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Effects Of Formulated Unripe Plantain And Millet Dietary Feeds In Alloxan-Induced Diabetic Albino Rats

Naomi Ngozi Nnadi

Chinwe Nonyelum Ezekwesili

Obiajulu Christain Ezeigwe

Department of Applied Biochemistry, Faculty of Biosciences,
Nnamdi Azikiwe University Awaka, Anambra State, Nigeria

Abstract: ***Background: Diabetes mellitus is one of the leading causes of deaths worldwide with an estimated prevalence of 700 million projected by 2045. The purpose of this study was to investigate the effects of formulated unripe plantain and millet feeds on lipid profiles in alloxan-induced diabetic albino rats.***

Methods: Twenty-five (25) male albino rats (8-14 weeks) of average weight 135g were randomly divided into five groups (A-E) of five rats each. Group A was the normal control, group B was negative control (diabetic untreated), group C was positive control treated with 100mg/kg bodyweight metformin, group D was fed with unripe plantain + millet formulated feeds (1:1) and group E was fed with unripe plantain + millet incorporated feeds (2:1). The phytochemical and the proximate constituent of the feeds were identified using the standard method of AOAC. The glucose levels of the animals were monitored using a Fine Test Glucometer and the weights were measured using a Search Tech weighing balance.

Results: The result obtained showed that unripe plantain + millet formulated feeds (1:1 and 2:1) significantly ($p<0.05$) decreased the blood glucose level by 50.95% and 42.34% respectively at day 28 in groups D and E rats respectively.

Conclusion: The study thus showed the potentials of unripe plantain and millet formulated feeds at different ratio (1:1 and 2:1) in the management of diabetes mellitus.

Keywords: Diabetes mellitus, plantain, millet, alloxan

I. INTRODUCTION

Diabetes mellitus (DM) is a long-term metabolic disorder that poses a great threat globally, with no regard to socioeconomic status. It is a chronic condition that occurs when there is a raised level of blood glucose, due to the inability of the body to produce enough insulin or its inability to effectively utilize insulin produced. It is one of the causes of death worldwide [1] with about 50% of DM undiagnosed [2].

The incidence of diabetes mellitus keeps rising globally. In 2017, 451 million (age 18–99 years) people were estimated to be living with diabetes worldwide with a death toll of about 5.0 million [3]. As at 2019, the prevalence of diabetes globally was estimated to be 463 million people [3]. It has been predicted that by the year 2030 and the year 2045, it will rise to 578 million and 700 million respectively. The prevalence is higher in urban (10.8%) than rural (7.2%) areas, and in high-income (10.4%) than low-income countries (4.0%) [4].

In Africa, an estimated 19.4 million adults are living with diabetes. A systematic review and meta-analysis reported the prevalence of diabetes mellitus in Nigeria to be 3.0% in the north-west, 5.9% in the north-east, 3.8% in the north-central zone, 5.5% in the south-west, 4.6% in the south-east, and 9.8% in the south-south zone. Unhealthy dietary habits were

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found to be the major risk factor having a pooled prevalence of 8.0% [5].

Uncontrolled hyperglycaemia affects several organs, tissues and systems of the body. Individuals living with diabetes mellitus are vulnerable to life threatening complications such as diabetic retinopathy, diabetic foot, peripheral neuropathy that affects the distal nerves of the limbs, cancer, cerebrovascular disease, heart-related problems, kidney disease, diabetes mellitus-related amputations. When not controlled, it can cause atherosclerosis which can lead to high blood pressure [6. 7].

Glycaemic control has been reported to improve the health condition of type 2 diabetic patients. High glycaemic index (GI) diets elevate glucose-induced insulinotropic peptide (GIP) causing postprandial inflammation, fatty liver, and insulin resistance [8]. Avoiding food high in GI, lowers body weight in obese patient, in diabetic patient and in excessive birth weight (macrosomia). It also reduces insulin usage in gestational diabetes mellitus patients [9' 10]. Several studies have proved the fact that high glycaemic index is a risk factor in the development of complications that come along with diabetes mellitus such as cardiovascular disease (CVD), coronary heart disease (CHD) and cancer [6, 11].

Plantain *(Musa paradisiaca)* is a tropical plant that is mainly grown in tropical and subtropical countries. Its fruits, 5-7cm long, are oblong and fleshy. The fruits as well as other part of the plant have been used in traditional medicine to treat dysentery, uremia, and diarrhea, intestinal lesion in ulcerative colitis, diabetes mellitus, gout, nephritis and cardiac disease.

Pearl millet (*Pennisetum glaucum* (L.) R. Br.) is a staple food in Africa and India where it is used to make flour, bread, porridge and "couscous". It is enriched with vital nutrients such as Vitamin-B and rich in minerals such as iron, and zinc which may help in increasing hemoglobin level. It has the highest folic acid amongst all the cereals, which makes it the diet of choice for pregnant women [12]. It has a high fiber content and the protein contents can modulate glycemic control and insulin secretion [13]. It contains high antioxidant levels which enhance insulin activity, and helps prevent cancer, cardiovascular disease and are anti-fungal and anti-ulcerative [14]. A study carried out at University of Eastern African Baraton by Niduka and Ngule [15] reported that Pearl millet inhibited the growth of *Serratia marcescens*, *Salmonella typhi*, *Proteus vulgaris* and *Staphylococcus epidermidis*.

The presence of these phyto-constituents makes them (plantain and millet) a target for nutritional and therapeutic researches. Thus, this study investigated the most effective way through which formulated unripe plantain and millet diet could help to reduce blood glucose level in diabetic rats.

II. MATERIAL AND METHODS

A. STUDY SITE

This research was carried out at Natural Products Research and Development Laboratory, Special Research Centre, Nnamdi Azikiwe University, Awka.

B. COLLECTION AND IDENTIFICATION OF SAMPLE

The unripe plantain variety (*Musa paradisiaca*) and millet (*Pennisetum glaucum*) were obtained from Eke Market, Awka, Nigeria. The samples were identified and authenticated at the Department of Botany, Nnamdi Azikiwe University, Awka by Dr B. I. Aziagba. The voucher numbers as deposited in the herbarium of the Department of Botany, Nnamdi Azikiwe University, Awka, Nigeria, were 07^{B} and 06^{B}.

C. PREPARATION OF SAMPLE

Both samples of unripe plantain and pearl millet were washed with tap water to remove contamination and dirt. They were afterwards peeled and sliced thinly. The slices were oven dried and then milled into fine flour and stored in air-tight plastic containers.

D. FORMULATION OF FEED

The feed was formulated as given below:
Plantain: Millet (1:1) (sample A)
40% top feed + 30% unripe plantain +30% millet
Plantain: Millet (2:1) (sample B)
40% top feed + 40% unripe plantain + 20% millet

E. PROXIMATE ANALYSIS

The moisture, ash, crude fiber and crude fat were determined using standard methods according of the Association of Official Analytical Chemists [16]. Crude protein was determined by the Micro-Kjeldahl method as proposed by AOAC [16]. The total percent carbohydrate content was estimated by the difference of 100 of the other proximate components as reported by Yerima and Adamu [6] using the following formula:

Total Carbohydrate (%) = 100 - (% Moisture + % Ash + % Crude fibre + % Crude protein + % Fat)

F. QUANTITATIVE PHYTOCHEMICAL ANALYSIS

Saponins was determined as described by Obadoni and Ochuko [17] while tannins were estimated as described by Pearson [18]. Oxalate was analyzed as described by Harborne [19]. Flavonoids was determined as described by Boham and Kocipai [20] and the phytate content was determined using the method of Young and Greaves [21]. The quantity of phenols and alkaloids was determined as described by Harborne [19].

G. EXPERIMENTAL ANIMALS

Twenty-five (25) adults male Wistar albino rats (8-14 weeks) of average weight of 135g were obtained from Chris Farms at Mgbakwu, Anambra State. The animals were housed in standard animal cages in the animal house of Department of Applied Biochemistry, Nnamdi Azikiwe University. They were allowed 7 days for acclimatization with standard rat feed.

a. GROUPING OF ANIMALS

The alloxan monohydrate-treated rats with stable diabetic condition were divided into 4 subgroups (Groups B to E) comprising of five animals per group while the non-diabetic group served as the normal group as follows:

Group A: Normal rats fed standard rat feed and water (non-diabetic control).

Group B: Diabetic control rats which also received standard rat feed and water.

Group C: Diabetic rats fed with standard rat feed and water and treated with 100 mg/kg bodyweight metformin (a standard antidiabetic drug used for the treatment of diabetes).

Group D: Diabetic rats fed with unripe plantain + millet incorporated feeds (1:1) and water

Group E: Diabetic rats fed with unripe plantain + millet incorporated feeds (2:1) and water daily for a period of 28 days respectively. At the end of the treatment period, the animals were anesthetized and blood was collected by cardiac puncture.

H. INDUCTION OF DIABETES

Diabetes mellitus was induced intraperitoneally with alloxan monohydrate (120 mg/kg *b.w.*) after measurement of the baseline fasting blood sugar levels of the rats. The onset of diabetes was established with increase in the fasting blood sugar level above 200 mg/dl. Two days after induction with alloxan monohydrate, the weights of the rats, the blood glucose level as well as other symptoms of diabetes were determined and monitored.

I. MONITORING OF BLOOD GLUCOSE AND BODY WEIGHTS

The glucose levels of the animals were monitored using a Fine Test Glucometer and the weights were measured using a Search Tech weighing balance. Before induction, the weights and blood glucose levels of the animals were measured and then afterwards recorded on a seven-day interval until the end of the experiment.

J. ANIMAL SACRIFICE AND BLOOD COLLECTION

The animals were anaesthetized with chloroform and blood samples collected via cardiac puncture. The samples were collected into the universal bottles and allowed to clot, after which they were centrifuged for 10 minutes at 4000 rpm. The sera obtained were transferred into another set of test tubes. The sera were used for the biochemical analysis on the same day.

K. DATA ANALYSIS

Data obtained from the experiments were analyzed using the Statistical Package for Social Sciences (SPSS) software for Windows version 21 (SPSS Inc., Chicago, Illinois, USA). All the data were expressed as Mean ± SD. Statistical analysis of the results obtained was performed by using one-way analysis of variance test to determine if significant difference exists between the mean of the test and control groups. The limit of significance was set at $p<0.05$.

III. RESULTS

A. PROXIMATE ANALYSIS OF FORMULATED FEED FROM UNRIPE PLANTAIN AND MILLET

The proximate analysis of the formulated feed in the appropriate ratios is presented in Table 1. The findings are expressed as Mean ± Standard deviation of triplicate determinations. The percentage ash, moisture, crude fiber, crude protein and total carbohydrates with mean values of 24.95 ± 0.03, 13.98 ± 0.28, 0.69 ± 0.17, 8.40 ± 0.22 and 48.99 ± 0.04 respectively, were obtained for the feed formula in the ratio of 1:1. For the feed formula of 2:1, the ash, moisture, fibre and carbohydrates were found to be 21.21, 12.87, 1.63 and 53.55 respectively. However, the total carbohydrates, protein, fibre were found to be higher in sample B than sample A while crude fat, fibre and moisture were considerably higher in sample A than sample B.

***Constituents* (%)**	***Sample* A**	***Sample* B**
Carbohydrate	48.99	53.55
Protein	8.40	9.10
Fat	2.98	1.64
Fibre	0.69	1.63
Moisture	13.98	12.87
Ash	24.95	21.21

Results are expressed as Mean ± Standard deviation of triplicate determinations

Table 1: Proximate Analysis of formulated feed from unripe Plantain and millet

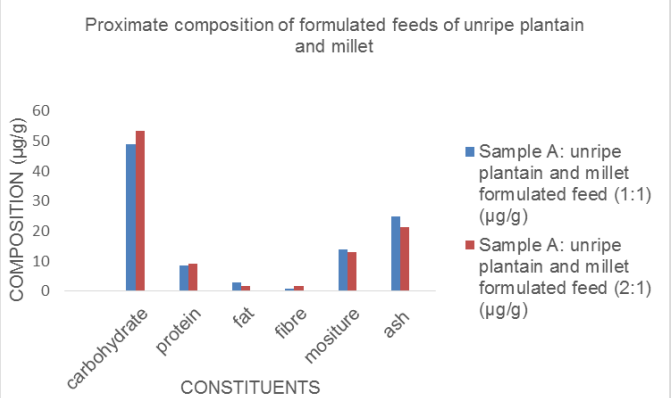

Figure 1

B. PHYTOCHEMISTRY OF FORMULATED UNRIPE PLANTAIN AND MILLET FEED

The phytochemical analysis of the formulated feed samples of unripe plantain and millet feed is presented in Table 2 below. Generally, from the investigations, both sample feed formulas expressed considerable amounts and presence of phytochemicals. Catechin, oxalate, flavon-3-ol and rutin were clearly absent in sample A but present in sample B. Only steroids were observed to be absent in sample B. Both formula ratios had high contents of anthocyanins. There was a significant difference in anthocyanins,

proanthocyanins and naringenin when the two extracts were compared ($P = 0.05$).

Component	Sample A (µg/g)	Sample B (µg/g)
Sapogenin	4.01	9.00
Flavonones	8.29	10.45
Phytate	2.30	5.88
Lunamarin	10.41	12.98
Kaempferol	3.12	7.77
Flavone	8.34	9.75
Quinine	18.94	20.16
Anthocyanin	28.40	40.36
Tannins	5.72	6.22
Catechin	-	8.69
Naringin	13.28	15.09
Proanthocyanin	5.58	13.67
Oxalate	-	0.27
Flavan-3-ol	-	1.17
Steroids	8.81	-
Rutin	-	18.09
Resveratrol	3.54	5.37
Phenol	39.98	33.65
Epicatechin	7.61	6.42
Ribalinidine	30.23	32.38
Naringenin	8.46	21.03

Results are expressed as Mean ± Standard deviation of triplicate determinations

Table 2: Phytochemical Analysis of formulated unripe Plantain and Millet feed

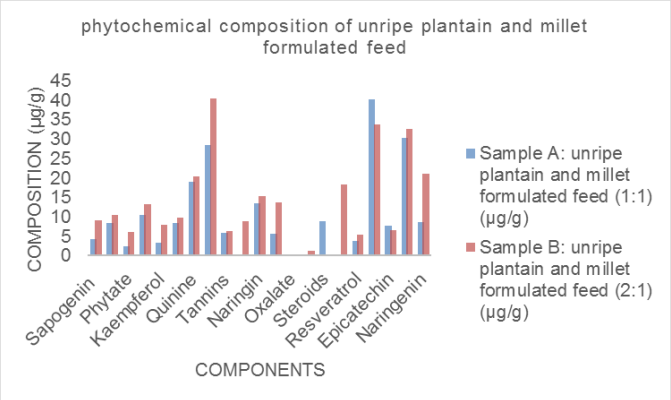

Figure 2

C. EFFECT OF THE FORMULATED FEED OF UNRIPE PLANTAIN AND MILLET ON BODY WEIGHTS OF THE RATS

The table below shows the average weights of each of the rat groups through the experimental period. There was no significant difference in the initial weights of the animals ($P > 0.05$). The least average initial weight was observed in group B with a value of 132.4 ± 2.48 while the group D rats had the highest average initial weight. After the induction of diabetes using alloxan, there was a drastic reduction in weights in days 1 and 2 in all the groups except the normal group. The weights began to increase from Week 1 and continued on a steady rise till the end of the experiment except in the untreated group. The body weights were also found to be significantly different ($P = 0.05$).

GROUP	*Initial* weight (g)	Weight (g) Week 0	Weight (g) Week 1	Weight (g) Week 2	Weight (g) Week 3	Weight (g) Week 4
Group A	132.6 ± 2.20	135.2 ± 2.63	146.8 ± 2.91	155.8 ± 1.88	165.2 ± 2.44	181.4 ± 5.70
Group B	132.4 ± 2.48	118.2 ± 1.46	122.6 ± 1.17	122.8 ± 1.59	128.6 ± 1.96	132.6 ± 2.38
Group C	135.0 ± 3.49	121.8 ± 4.04	126.8 ± 6.25	133.0 ± 5.55	138.2 ± 6.21	143.4 ± 6.49
Group D	140.4 ± 1.69	124.2 ± 3.17	130.0 ± 3.24	141.0 ± 5.43	149.0 ± 7.50	156.0 ± 7.36
Group E	138.6 ± 2.80	119.2 ± 3.54	126.8 ± 4.03	134.6 ± 2.98	144.2 ± 4.32	153.4 ± 3.80

Results are expressed as Mean ± Standard deviation of triplicate determinations

Table 3: Body Weight Changes of formulated unripe Plantain and Millet feed through experiment period

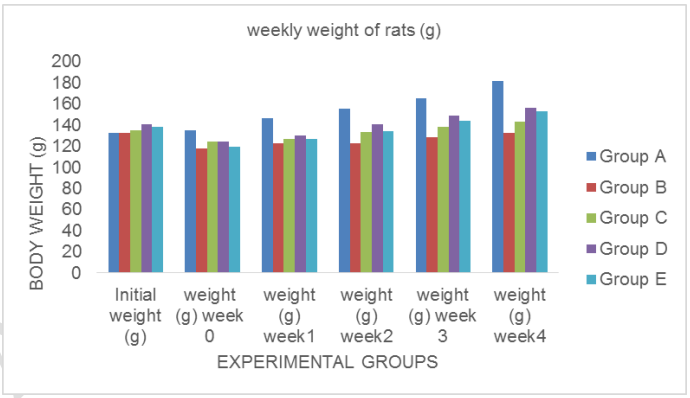

Figure 3

D. EFFECT OF THE FORMULATED FEED OF UNRIPE PLANTAIN AND MILLET ON BLOOD GLUCOSE LEVELS OF THE RATS

The table presents the mean blood glucose levels in the various rat groups over the period of the experiment. The control group remained below 100 mg/dl throughout the experiment while the other groups clearly increased markedly above 200 mg/dl after two days of successful induction of diabetes. Except for the diabetic control (group B), mean blood glucose levels were observed to markedly decrease in groups C, D and E till the end of the experiment. By the last day of administration, the blood glucose levels in the experimental groups had dropped significantly. The untreated group had the highest final glucose level of 503.8 ± 28.44 mg/dl while the control was the least at 81.4 ± 6.56 mg/dl. The difference in final glucose levels were also significant ($P = 0.05$) when all the treatment groups were compared with the negative control. By the 28th day of experiment, the rat groups D and E showed a 50.95% and 42.34% drop in mean blood glucose levels respectively from the induction of experimental diabetes, which was also observed to be significant ($P = 0.05$).

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Group	Initial	Day 4	Day 8	Day 12	Day 16	Day 20	Day 24	Day 28
A	89.6 ± 5.74	81.4 ± 3.67	82.6 ± 5.52	86.0 ± 6.19	85.2 ± 7.12	88.8 ± 6.34	85.4 ± 5.46	81.4 ± 6.56
B	83.2 ± 5.07	507.2 ± 50.24	453.4 ± 59.85	555.6 ± 22.21	484.2 ± 53.65	430.2 ± 59.08	481.6 ± 45.39	503.8 ± 28.44
C	88.6 ± 7.06	531.8 ± 34.40	324.4 ± 48.44	399.2 ± 80.74	310.8 ± 98.17	333.0 ± 79.77	304.2 ± 58.41	367.6 ± 90.89
D	91.6 ± 7.12	450.0 ± 88.62	467.7 ± 128.35	269.5 ± 99.42	248.0 ± 91.65	207.3 ± 81.85	249.5 ± 104.51	232.0 ± 35.63
E	93.0 ± 6.75	46.4 ± 7.24	314.8 ± 58.14	286.0 ± 41.38	275.2 ± 77.71	273.0 ± 87.41	297.6 ± 68.68	294.2 ± 34.30

Results are expressed as Mean ± Standard deviation of triplicate determinations

Table 4: Blood Glucose Levels of Rats through the experiment period

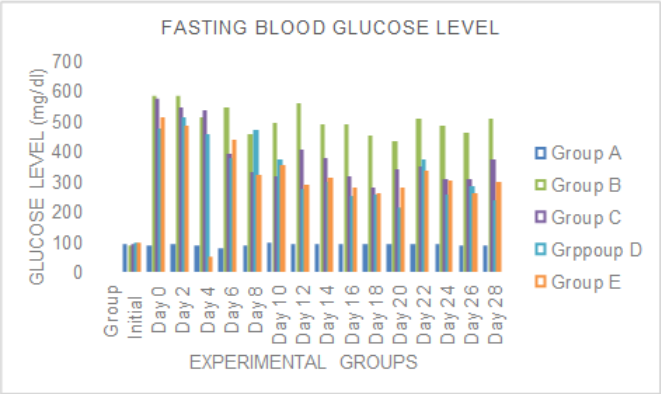

Figure 4

E. PERCENTAGE CHANGE IN BLOOD GLUCOSE LEVEL

The percentage change in mean blood glucose level is presented in Table 5 below. It shows the highest percentage change in group D of 50.95 greater than that of group E at 42.34 while the lowest change was observed for normal control at 4.01.

GROUP	Baseline *level*	Glucose level after alloxan	Final glucose level at day 28	Percentage change of blood glucose at day 28
Group A	89.6 ± 5.74	84.8 ± 2.63	81.4 ± 6.56	+4.01
Group B	83.2 ± 2.07	580.6 ± 19.4	503.8 ± 28.44	+13.23
Group C	88.6 ± 7.06	567.0 ± 21.99	367.6 ± 90.89	+35.17
Group D	91.6 ± 7.12	473.2 ± 55.05	232.0 ± 35.63	+50.95
Group E	93.0 ± 6.75	510.2 ± 54.37	294.2 ± 34.30	+42.34

Results are expressed as Mean ± Standard deviation of triplicate determinations

Table 5: Percentage change in blood glucose level at day 28

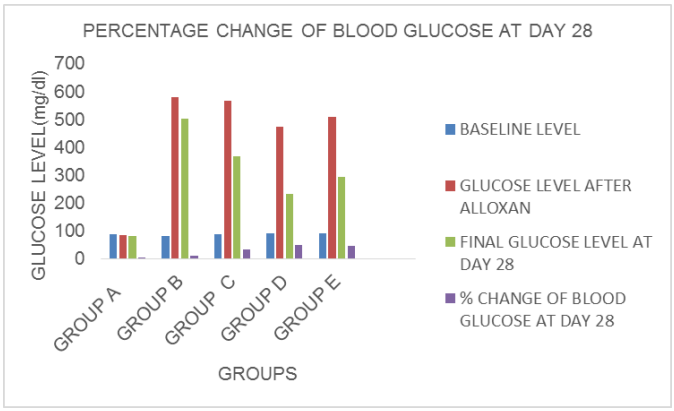

Figure 5

IV. DISCUSSION

In this study, there was weight loss in diabetic control rat after induction with alloxan (table 1) which is in line with several studies [24] This could be as a result of reduction in the level of protein synthesis due to declined amino acid uptake by tissues and resulting to lipolysis in adipose tissues and protein breakdown [25, 26]. The formulated feed of unripe plantain and millet (1:1) with low carbohydrate content decreased the glucose level more than that of the formulated feed of unripe plantain and millet (2:1) having high carbohydrate content (table1). The regular frequent consumption of carbohydrate results in hyperglycemia due to rapid digestion, which triggers the release of free radicals.

Phytochemical screening of the formulated feeds (plantain + millet 1:1 and plantain + millet 2:1) revealed the presence of saponins, epicatechins, flavonoids, tannins, alkaloids, steroids, terpenoids among others (table 3). Saponin have been reported to lower glucose level by slowing gastric emptying through inhibiting carbohydrate digestive enzymes and stimulating of insulin secretion [27]. Epicatechins are effective scavengers of free radicals; they decrease the oxidation of low-density lipoprotein. They also regulate the metabolism of carbohydrate, protein and fat [28, 29].

Flavonoids are known to act against diabetes mellitus either through their capacity to avoid glucose absorption (inhibition of α-glucosidase activity in the intestine), or to improve glucose tolerance. It also acts as insulin secretagogues or insulin mimetics, by pleiotropic mechanisms, to halt diabetic complications. Tannins are excellent free radical scavengers while anthocyanin exert their effects through the following improvement of insulin signaling, increase of plasma insulin levels and induction of insulin release from the pancreas, as well as inhibition of disaccharides activity, activation of glycogen synthesis, inhibition of α- glucosidase activity and inhibition of mRNA expression of glycogen phosphorylase [30]. Hence, the biological effects of formulated feeds are connected with their active components. This finding is in line with those of the previous studies carried out on antidiabetic and antihyperglycemic activity of plantain and millet. Studies from Shodehinde *et al.* [31] reported that unripe pulp of M. paradisiaca reduced blood glucose levels by inhibiting intestinal α-glucosidase, pancreatic α-amylase, and

angiotensin-I-converting enzyme (ACE) in diabetic adult male Wistar rats after 14 days of oral administration due to the polyphenolic content.

According to Bhinge *et al*. [32] unripe pulp extracts of plantain possess better antidiabetic effect over ripe pulp extract. Other reports have supported the claimed of antidiabetic effect of plantain [33-35].

The fasting blood glucose level of group B (Diabetic rats fed with standard rat feed) significantly increased after the administration of alloxan. Alloxan induce DM by destruction of pancreatic beta cells selectively via disruption of the cell membrane integrity and thereby causing a primary deficiency in insulin without affecting other types of islets. One of the mechanisms for its cell destruction is by intracellular generation of free radicals [36]. These free radicals damage the pancreas by causing reduction in the synthesis and release of insulin. The pancreatic beta – cells, stores, synthesize, and release insulin, a peptide hormone regulating protein and carbohydrate [37].

The fasting blood sugar decreased when the rats were treated and fed with metformin and the formulated feed respectively. Metformin alleviates hyperglycemia via suppression of hepatic gluconeogenesis and enhancement of tissue glucose uptake. Metformin has also been shown to increase AMP-activated kinase (AMPK) phosphorylation and downstream responses of glucose and hepatic lipid regulation, including cholesterol and triglycerides in clinical studies [38]. According to Ajiboye *et al*. [34], *M. paradisiaca*-based diet significantly (P = .05) reversed the levels of fasting blood glucose, with significant (P = 0.05) increase in insulin and glycogen concentrations.

V. CONCLUSION

The study showed the potentials of unripe plantain + millet formulated feeds at different ratio (1:1 and 2:1) in the management of diabetes mellitus, in which the formulated feed of unripe plantain and millet (1:1) decreased the blood glucose level more than that of the formulated feed of unripe plantain and millet (2:1). This could be as a result of the high polyphenolic contents in the phytochemicals whose antioxidant activity is directly proportional to the total phenol contents. Also, it could be as a result of its low carbohydrate content, as reducing the intake of carbohydrate help stabilize blood glucose.

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