min. Similarly, the blood glucose of the normal rats fed breadfruit also achieved a maximum peak (146.25 mg/dl) at 30 min following oral glucose loading but was elevated (130.75 mg/dl) after a further 90 min.

The body weights and percentage change in the body weights of the rats investigated in this study are shown in Table 2.

As shown in the figure, the initial body weights of all the rats in the respective groups were not significantly different from each other ($P > 0.05$) at the commencement of the experiment. However, at the end of the experiment, the final body weights of the diabetic control (31.32% decrease) were significantly decreased ($P < 0.05$) when compared with the normal control that recorded a 12.5% increase in body weight, while the body weights of the normal rats fed breadfruit alone (15.13% increase) were not significantly different ($P > 0.05$) from that of the normal control.

In addition, the body weights of the diabetic rats of group 3 fed the test diet (12.32% decrease) were also not significantly different ($P > 0.05$) from that of the diabetic control.

The relative tissue weights of the rats investigated in this study are shown in Table 3.

There were significant increases ($P < 0.05$) in the relative liver weights of the diabetic control in comparison with the normal control, but no significant difference ($P > 0.05$) in the relative liver weight of the

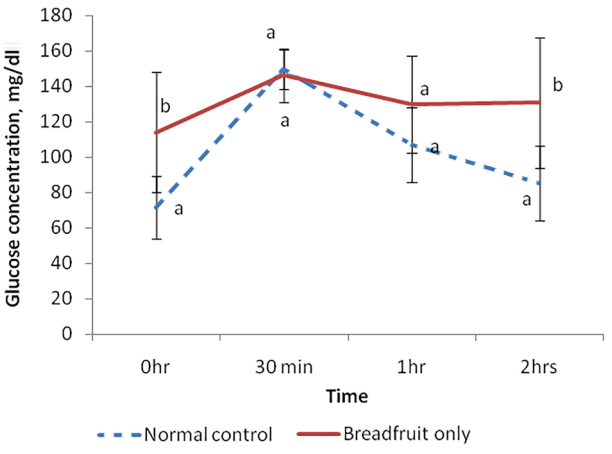

Fig. 2. Effect of cooked breadfruit on oral glucose tolerance test in glucose-loaded normal rats. [a–b]Means with different superscripts are significantly different for each group ($P < 0.05$)

Table 2. Body weights and percentage change in the body weights of rats, g

Groups	Initial	Final	Percentage change
Normal control	140.00 ±10.22[a]	160.00 ±24.97[b]	12.5 (increase)
Diabetic control	180.55 ±8.55[b]	124.00 ±34.41[a]	31.32 (decrease)
Test group	130.60 ±6.44[a]	114.50 ±28.87[a]	12.33 (decrease)
Breadfruit alone	150.00[ab] ±3.22	176.75 ±21.97[b]	15.13 (increase)

Values are means ±SD.
[a–b]Means with different superscript letters along each column are significantly different ($P < 0.05$).

Table 3. Relative tissue weights of rats, g/100 g wet weight

Groups	Liver	Kidney
Normal control	3.73 ±0.11[a]	0.75 ±0.09[a]
Diabetic control	5.12 ±1.86[b]	0.99 ±0.17[b]
Test group	4.91 ±0.53[b]	1.08 ±0.08[b]
Breadfruit alone	3.16 ±0.24[a]	0.69 ±0.04[a]

Values are means ±SD.
[a–b]Means with different superscript letters along each column are significantly different ($P < 0.05$).

normal rats fed the breadfruit diet compared to the normal control.

Consumption of the breadfruit diet by the diabetic rats of group 3 did not significantly reduce ($P > 0.05$) their elevated liver weights when compared with the diabetic control.

As shown in the table, there were significant increases ($P < 0.05$) in the relative kidney weights of the diabetic control when compared with the normal control but no significant difference ($P > 0.05$) in the relative kidney weight of the normal rats fed rats fed breadfruit compared to the normal control. However, consumption of breadfruit by the diabetic rats of group 3 did not significantly reduce ($P > 0.05$) their elevated kidney weights when compared with the diabetic control.

The proximate composition of the breadfruit seeds that were used for this study had earlier been reported to be: 1.64% ash, 18.58% crude protein, 1.33% fat, 78.53% carbohydrate and 1.33% crude fiber with an energy value of 400.41 Kcal/100 g (at 10% moisture content; Ijeh et al., 2010) while the standard rat feeds that were used for the study contained: 15% crude protein, 7% fat, 33% carbohydrate and 10% crude fibre with an energy value of 255 Kcal/100 g.

DISCUSSION

The cooking method used in this study reflects the conventional method in which African breadfruit seed is cooked in typical Nigerian diets prior to its consumption as a meal.

In recent times, there has been increased interest in functional foods due to their roles in ameliorating metabolic disorders, one of which is type 2 diabetes (Eleazu et al., 2016).

Oboh et al. (2015) reported the glycemic index (GI) of breadfruit seed to be about 64.5, which places it as an intermediate GI crop based on the classification of GI by Brand-Miller et al. (2003). On the other hand, Ajiboye et al (2016) reported the hypoglycemic action of this plant in experimentally induced diabetic rats, and the findings of this study suggest that the processing of this plant by boiling (which is the form in which it is eaten in typical diets) affects its reported hypoglycemic action. This variation between our results and those of Ajiboye and colleagues could be attributed to the fact that, while Ajiboye and colleagues worked on raw seeds, we worked on cooked seeds, and cooking has been reported to affect the nutrient constituents and the digestibility of starches in foods, which could also affect their glycemic indices (Capriles et al., 2008; Eleazu et al., 2016; Eleazu et al., 2017).

To further explore the biochemical basis of the effect of processing this plant on blood glucose, the effect of cooked breadfruit seed on oral glucose tolerance was also studied in glucose-loaded normal rats. The oral glucose tolerance test measures an individual's ability to utilize ingested glucose over a period of time. For normal tolerance to blood glucose, blood glucose at 2 h post oral glucose loading is about 110 mg/dl, while for impaired tolerance, blood glucose rises above 110 mg/dl due to lack of or insensitivity to insulin, which results in reduced glucose uptake and its utilization by the peripheral tissues (Shivananda and Shivananda, 2007). Since impaired oral glucose tolerance is indicative of the predisposition of an organism to diabetes, medicinal plants that possess antidiabetic actions will improve glucose tolerance, thereby arresting the progression of impaired glucose tolerance to diabetes (Olorunfemi et al., 2010). In this regard, the findings of this study, which indicated that the blood glucose levels of the rats fed breadfruit were elevated (>110 mg/dl) at 2 h following oral glucose loading, suggest that the boiled form of African breadfruit seed does not have the ability to improve impaired glucose tolerance. This finding therefore explains the inability of this plant to ameliorate the elevated serum glucose levels of the diabetic rats fed with this diet.

The decreased body weights of the diabetic control and diabetic rats fed the breadfruit-incorporated diet

could be associated with the breakdown of tissue proteins in an attempt to arrest the STZ assault, while the increased body weights of the normal rats fed standard rat feeds or breadfruit diet suggests increased synthesis of tissue proteins in these groups of rats.

Organ weight can be the most sensitive indicator of the effect of drug toxicity, as significant differences in organ weights between treated and control animals may occur in the absence of any morphological changes or may precede morphological changes (Kalu et al., 2016).

In addition, liver hypertrophy is a well known complication of diabetes with a reported frequency of 40–70% (Chatila and West, 1996).

Therefore, the increased liver weight of the diabetic control could be attributed to increased mobilization of fatty acids from the adipose tissue, leading to their accumulation in the liver due to the absence of insulin. Moreover, STZ is also known to be toxic to the liver as the liver expresses glucose 2 transporter (Eleazu et al., 2013b). Any one or a combination of these two factors could have accounted for the liver growth demonstrated by the diabetic control in this study.

The liver growth demonstrated by the diabetic control could not be ameliorated by consumption of the bread fruit diet, which was evident from the non-significant difference of the relative liver weights of the diabetic rats fed the breadfruit diet compared to the diabetic control. In addition, the non-significant difference of the relative liver weights of the normal rats fed the breadfruit diet when compared with the normal control suggests the non-toxicity of breadfruit to the liver.

Diabetic renal hypertrophy constitutes an early development in the progression of glomerular pathology, which occurs in the absence of mesangial expansion (Eleazu et al., 2013a). Therefore, the increased kidney weights of the diabetic control suggest renal hypertrophy for this group of rats. This renal growth could not be ameliorated by the consumption of the breadfruit diet, which was seen from the non-significant difference of the relative kidney weights of the diabetic rats fed the breadfruit diet compared to the diabetic control. In addition, the non-significant difference in the relative kidney weights of the normal rats fed the breadfruit diet when compared with the normal control suggests the non-toxicity of breadfruit to the kidney.

The proximate composition of the breadfruit seed that was used for this study as reported by Ijeh et al. (2010) showed it to be low in ash, fat and crude fiber but high in proteins and carbohydrate with a considerable amount of energy value.

The proximate composition of the standard rat feed that was used for this study showed it to be rich in fat, proteins and crude fibre, with some energy value.

It is noteworthy that, despite a considerable amount of protein in both the African breadfruit seed and the standard rat feed, their consumption by the diabetic rats did not translate into any weight gain, which further suggests that the loss of weight by these groups of rats was a result of uncontrolled hyperglycemia (Eleazu et al., 2014).

To the best of our knowledge, this is the first report on the effect of dietary intake of cooked breadfruit on blood glucose response, which is the major strength of this article. The findings of this study suggest that the traditional method of boiling of African breadfruit in typical African diets negatively affects its hypoglycemic property.

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