Glycemic Index: Nano-Considerations and Impact in Rat Model of Type 2 Diabetes

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***Abstract*— Diabetes mellitus (DM) is a chronic metabolic disorder characterized by high blood glucose level and abnormalities in carbohydrate, protein and fat metabolism. The resulting hyperglycemia may lead to irreversible damage, dysfunction and failure of various organs. The objective of this study was to investigate the effects of low, medium and high glycemic index (GI) diets on normal as well as diabetic rats. The three diets were fed to the rats and the biochemical nano-variables and organ histology assessed at the end of the study (90 days). Our findings suggest that it may be possible to improve glycemic control, insulin secretion and histoarchitecture of pancreatic islets via consumption of low and medium GI diets.**

***Index Terms*—Glycemic index, diabetes, hyperglycemia.**

I. Introduction

Diabetes mellitus (DM) is one of the leading causes of death in many countries; therefore an effective method of management is of absolute importance. This metabolic disorder is characterized by high blood glucose level and abnormalities in carbohydrate, protein and fat metabolism [1,10]. Type 2 DM can be managed by lifestyle changes as well as the administration of expensive drugs such as metformin, which aids in the control of the blood glucose level [11,12]. Similarly, the administration of synthetic insulin helps individuals with type 1 DM to reduce their elevated blood glucose concentration. However, these oral antihyperglycemic agents have undesirable side effects and are ineffective in treating chronic diabetes patients. Insulin injection decreases glycemia, but does not physiologically maintain normal blood glucose levels [7,15]. Due to the limitations of current therapies for DM, there remains interest in alternative treatments. It has been reported that the consumption of low glycemic index (GI) foods is a possible inexpensive dietary alternative in the management of diabetes [2,5]. Therefore, the objective of this study was to investigate the effects of the consumption of low, medium and high glycemic index Jamaican foods on biochemical nano-variables and organ histology in high-fat diet-fed and streptozotocin-induced diabetic rats (HFD-STZ).

II. Materials and Methods

A. Food Samples

Freshly harvested, mature sweet yam (*Dioscorea alata* - high glycemic index), dasheen (*Colocasia esculenta* - high glycemic index), round leaf yellow yam (*Dioscorea cayenensis* - medium glycemic index), ripe plantain (*Musa paradisiaca* - medium glycemic index), green banana (*Musa sapientum* - low glycemic index) and sweet potato (*Ipomea batatas* - low glycemic index) were purchased from the local market in Kingston, Jamaica, processed and administered to the rats according to their groups [4].

B. Animals

Adult Sprague-Dawley rats between the ages of 6-8 weeks were acquired from the University of the West Indies Biotechnology Animal House and were used in agreement with the guidelines of Ethics Committee of the University Hospital of the West Indies and the Faculty of Medical Sciences at the University of the West Indies Mona Campus, Kingston, Jamaica. Diabetes induction (HFD-STZ, 35 mg/kg intraperitoneally) was done according to a protocol previously described by Zang et al. [16].

C. Design of experiment

Sixty four (64) adult Sprague-Dawley rats (32 males and 32 females) were divided into eight groups (Table 1) for the experimental study. The stainless steel cages that they were housed in were maintained daily and were placed in a animal room that was kept on a 12/12-hour light/dark cycle. Throughout the study, the rats had access to food and water *ad labitum*. Rats were acclimatized for a week prior to commencing study.

TABLE I. Animal Study Groups and Administered diets

Groups	Diets administered
LD	Low glycemic index food (Diabetic rats)
MD	Medium glycemic index food (Diabetic rats)
HD	High glycemic index food (Diabetic rats)
LN	Low glycemic index food (Non-Diabetic rats)
MN	Medium glycemic index food (Non-Diabetic rats)
HN	High glycemic index food (Non-Diabetic rats)
DC	Regular rat chow (Diabetic rats)
NC	Regular rat chow (Non-Diabetic rats)

D. Statistical Analysis

Data obtained from the experiments are expressed as mean ± SE. Differences between the control and the treatments in the experiments were analyzed using ANOVA and Duncan's

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multiple range test, while values of $P \leq 0.05$ were considered significant.

III. Results

Postprandial glycemic response to low GI diet showed improvement over that of medium and high GI diets (Fig. 1). No significant change was observed in cholesterol and triglycerides when animals fed low, medium and high GI diets were compared to diabetic controls (Table 2). Similarly, no significant change was observed in mean body weights and mean organ weights (Fig. 2 & Fig. 3). There was increased serum insulin (Fig. 4) in diabetic rats fed low (400±0.01 ng/L) and medium (410±0.04 ng/L) GI diets when compared to the diabetic control rats (340±0.00 ng/L) after twelve weeks. Pancreas histology (Fig. 5) of diabetic control rats showed degeneration with degranulation and vacuolation of islet β cells, while regeneration was observed in some β cells in the diabetic rats fed with low and medium GI diets.

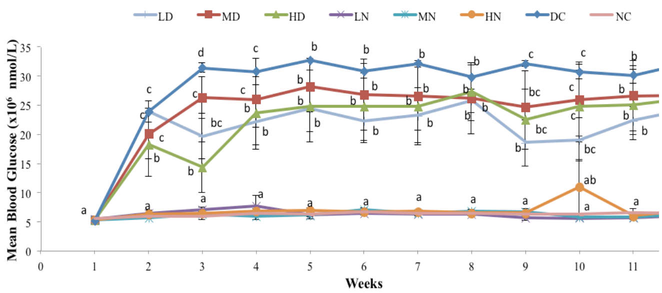

Fig. 1. Blood glucose concentrations over the 12 weeks experimental period.

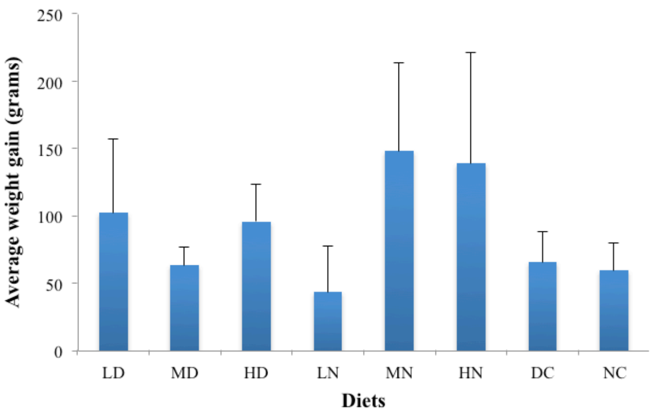

Fig. 2. Average weight gain for animals fed with normal, low, medium and high glycemic diets.

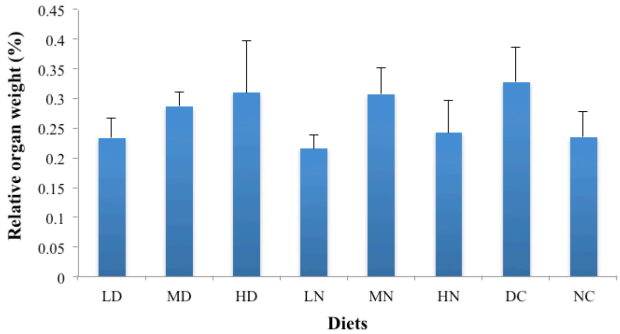

Fig. 3. Relative organ weight of pancreas for the experimental groups

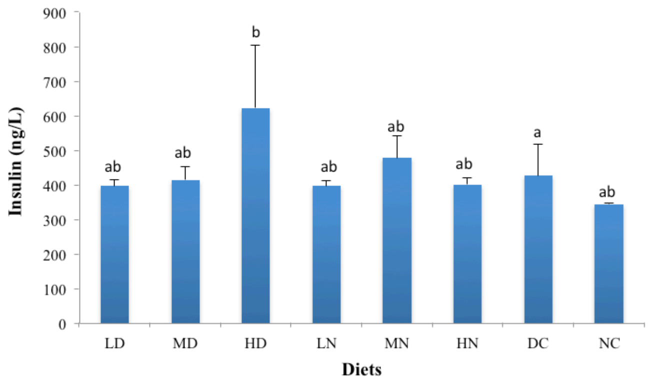

Fig. 4. Serum insulin concentration in animals fed low, medium and high glycemic index diets

TABLE 2. Effects of Low, Medium and High Glycemic Index Diet on Cholesterol, Triglyceride and Lipoprotein Levels in Serum.

Groups	Total Cholesterol ($x10^6$ nmol/L)	Triglyceride ($x10^6$ nmol/L)	HDL ($x10^5$ nmol/L)	LDL ($x10^5$ nmol/L)	VLDL ($x10^5$ nmol/L)
LD	2.33 ± 0.37^{b}	1.14 ± 0.31^{b}	9.1 ± 0.15^{b}	9.0 ± 0.11^{ab}	5.2 ± 0.14^{b}
MD	1.90 ± 0.12^{ab}	0.69 ± 0.16^{ab}	7.1 ± 0.15^{ab}	8.8 ± 0.15^{ab}	3.1 ± 0.07^{ab}
HD	1.98 ± 0.30^{ab}	0.87 ± 0.21^{ab}	7.0 ± 0.09^{ab}	8.8 ± 0.27^{ab}	4.0 ± 0.09^{ab}
LN	1.68 ± 0.10^{a}	0.65 ± 0.08^{ab}	6.1 ± 0.06^{a}	8.7 ± 0.06^{ab}	1.9 ± 0.07^{a}
MN	1.63 ± 0.11^{a}	0.72 ± 0.07^{ab}	5.7 ± 0.07^{a}	7.3 ± 0.04^{a}	3.3 ± 0.03^{ab}
HN	1.75 ± 0.12^{ab}	0.67 ± 0.02^{ab}	5.7 ± 0.06^{a}	8.8 ± 0.10^{ab}	3.0 ± 0.01^{ab}
DC	1.95 ± 0.05^{ab}	0.86 ± 0.12^{ab}	7.4 ± 0.04^{ab}	9.1 ± 0.03^{ab}	3.0 ± 0.03^{ab}
NC	2.13 ± 0.08^{ab}	0.61 ± 0.07^{a}	6.2 ± 0.02^{ab}	2.3 ± 0.13^{b}	2.8 ± 0.03^{a}

IV. Discussion

Diabetes is a chronic metabolic disorder that leads irregularities in carbohydrate, fat and protein metabolism. It poses a major global public health treat and its prevalence is rapidly increasing. It is of significant public importance because of the associated physiological complications. Which includes dysfunction in organs such as pancreas, intestine, liver and kidney [1,10].

In this study, high-fat diet-fed animals administered low dose streptozotocin were used to investigate the potential of GI diets as a low cost method of managing diabetes. The use of this type 2 diabetes animal model enables the opportunity to conduct detailed and mechanistic assessments, such as histopathology that is challenging or impossible to execute in clinical trials [5].

Postprandial hyperglycemia is a well-known indicator of type 2 diabetes and causes life-threatening complications that are linked to the disease. This parameter was assessed to determine the effects of the GI diets on postprandial hyperglycemia. Blood glucose levels in the diabetic groups were consistently higher than the non-diabetic groups. However, the GI diets did not revert the hyperglycemia at the end of the study. This may be due to the damage of the β-cells and the lack of insulin sensitivity in tissues caused by streptozotocin and existing hyperglycemia [3,14]. It is however important to note that, the diabetic animals fed with low GI diet had the lowest level of hyperglycemia throughout the study when the diabetic groups are compared. Body weight was monitored weekly. The data reveals no statistical difference between groups studied. This indicates that there were no observable effects of low, medium and high GI diets on overall body weight changes when compared to the normal diet, when animals were given food *ad libitum*. Altered lipid levels in diabetes are often important in assessing the progression of diabetes. However no significant change was observed in cholesterol and triglycerides when animals fed low, medium and high GI diets were compared to diabetic controls (Table 2). Relative pancreas weight was assessed to determine if the different GI diets had any effects on organ integrity. There was also no significant change in relative pancreas weight in this study.

Insulin produced by the pancreatic β-cell (Fig. 4), is an important hormone that regulates the control of metabolism and the maintenance of normal concentration of glucose and lipid in the blood. Loss of functional β-cell mass via apoptosis and impaired proliferation is documented as the cause for hyperglycemia that leads to the development of type 1 and type 2 diabetes mellitus. Uncontrolled hyperglycemia is toxic to β-cell, leading to further deterioration in β-cell function and hence worsen blood glucose control [1,9]. In this study there was a decrease in serum insulin in the diabetic control group. However, the diabetic groups LD, MD and HD showed increase serum insulin levels. This may be due to a defensive action against streptozotocin and hyperglycemia induced damage to the β-cells in the pancreatic islets, possible regeneration of damage beta cells (Fig. 5), an increase in pancreatic secretions of insulin from β-cells or release of bound insulin [1,8,13].

The present biochemical and histopathological experiments on diabetic rats suggest that it may be possible to improve glycemic control, insulin secretion and histoarchitecture of pancreatic islets via consumption of low and medium GI diets. Incorporating boiled banana, sweet potato, yellow yam and ripe plantain in diabetic menu may aid in better management of type 2 diabetes mellitus.

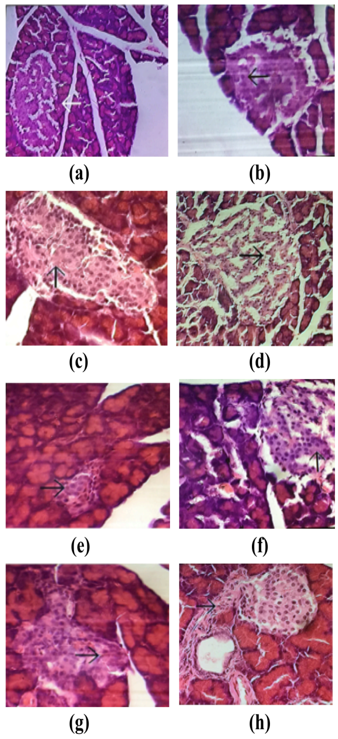

Fig. 5. Photomicrographs of pancreatic islet tissue (stained with haemotoxylin-eosin) of rats from different experimental groups at the end of the experimental period (12 weeks). (a) Normal control rats (NC). (b) Normal rats fed with low glycemic index diet (LN). (c) Normal rats fed with medium glycemic index diet (MN). (d) Normal rats fed with high glycemic index diet (HN). (e) Diabetic control rats (DC). (f) Diabetic rats fed with low glycemic index diet (LD). (g) Diabetic rats fed with medium glycemic index diet (MD). (h) Diabetic rats fed with high glycemic index diet (HD). Magnification x 400.

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