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Hypoglycemic Effects of Unripe Pawpaw on Streptozotocin Induced Diabetic Albino Rats

[1,2]H.B. Osadolor, [1]I.I. Ariyo, [2]M.A. Emokpae and [2]K.C. Anukam

[1]Department of Medical Laboratory Science, Ambrose Alli University, P.M.B. 14, Ekpoma, Nigeria
[2]Department of Medical Laboratory Science, School of Basic Medical Sciences, University of Benin, Benin City, Nigeria

Corresponding Author: H.B. Osadolor, Department of Medical Laboratory Science, School of Basic Medical Sciences, University of Benin, Benin City, Nigeria

ABSTRACT

This study was carried out to evaluate the hypoglycemic effect of unripe pulp of *Carica papaya* on streptozotocin induced diabetic albino rats. Thirty male albino rats were used for this study. The animals were examined by a veterinary doctor and allowed to acclimatize for two weeks. The animals were divided into three groups of 10-animals each. Group 1 (test), group 2 (induced control) and group 3 (normal control). Group 1 was fed with unripe pulp of pawpaw while group 2 and 3 were fed with a commercial feed (grower marsh). Samples from five animals were collected from each group after three weeks, another five samples were collected from each groups after five weeks. Plasma glucose level was determined by glucose oxidase method. The mean and standard deviation of the values obtained from group 1 (test) at week 3 and 5 were 56.0±6.0 and 35.8±6.9. The mean and standard deviation of the values obtained for group two (induced control) at week 3 and 5 were 155.0±8.0 and 159.0±4.3 and the mean and standard deviation of the values obtained for group 3 (normal control) were 113.2±3.4 and 112.0±3.2. All the results were statistically significant ($p<0.05$) at week 3 and 5 when compared with controls. This study revealed the hypoglycaemic effects of the pulp of unripe *Carica papaya*. Therefore, there is urgent need to conduct double-blind, randomized placebo-controlled human trial to decipher whether the same hypoglycemic effects could be obtained in human subjects.

Key words: Hypoglycaemia, plasma glucose, pawpaw, diabetes, albino rats, streptozotocin

INTRODUCTION

Focus on plant research has increased worldwide in recent times and a large body of evidence has been collected to show the immense potentials of medicinal plants used in various traditional systems. Various medicinal plants have been studied using modern scientific approaches. Results from these plants have revealed the potentials of medicinal plants in the area of pharmacology (Dahanukar *et al*., 2002; Auddy *et al*., 2003; Somova *et al*., 2003; Fatahi *et al*., 2003).

Synthetic hypoglycemic agents can produce serious side effects including hematological effects, hypoglycemic coma and disturbances of liver and kidney. In addition, they are not suitable for use during pregnancy (Davis and Granner, 2001). Compared to synthetic drugs, herbal preparations are frequently considered to be less toxic with fewer side effects. Glyoherb is claimed to be a single unique formulation that provides a holistic management of blood glucose- and diabetes-related

complications (Thakkar and Petal, 2010). From primodial times, the healing power of herbs has been recognized and botanic medicine has been one of the oldest practiced professions by mankind (Oduola *et al*., 2007).

Medicinal herbs used in indigenous medicines for the management of diabetes mellitus contain both organic and inorganic constituents. Some of these inorganic trace elements possess antidiabetic properties, which accounts for the activity of medicinal herbs. The hypoglycemic efficacy of the inorganic part was tested by the glucose tolerance test on streptozotocin-induced diabetes. Elements such as zinc, chromium, vanadium, potassium and sodium, possessing hypoglycemic activity, were present in the seed. The E. jambolana seed ash treated diabetic rats exhibited normoglycemia and better glucose tolerance (Ravi *et al*., 2004).

In a similar study, Arul *et al*. (2004), also found *Semecarpus anacardium linn* to lower blood glucose in streptozotocin induced diabetes mellitus *Carica papaya*, popularly known as pawpaw and more commonly known as the papaya (Watson, 1997), is common in tropical and sub-tropical countries (Sofowora, 1996). Its biologically active constituents include chymopapain and papain, which are used in the treatment of arthritis and digestive disorders. In folkloric medicine, extracts of the fruits are used for a variety of medicinal purposes ranging from treatment of ringworm, malaria and hypertension (Sofowora, 1996).

The pathogenesis of diabetes mellitus and the possibility of its management by the oral administration of hypoglycemic agents have stimulated a greater interest in recent years. Herbal remedies from medicinal plants have been used traditionally in many parts of the world where access to formal healthcare is limited, especially in tropical Africa. There are several reasons why the use of medicinal plants should be studied: herbal remedies may have recognizable therapeutic and less toxic side effects (Thakkar and Petal, 2010).

This study seeks to evaluate the effect of unripe pulp of pawpaw in glycemic control in streptozotocin induced diabetes mellitus in rats. Considering the fact that most Africans live below poverty level on the economic front, as it is already known world-wide that more than 75% of tropical Africans live on less than one dollar per day. Also, the nontoxic nature of pawpaw from the nutritional and medical point of view gives credence to this study.

MATERIALS AND METHODS

Thirty weaned male albino rats Wistar rats were obtained from the animal farm, College of Medicine, Ambrose Alli University, Edo state, Nigeria in July, 2009 and the animals were taken to the laboratory where they were housed in a plastic cage and placed on commercial feeds (growers marsh from the Bendel Feed and Flour Mill, Ewu, Nigeria) and allowed to drink water freely till the end of the experiment. They weighed between 80 to 100 g. The albino rats were examined by a veterinary doctor and allowed to acclimatize for 2 weeks prior to the commencement of the experiments. At the end of acclimatization, the animals were divided into three groups of 10 each. Group 1 was fed with grated unripe pulp of *Carica papaya* while groups 2 and 3 were fed with growers' marsh. Treatment of the animals was in accordance with the principles of laboratory Animal care. Diabetes mellitus was induced in the albino rats in groups 1 and 2 by subcutaneous injection of 2 mg kg^{-1} body weight of streptozotocin manufactured by Hangzhou Onicon Chemical Co Ltd., China. After 2 weeks, 3 mL of blood specimens were collected from the tails of all the animals (groups 1, 2 and 3). Blood glucose level was determined (Trinder, 1969) to ascertain the presence of hyperglycaemia in the groups 1 and 2 rats. The rats in group 1 were then fed with

grated unripe pulp of pawpaw for five weeks. While, groups 2 and 3 were fed with growers' marsh for the same period. Blood specimens (3 mL) were collected at 7 days interval into fluoride oxalate containers. Fasting blood glucose was measured using glucose oxidase reagent kit supplied by Randox Laboratories, UK. Fasting was achieved by withdrawing all foods from the rats after the last feeding by 8.00 p.m. till 7.00 a.m. the following morning. All glucose determinations were done in duplicate and the mean values were calculated. The test was controlled using quality control reagent kit (Randox Laboratories, UK).

Statistically, the mean and the standard error of mean were calculated at 95% confidence limit.

RESULTS AND DISCUSSION

At the end of this research, it was observed from the results that the rats used lost weight progressively as the diabetes mellitus induced with streptozotocin progressed (Table 1), while the normal control rats gained weight. Table 2, shows unequivocally that diabetes mellitus was induced by streptozotocin within two weeks after administration. Table 3, it clearly shows the therapeutic effects of streptozotocin from weeks 3-5 in the test (induced) group of rats, i.e., those that fed on unripe pulp of pawpaw, the induced control diabetes remained unabated compared with the normal control and the test induced groups respectively. The results show from the tables below that streptozotocin can induce diabetes mellitus and therapeutic potency of unripe pulp of pawpaw:

Table 1: Body weight of albino rats (g) during feeding trials

	Weeks (n = 5)					
Groups	0	1	2	3	4	5
Test (induced)	89.9±5.8	112.2±2.7	130.0±5.6	141.1±5.6	120.6±5.5	98.6±7.0
Induced control	90.5±6.2	123.4±3.3	137.8±3.0	154.4±4.2	140.0±4.1	145.2±4.1
Normal control	89.6±6.4	146.5±4.6	183.8±4.3	193.0±6.4	216.0±4.0	221.65.3
Analysis						
Test (induced) vs. normal control	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05
Induced control vs. normal control	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05

Table 2: Plasma glucose after streptozotocin induction of DM

	Week	
Groups	1	2
Test induced DM (group 1)	159.2±5.0	174.0±4.1
Induced control DM (group 2)	160.3±2.3	172.4±6.2

Table 3: Plasma glucose levels (mg dL^{-1}) of rats on feeding trials

	Week				
Groups	1	2	3	4	5
Test induced	112±3.0	78.5±2.0	56.6±6.0	48.4±2.3	35.8±6.9
Induced control	143.6±4.0	145.5±5.0	155.0±8.0	156.3.0±5.0	159.0±4.3
Normal control	90.5±3.2	96.6±4.0	113.2±3.4	113.0±2.3	112.0±3.2
Analysis					
Test (Induced) vs. normal control	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05
Induced control vs. normal control	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05

There was a general reduction in weight between the test group and the induced group. The test group lost more weight due to the effect of the unripe pulp of *Carica papaya* they were fed with. This was statistically significant at $p<0.05$. The induced group had a normal weight loss from day 1 to 35 ($p<0.05$) because they were diabetic (Akhere and Iyere, 2008).

The dissected test animals showed prominent reduction of subcutaneous fat compared to the control animals. This was noticed during dissection, although this was not part of the original design of the study. The weight reducing effects of the medicinal plants in this study may be an enhancement of their hypoglycemic effect, since obesity is a predisposing condition in some types of diabetes (Akhere and Iyere, 2008). There was an obvious reduction in plasma glucose for the test group that was fed on unripe pulp of *Carica papaya* at week 3 and 5 ($p<0.05$) with the induced control group (diabetic group) remained diabetic at week 3 and 5 ($p<0.05$). From this study, it shows that diabetic albino rat fed with unripe pawpaw (*Ccarica papaya*) for as long as 3 weeks led to hypoglyceamia ($p<0.05$). Arul *et al.* (2004), demonstrated similar hypoglycemic effect using *Semecarpus anacardium* Linn. on streptozotocin induced diabetes in rats.

Thus, the unripe pulp of *Carica papaya* may probably contain active substances that possess blood glucose lowering activities (Olayede, 2005; Auddy *et al.*, 2003). This study is further supported by Baustista (2002), when he used *Urena lobata* Linn. to demonstrate hypoglycemia.

Unripe pulp of pawpaw (*Carica papaya*) has shown that it could be very effective in the treatment of diabetes mellitus. This observation was corroborated by Fakeye *et al.* (2007), clearly showing that this medicinal plants have hypoglycemic effects.

More than 400 plant species having hypoglycemic activity are available in literature (Oliver-Bever, 1986), However, searching for new anti diabetics drugs from natural plants is still attractive because these natural occurring plants are cost effective in the treatment of diabetes mellitus in resource limiting societies.

The results obtained in this study have established that the intake of unripe pulp of *Carica papaya* in the treatment of diabetes mellitus could be effective. During the course of the study, unripe pulp of *Carica papaya* has also shown that it could be effective in weight reduction.

CONCLUSION

The hypoglycemic effect of unripe pulp of *Carica papaya* has been revealed by this study and it could be recommended as remedy for diabetes in humans pending human clinical randomized placebo-controlled trial. In addition further studies are needed to ascertain the hypoglycemic substances present in the plant.

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