

ANTIHYPOGLYCEAMIC EFFECT OF SOME FRUITS IN ALLOXAN INDUCED DIABETICALBINO MICE.

Abstract

There is always paranoid by individuals suffering diabetes mellitus of any type whether to eat fruits or not, to avoid having above normal glycemic index. Glycemic index of four most and regularly consumed fruits in Nigeria were evaluated in twenty alloxan-induced diabetes mellitus healthy male albino mice matched with parity group. This was a parallel study comprising of intraperitoneally administration of single standard dose of alloxan monohydrate to test animals and equal volume of normal saline to parity matched control group. There was no disparity in glycemic index of the two study groups (test and control). Good diet plan by diabetic individuals is a panacea to maintaining good glycemic index.

Key Word: Antihypoglyceamic Effect, Alloxan Induced, Diabetic Albino Mice, diabetes mellitus

Introduction

Diabetes mellitus is a chronic disease caused by inherited or acquired deficiency in production of insulin by the pancreas, or by ineffectiveness of the insulin produced. It is a metabolic disorder of multiple aetiology characterized by chronic **hyperglycemia** with disturbances of carbohydrate, fat and protein metabolism. The abnormal metabolism results in increased concentration of glucose in blood, which in turn damages many of the body systems (Rockefeller, 2005).

The disease was first classified into three types mainly, using age as the sole criterion without regard to the pathogenesis. Individual who developed the disease at any age below thirty years is said to be suffering from Juvenile-onset diabetes mellitus and those at between thirty and forty years were said to have Maturity-onset diabetes mellitus while those who acquired the disease after forty years of age is said to suffering from Adult-onset diabetes mellitus.

Not long afterward, the classification of diabetes mellitus shifted emphasis from age as the sole criterion to a more pathogenic view with biochemical, clinical and immunological background. The present day classification based on biochemical and clinical background considers diabetes into variants: insulin-dependent diabetes mellitus also known as type one, (Lambert and Bingley,2002) and non-insulin dependent diabetes mellitus also known as type two, (Knowler et al,2002).

However, diabetes mellitus is associated with clinical signs and symptoms such as polydipsia, polyuria, polyphagia weight loss, **fatigue**, anorexia and nocturia. Keto-acidosis and infection are often serious complications associated with **insulin-dependent** diabetes mellitus if not treated or poorly treated and may result in death of the patient, (Bears *et al.*, 2004). Cerebro-vascular disease, coronary artery disorder, neurological complications, blindness and renal failure are also common in an untreated or poorly treated diabetes mellitus especially type one (Cryer, 2006).

As the number of people with diabetes multiplies worldwide, the disease takes an ever-increasing proportion of national and international health care **budgets**.

It is estimated to be one of the **world's** main disablers and killers within next 25 years,(Wild et al,2004). Regions with highest potential are Asia and Africa where the disease is multiplying two to three folds with inadequate treatment facilities,(Chen et al,2004). More so, high cost of conventional drugs with their relatively high incidence of side effects is one important challenge with modern medicine,(Mahler and Adler,1999).The management of diabetes mellitus without any side effect is still, therefore, a major challenge.

Use of plants to treat diabetes mellitus represents a valuable alternative for control of the disease,(Dewanto et al,2002).Guided nutritional regimen has been highlighted as an alternative approach to management of **diabetes**. **The antidiabetic** potential of watermelon showed high reduction in blood glucose in experimental albino rats fed rind ethanol extract of the fruit.

Glycemic effect of fruits in diabetic patients is largely not clear and hence the basis of this study.

Materials and Method.

Laboratory method

There was carried out from July to August, 2017. Forty healthy male wistar albino mice that weighed between 34 and 36 grams were used.

Inclusion criteria:

1. Male wister albino mice that weighs between 34 and 36g.
2. No signs and symptoms of illness or infirmity

Exclusion criteria:

1. Male wister mice that weighs below 34g or above 36g.
2. Mice with signs and symptoms of illness or infirmity.

The mice were purchased from Animal farm of Ebonyi State **University, Abakaliki** and kept in our **laboratory, well** fed and with water for 7days for proper acclimatization.

One hundred milligram of alloxan monohydrate, purchased from Adrich Laboratory LTD,UK, was dissolved in 8ml of distilled-deionised water to a dosage of 3mg/g body weight of the study animals.

Healthy fresh **water-melon, pineapple, orange** and banana fruits were bought regularly according to demand at major market in Abakaliki metropolis.

The animals were acclimatized for 7days.

Study design and treatment.

This was a single blind and parallel group animal study comprising one day intraperitoneally administration of single standard dose of alloxan monohydrate to twenty study animals to induce diabetes mellitus verses administration of same volume of normal saline to twenty parity control group. Pre-test blood glucose of both groups was measured by glucose oxidase method. Thereafter, blood glucose level of both test and control animals were measured every other day for one week using the same method.

Mechanism of action of alloxan monohydrate.

Alloxan-induced diabetes in rodents has been commonly employed as an experimental model of insulin dependent diabetes mellitus,(Loreto and

Elina,2009).It is a toxic glucose analogue that selectively destroys insulin-producing cells in the pancreas (that is beta cells) when administered to rodents and many other animal species,(Lenzen and Panten,1988).It preferentially accumulates in pancreatic beta cells via Glut 2 glucose transporter and causes diabetes in animal models similar to type 1 diabetes in humans,(Dunn et al,1943).In the presence of intracellular thiols, especially glutathione, alloxan generates reactive oxygen species (ROS) in a cyclic redox reaction with its reduction product, dial uric acid. Autoxidation of dial uric acid generates superoxide radicals, hydrogen peroxide and iron-catalyzed reaction step (hydroxyl radicals),(Wohler and Liebig,1838). These hydroxyl radicals are ultimately responsible for death of beta cells, which have low anti-oxidative defense capacity and ensuing state of insulin-dependent alloxan diabetes.

Results

Follow-up:

The animals were fed four types of fruits (water melon, **pineapple**, orange and banana) and water for 14 days. Blood specimens were taken every other day from the animals by passaging for glucose evaluation.

Laboratory procedure:

Blood glucose estimation was carried out using a rapid glucose meter (Accu-Chek from BoehringerIngelheim, Germany).This was done once daily for five days and mean of the five day results calculated as the final blood glucose of each study animal.

The anthropometric and baseline characteristics of the study animals are displayed in Table 1. There was no reported adverse reaction following alloxan administration. However, two test animals died immediately after receiving alloxan injection. The alloxan dosing of 2.5 mg/g was safe and well tolerated by the animals. Comparison of **glycemic** index of the test animals (n=20) with the control animals (n=20) by student t-test showed no significant difference at $P < 0.05$. Five days **glycemic** index of both the test animals and control animals after treatment is shown in Figure 1.

Table 1. Basic Characteristics of the Study Animals.

Characteristics	Treatment Groups		P-value
	Control n=20	Test. n=20	
Age(days)	18-20	18-21	
Weight (grams)	32-36	32-36	
Treatment dose	1ml of 0.9mg of Nacl	1ml of 2.5mg of alloxan	
Blood Glucose (mg/dL),day 0: mean	89.00	86.80	
	SD 3.34	5.00	
	SEM 0.75	1.12	
day 1: mean	87.00	92.90	
	SD 3.34	5.41	
	SEM 0.75	1.21	
day 2: mean	86.70	96.05	
	SD 2.26	4.50	
	SEM 0.59	1.02	
day 3: mean		85.90	99.75
	SD 3.21		5.60
	SEM 0.721		.250
day 4: mean		87.60	100.00
	SD 1.90		4.74
	SEM 0.43		1.960
day 5: mean		87.60	102.45
	SD 1.79		5.36
	SEM .040		1.870

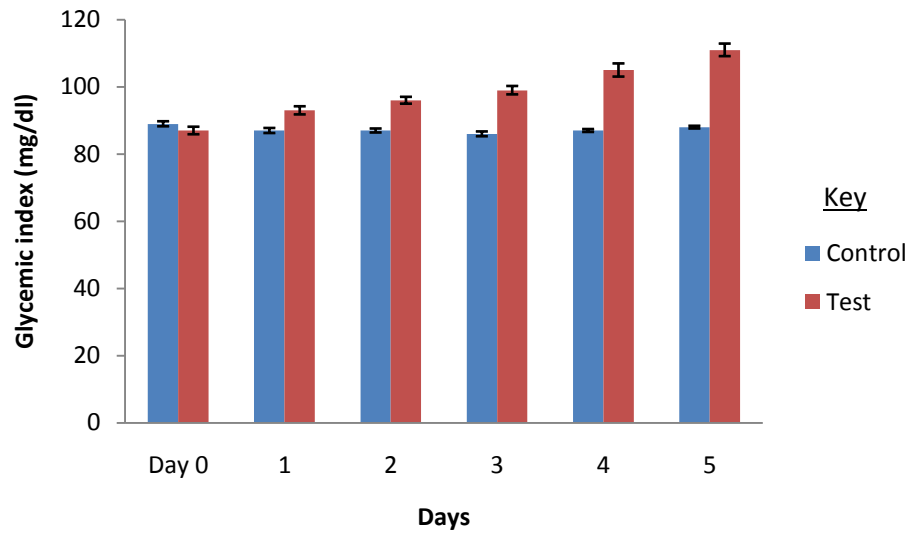


Figure 1: Mean value of glycemic index of the study animal

Discussion:

Maintaining a healthful diet is an important part of managing diabetes. Along with vegetables, fruit is one of the healthiest food groups and contains an important source of vitamin c which helps to keep our cells healthy.

Disparity of blood glucose levels of our study animals (treated and control) did not show significant difference ($p \leq 0.05$). Largely, a combination of a fruit with low glycemic index (watermelon) with those with high glycaemic index (**pineapple, orange** and banana), (Diabetes myths.2018.<http://www.diabetes.org/diabetes-basics/myths/>), were used in the study. Nevertheless, significant difference **was not** observed between blood glucose levels of the two study groups.

Fruit contains carbohydrates and sugars, and a person with diabetes mellitus may want to consider this when putting together a meal plan. Fruit, however, is high in fibre, and foods that contain fibre take longer time to digest, so they raise blood glucose more slowly, Fruits.(2016). <http://www.diabetes.org/food-and-fitness/food/what-can-I-eat/making-health-food-choices/fruits.html> .Most tropical fruits are taken along their fibres and such may slowly increase blood glucose to non significant level because of the effect of fibre on digestion. Most fruits have low glycemic index score but some tropical fruits are in the high range. Therefore, it may be a good idea to eat these fruits less or limit their proportion and frequency of their consumption. Processed foods, fruit juices and dried fruits tend to contain more **glucose than the unprocessed (whole fruit)**. **Despite** the recent accumulation of evidence in support of some fruits having high glycemic index score, combination of fruits that have a high scoring with low-scoring foods can be a healthier choice.

Conclusion.

Consumption of fruits of both high and low glycemic index scoring does not significantly increase glycemic index of diabetes. More so, consumption of whole fruit than processed or fruit juices is therapeutically safer because fibre contents of whole fruit reduces its absorption.

However, regimented consumption of fruits by diabetes is highlighted.

Ethical Approval

Animal Ethic committee approval has been collected and preserved by the author(s)

References:

1. Bearse, M.A. Jr., Han. Y., Schneck, M.E., Barez. S., Jacobsen. C. (2004). Local multifocal oscillatory potential abnormalities in diabetes and early diabetic retinopathy. *Investigation ophthalmology Visceral Science* 45:3259-3265.
2. Chew E.Y, Ambrosius W.T., Davis M.D., Danis R.P. (2010). Effects of medical therapies on retinopathy progression in type 2 diabetes. Accord Eye Study Group. *North England Journal Medical*, 363:233-244.
3. Cryer P.E., (2012). Mechanism of sympathoadrenal failure and hypoglycaemia in diabetes. *Journal of Clinical Investigation*, 116:1470-1473.
4. Dewanto V, Wu X, Adom K.K., and Liu R.H, (2002). Thermal processing enhances the nutritional value of tomatoes by increasing total antioxidant activity. *Journal of Agricultural food Chemistry*. 50: 3010-3014.
5. Dunn J.S., Sheehan H.L, McLetchie N.G.B, (1943). Necrosis of Islets of Langerhans Produced experimentally. *Lancet*, 241: (6242) 484-487.
6. Fruits. (2016). <http://www.diabetes.org/food-and-fitness/food/what-can-I-eat/making-health-food-choices/fruits.html> .
7. Knowler W.C., Barrett-Connor E, Fowler S.E, Hamman R.F., Lachin J.M, Walker E.A., Nathan D.M. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *North England Journal of Medicine*, 346(6) 393-403.
8. Lambert P and Bingley P.J. (2002). What is type 1 diabetes?.

Medicine 30:1-5

9. Lenzen S and Panten U. (1998). Alloxan: history and mechanism of action. *Diabetologia*; 31:337-42.
10. Loreto D, and Elina V. (2009). Experimental surgical models in the laboratory rat. Boca ration: CRC Press.
11. Mahler R.J and Adler M.L. (1999). Clinical review 102; type 2 diabetes mellitus: update on diagnosis, pathophysiology and treatment. *Journal of Clinical Endocrinology Metabolism*. 84:1165-1171.

12. Rimando A.M, and Perkins-Veazie P. (2005). Determination of citruline in watermelon rind. *Journal of Chromatography Analysis*, 1078:196-200.

13. Wild S, Roglic G, Green A, Sicree R, King H,. (2004). Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*, 27:1047-1053.

14. [http://www.diabetes.Org/food and fitness/ food/ what can I eat/making-health-food-choices/fruits.html](http://www.diabetes.Org/food%20and%20fitness/food/what%20can%20I%20eat/making-health-food-choices/fruits.html).

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