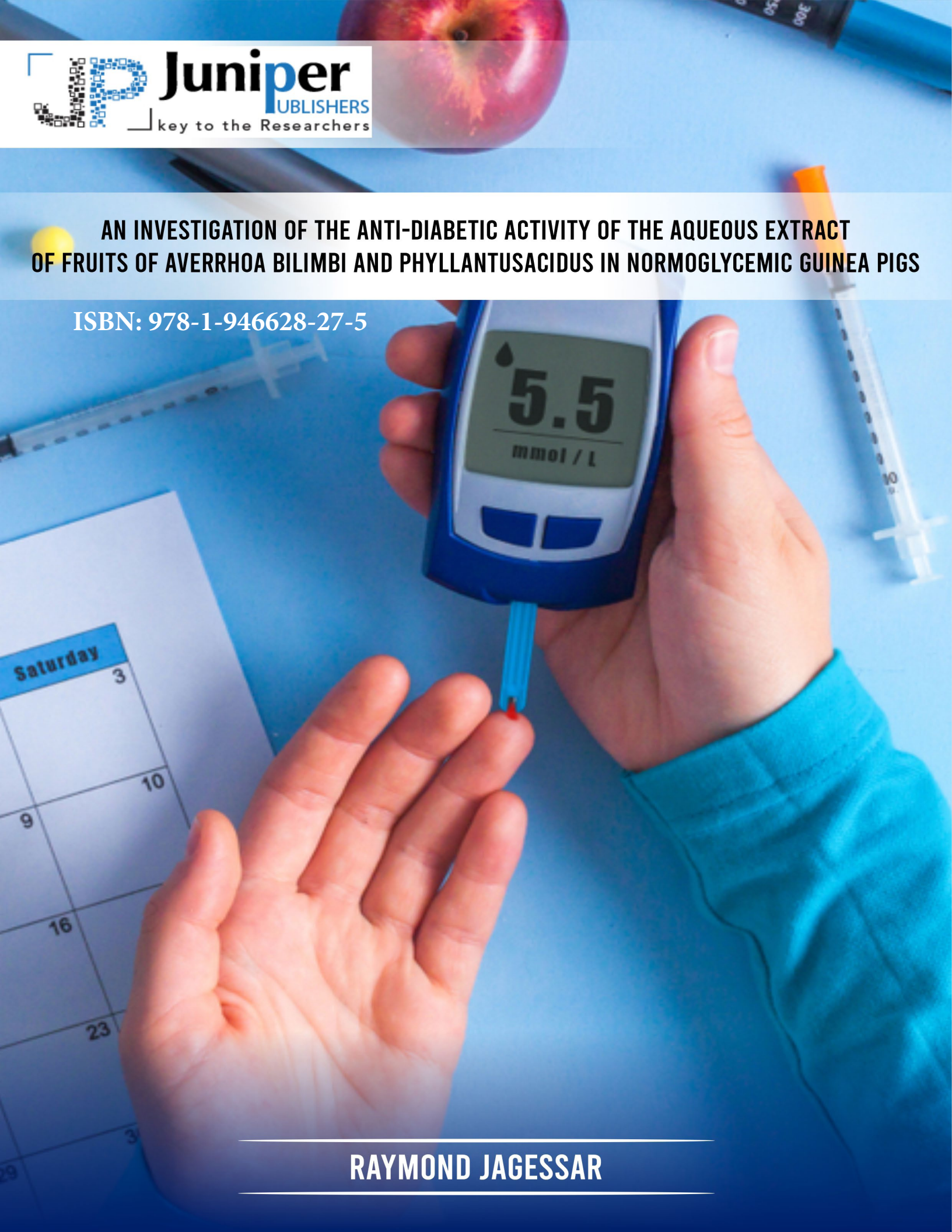


AN INVESTIGATION OF THE ANTI-DIABETIC ACTIVITY OF THE AQUEOUS EXTRACT OF FRUITS OF AVERRHOA BILIMBI AND PHYLLANTUSACIDUS IN NORMOGLYCEMIC GUINEA PIGS

ISBN: 978-1-946628-27-5



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An Investigation of the Anti-Diabetic Activity of the Aqueous Extract of Fruits of *Averrhoa bilimbi* and *Phyllanthus acidus* in Normoglycemic Guinea Pigs

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Published By
Juniper publishers Inc.
United States
August 29, 2019

Content Inside

Abstract	01
Introduction	03
Procedure	04
a. Research Design	
b. Methodology	
c. Variables	
i. Independent Variables	
ii. Dependent Variables	
d. Population	
e. Sample	
f. Experimental Treatment	
g. Plant collection and extraction	
i. <i>Averrhoa bilimbi</i>	
ii. <i>Phyllanthus acidus</i>	
h. Animals and Diet	
i. Blood Glucose Concentration Test (BGCT)	
j. Blood Collection and Analysis	
k. Statistical Analysis	
l. Validity	
i. Reliability	
m. Animals and Diet	
Results	06
Anova Analyses	08
Discussion	18
Conclusion	19
References	20

Abstract

Type 2 Diabetes mellitus (insulin resistance) due to unresponsiveness of receptor on target tissues is a global problem. Diabetes is a common endocrine disorder worldwide. Selected plants are a potential complementary source of hypoglycemic drugs to combat diabetes, in addition to the use of synthetic drugs: insulin, metformin etc. This research focused on the hypoglycemic effect of the aqueous extract of the pulp of *Averrhoa bilimbi* and *Phyllanthus acidus* on normoglycemic guinea pigs. Twelve guinea pigs were divided into five groups of three: Control group, *A.bilimbi* treated group, *Pacidus* treated group and Glibenclamide treatment group and Non-diabetic treated group. The *A.bilimbi* treated group showed 33.48 % reduction in blood glucose level from (148.33±8.18 mg/dl to 98.67±9.81 mg/dl) over the 21 days period. The Glibenclamide treated group showed 14 % reduction of blood glucose level from (126.64±36.71 to 112.00±8.29 mg/dl). The control group showed 0% reduction in blood glucose level. There was an increase in body weight in all cases. For the *A.bilimbi* treated group, this surged from (0.70±0.16 kg to 0.77±0.19 kg). The Glibenclamide treated group showed an increased from (0.63±0.05kg) to 0.68±0.05 kg). For the normal group, this increase from (0.64±0.04 kg) to (0.71±0.04kg). The *Pacidus* treated group showed an hypoglycemic effect in blood glucose level from 120.00±11.31 mg/dl to 99.33±3.68 mg/dl. The Glibenclamide treated group showed 11.58 % reduction in blood glucose level from (126.67±36.1 mg/dl to 112.00±8.29 mg/dl) over the 21 days period. For the control group, there was a reduction in the blood glucose level from (105.67±7.41 mg/dl) to (96.00±4.90 mg/dl) on Day 18th. The Body weight showed an increase for all three groups. For the *Pacidus* treated group, this increase from (0.63±0.12 kg to 0.68±0.11kg over the 21 days period. For the Glibenclamide treated group, this increase from 0.63 ± 0.05Kg to 0.68 ± 0.05 kg. The control group showed an increase from 0.64±0.04kg to 0.71±0.04kg. For the Fasting Blood Glucose Level for Controlled VS. No. Treatment Diabetic group, there was an increase in blood glucose level from (119.67±25.04 mg/dl to 133.33±2.05 mg/dl over the 21 days period. For the corresponding Glibenclamide treated groups, this decrease from 126.67±36.71 mg/dl to 112.00±8.29 mg'dl. For the control group, this decrease from 105.67±7.41 to 105.00±7.48 mg/dl. Both plant aqueous extract did induced a hypoglycemic effect in both cases.

Keywords: Diabetes mellitus; *Psidium guajava*; *Tamarindus indica*; *Averrhoa bilimbi*; Blood glucose; Hypoglycemic activity; Glibenclamide; Guinea pigs; Islet of Langerhans; Hyperglycemia; Pancreas; Glycosuria; Glucosidase inhibitors

Abbreviations

DM: Diabetes Mellitus;
WHO: World Health Organization;
STZ: Streptozotocin;
Abe: *Averrhoa bilimbi*;
HFD: High Fat Diet;
BWM: Body Weight Mass;
BGCT: Blood Glucose Concentration Test;
RBS: Random Blood Sugar;
ANOVA: Analysis of Variance;
BW: Body Weight;
FBG: Fasting Blood Glucose

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Introduction

Diabetes mellitus is a chronic health problem with long term consequences that are potentially preventable. It is a heterogeneous group of disease, characterized by high blood glucose levels, resulting from impaired insulin secretion, impaired insulin action, or both [1-4]. It is associated with the deterioration and loss of proper functioning of the β -cells of islet of Langerhans of the pancreas and as a result of receptor malfunctioning. Thus, glucose is not taken up by the tissues and the glucose level in the blood increases causing hyperglycemia which is a major symptom of diabetes mellitus. As such, prolonged and more severe hyperglycemia contributes to other pathological conditions associated with diabetes mellitus. In addition, other factors such as oxidative stress pose damages insulin-producing cells of the pancreas which is also a determining factor for the progression of diabetes. In a hyperglycemic state, the body tries to remove excess glucose by excreting in the urine.

This increases urine output, causing glycosuria and result in frequent thirst. In addition, the body is deprived of glucose energy and seeks alternative energy sources such as fats and muscle tissues, leading to weight loss [5]. A diminishing growth effect and increased predisposition to certain infections, may also be present with chronic hyperglycemia [4]. These combinations along with polyuria, polydipsia, polyphagia, and blurry vision produces the common symptoms of diabetes [6]. As this disease progresses, vascular damage ensues leading to severe diabetic microvascular and macrovascular complications [7]. Therefore, diabetes covers a wide range of diseases which are the major causes of chronic morbidity and death in diabetic subjects [8].

Being described as the “the perfect epidemic” this condition affects an estimated 387 million people worldwide. According to the WHO [9], the incidence of diabetes has risen dramatically over the past years with a current prevalence of 9% and it is expected to affect more than 500 million adults by 2030. North America and the Caribbean are the regions with a higher prevalence of 11%, having 37 million people affected. In 2012, an estimated 1.5 million deaths were directly caused by diabetes, with 80% deaths occurring in low and middle-income countries [9]. A national survey revealed the total number of diagnosed diabetic cases in Guyana as 49,800, with an estimated number of 1025 deaths; a substantially high value for a population as small as that of Guyana's [10].

Although, antidiabetic agents such as insulin, biguanides, thiazolidinediones and a glucosidase inhibitors are available in Guyana to treat diabetes, a safe and effective treatment paradigm is yet to be achieved [11]. This is due to that fact that these drugs fail to significantly reduce the course of diabetic complications and have limited use because of their undesirable pathological conditions and high secondary failure rates. Therefore, it is essential to discover more effective antidiabetic agents with few adverse effects, low costs and ease of accessibility [12].

In recent years, there has been a resurgence of interest in medicinal plants for the treatment of diseases [12]. A World Health Organization (WHO) study shows that 80% of the world's population solely relies on medicinal plants for their primary health care needs [13]. Medicinal plant extracts, having antidiabetic properties can be a useful source for the development of oral hypoglycemic agents in both animal models and human subjects [14]. Over 350 plants are used in the treatment of diabetes mellitus, but only a small number of these plants had gained scientific and medical evaluation to assess their effectiveness and efficacy. For the management of diabetes, the World Health Organization [15] (WHO) has recommended the evaluation of traditional plant treatments as they are effective, non-toxic, with little or no side effects and are considered to be excellent candidates for oral therapy [16].

Synthetic drugs currently in use for diabetic treatment include sulfonylureas (such as Glibenclamide). Glibenclamide stimulate the release of insulin from β -cells of the pancreas via the mechanism of action responsible of the inhibition of the potassium (K^+) channels, causing the calcium ion (Ca^{2+}) induced depolarization of the cells which in turn permit the release of insulin. However, these antidiabetic medications have undesirable side effects, including weight gain, hypoglycemia, nausea and diarrhea. These contributes a great deal to non-compliance in patients which can lead to further deleterious progression of their condition and result inevitably, in the increased mortality rate of the disease. As such, alternative modes of treatment using natural extracts form *Averrhoa bilimbi* and *Phyllanthus acidus* to lower blood glucose levels and stimulate insulin production is sought. Both plant extracts should contain hypoglycemic compounds which should act singly or in combination to stimulate insulin production and lower blood glucose level. Should the extracts provide a positive response, the population will be enlightened on the value of local fruits as alternatives that are readily available for their hyperglycemia remedies. With the improvement of Diabetes Management and lessened need for pharmacological intervention, complications associated with the disease and medications used will be diminished.

This research paper aims to explore the hypoglycemic activity of the aqueous extracts of the fruits of *Phyllanthus acidus* and *Averrhoa bilimbi* in guinea pigs with normal blood glucose in comparison to standard synthetic treatment of glibenclamide used in Guyana. To the best of our knowledge, no study was conducted to assess the effectiveness of local fruits to lower blood glucose levels. Therefore, the objective of this study was to determine the hypoglycemic effects of the aqueous extracts of selected fruits in guinea pigs, to explore to what extent these extracts reduce blood glucose level in guinea pigs with normal blood glucose, to compare the hypoglycemic activity of the selected extracts with a standard anti-diabetic drug (glibenclamide), to examine the body weight of the guinea pigs before and after administering each fruit extracts. To increase public awareness of local and easily accessible fruits that can be incorporated into the diet to lower blood glucose levels

and manage diabetes, and to determine the time it takes for each plant extract to exhibit minimum blood glucose level after the administration of glucose. It is assumed that the guinea pigs are healthy, free from disease and infections. Also, the syringes used for injection are aseptic and sterilized and the aqueous solvent of the fruits does not hinder experimental results.

There is little or no report on the antidiabetic activities of *P. acidus*. However, the antidiabetic activities have been reported on other species such as *Phyllanthus amarus* and *Phyllanthus emblica*. Antidiabetic effect of the ethanolic extract of *Phyllanthus emblica* fruits in evan rats has been reported and is dose dependent [17]. The anti-hyperglycemic effect of Quercetin, a major constituent of the methanolic extracts of *Phyllanthus emblica* fruit in Streptozotocin (STZ) induced diabetic rats were determined [18]. The aqueous leaf extract of *Phyllanthus amarus* have been shown to have antihyperglycemic effect in some laboratory animals [19]. *P. acidus* species was used because it is available in Guyana as opposed to *P. emblica*. Anti-diabetic activity of the semi-purified fractions of *Averrhoa bilimbi* in high fat diet fed-streptozotocin-induced diabetic rats has been reported [20]. The present study was designed to investigate the hypoglycemic and hypolipidemic activities of the semi-purified fractions of an ethanolic leaf extract of *Averrhoa bilimbi* (ABI) in high fat diet (HFD)-streptozotocin (STZ)-induced diabetic rats.

Averrhoa bilimbi fruits attenuate hyperglycemia-mediated oxidative stress in streptozotocin-induced diabetic rats [21]. Hyperglycemia-mediated oxidative stress plays a major role in the development of diabetic complications. *Averrhoa bilimbi* Linn. (Oxalidaceae) is a medicinal plant with fruits reported to possess antidiabetic activity. This study evaluated the beneficial effects of the ethyl acetate fraction of *A. bilimbi* fruit (ABAEE) on the antioxidant/oxidant status in diabetes mellitus.

Procedure

Research design

This experiment featured a fixed effects model experimental design. The prospect of this experiment incorporated investigation of the hypoglycemic effect of two fruit extracts on animal models. The researchers' objective also included the comparison of the hypoglycemic effect of the fruit extracts against the standard drug treatment Glibenclamide.

Methodology

The subjects were divided into five groups of three guinea pigs:

Group I (Controlled group): Three guinea pigs were allotted to the respective cage. They were subjected to administration of pellets, vitamin C, water and green fodder/ Tanner Grass (*Brachiaria arrecta*) for twenty- one (21) days.

Group II (Aqueous (1:1) extracts co-administered): Three guinea pigs were subjected to induction of diabetes mellitus with the reagent Alloxan Monohydrate with a dose of 150mg/kg solublized in 0.2ml distilled water. After forty- eight (48) hours, their blood glucose concentration was tested using a Control- D glucometer and strips (ISO certified). They then received oral administration of the aqueous extracts at individual doses based on their body weights twice daily (every twelve hours) for twenty- one (21) days. This was conducted along with the standard administration of pellets, vitamin C, water and green fodder/ Tanner Grass (*Brachiaria arrecta*).

Group III (Aqueous (1:1) extracts co-administered): Three guinea pigs were subjected to induction of diabetes mellitus with the reagent Alloxan Monohydrate. After forty-eight (48) hours, their blood glucose concentration was tested using Control-D glucometer and strips (ISO certified). They then received oral administration of the aqueous extracts at individual doses based on their body weights twice a day (every twelve hours) for twenty- one (21) days. This was conducted along with the standard administration of pellets, vitamin C, water and green fodder/ Tanner Grass (*Brachiaria arrecta*).

Group IV (Glibenclamide co-treated (2.5mg/kg)): Three guinea pigs were subjected to induction of diabetes mellitus with the reagent Alloxan Monohydrate. After forty- eight (48) hours, their blood glucose concentration was tested using Control- D glucometer and strips (ISO certified). They then received Glibenclamide at a dose 2.5 mg/kg twice daily (every twelve hours) for twenty- one (21) days. The standard diet of pellets, vitamin C, water and green fodder/ Tanner grass (*Brachiaria arrecta*) was maintained.

Group V (No Treatment): Three guinea pigs were subjected to induction of diabetes mellitus with the reagent Alloxan Monohydrate. After forty-eight (48) hours their blood glucose concentration was tested using Control -D glucometer and strips (ISO certified). However, they received no treatment for the induced condition. The standard diet as aforementioned was maintained throughout. Before administration of extracts and supplements, the basal blood glucose levels were taken forty-eight (48) hours, after induction of diabetes mellitus with Alloxan Monohydrate for all the guinea pigs. The extracts and Glibenclamide were administered at six in the morning and again at six in the evening while feeding times followed the same time pattern.

Variables

Independent variables

The Independent Variables comprised of the two fruit extracts and standard drug treatment:

- a) *Averrhoa bilimbi*
- b) *Phyllanthus acidus*
- c) Glibenclamide 5mg

Dependent variables

The Dependent Variables were centered on the Blood Glucose Concentration and Body Weight of the guinea pigs.

Population

The targeted population were guinea pigs sourced from Mandela Avenue, Georgetown, Guyana. The subjects consisted of fifteen (15) males and their Body Weight Mass (BWM) ranged from 560-900g.

Sample

A total of fifteen (15) guinea pigs were randomly selected from a single farm located on Mandela Avenue, Georgetown, Guyana.

Experimental treatment

Two aqueous fruit extracts were used in the conduction of this experiment:

- a. *Averrhoa bilimbi*
- b. *Phyllanthus acidus*

Plant collection and extraction

The fruits of the *Phyllanthus acidus*, and *Averrhoa bilimbi* were picked from trees in Polder, Canal No.2, West Bank Demerara in May.

***Averrhoa bilimbi*:** The fruit was washed thoroughly using warm distilled water to remove any residual pesticide, dirt or bacterial/fungal growth from the surface. They were weighed to reach a mass of 250g and cut into tiny pieces for easy blending in an electric blender. The chopped fruit and 1000ml of distilled water were added to the blender and the mixture was pureed for approximately seven minutes. The mixture was filtered using a kitchen strainer and further filtered with Whatman Qualitative filter paper # 1. The extract was placed in a large glass bottle, labelled with its name and stored in a refrigerator.

***Phyllanthus acidus*:** The fruits were washed thoroughly with warm distilled water and any stems were plucked out and thrown away. They were weighed until they attained 250g and placed into an electric blender with 1000ml distilled water. The mixture was pureed for five minutes and filtered using gauze. This filtrate was further filtered using Whatman Qualitative filter paper # 1 and poured into a large glass bottle appropriately labelled to be stored in the refrigerator.

Animals and diet

The Code of Practice for the Housing and Care of Laboratory Mice, rats, Guinea Pigs and Rabbits (6 December 2004) and Laboratory Animal Medicine- and Science- Series II Guinea Pigs: Care and Management 29 April, 2015 were followed throughout the experiment. Fifteen (15) guinea pigs were selected for this experiment with weights ranging from 560-900g. Before the commencement of the experiment, the animals were kept for an acclimatization period of one week as advised by project supervisor Professor Raymond Jagessar.

The guinea pigs were housed in colony cages (three pigs per cage), measuring 24.5x30.5x48.28 cm. They were made of wood and mesh with ventilated floors and provided by the project supervisor. The animals were stored in an environment ranging from 23- 28°C, while being exposed to twelve hours light and twelve hours darkness. They were fed a standard diet consisting of green fodder/ Tanner Grass (*Brachiaria arrecta*), pellets, vitamin C and distilled water.

The cage pans of each group were cleaned daily and the animals were cleaned three times a week.

Blood glucose concentration test (BGCT)

The Blood Glucose Concentration Test was carried out for the Data Collection. The researchers bought a handheld device i.e. Control-D glucometer and strips. The guinea pigs were divided into five groups containing three pigs each:

Group I (Controlled group): The three guinea pigs were subjected to being pricked on the underside of their rear lower extremity. This occurred every three days as well as weighing of each subject.

Group II (Aqueous (1:1) extracts co-administered): The three guinea pigs were subjected to being pricked on the underside of their rear lower extremity followed by *Averrhoa bilimbi* at tailored individual doses appropriate for their body weights. Testing occurred every three days as well as weighing of the subjects.

Group III (Aqueous (1:1) extracts co-administered): The three guinea pigs were subjected to being pricked on the underside of their rear lower extremity, followed by *Phyllanthus acidus* at tailored individual doses appropriate for their body weights. Testing occurred every three days as well as weighing of the subjects.

Group IV (Glibenclamide co-treated (2.5mg/kg)): The three guinea pigs were subjected to being pricked on the underside of their rear lower extremity followed by Glibenclamide dose of 2.5 mg/kg. Testing occurred every three days as well as weighing of the subjects.

Group V (No treatment): The three guinea pigs were subjected to only being pricked on the underside of their rear lower extremity with no treatment. Testing occurred every three days as well as weighing of the subjects.

Blood collection and analysis

Random blood sugar (RBS) testing was done at every 3 days intervals for the 21 days period. Blood samples were collected from the underside of the rear lower extremity. Glucose concentrations were determined using Control- D Glucometer and Strips (ISO certified). The readings were expressed in units of milligram per deciliter of blood (mg/dL).

Body weight of each guinea pig was measured every 3 days interval for 21 days using a top loading scale.

Statistical analysis

The results were recorded as Mean and Standard Deviation. All data analysis was analysed using 1- way analysis of variance (ANOVA). A P- value or Significant Value of <0.05 will be considered significant.

Validity

The validity of the study is unambiguous as the methodology was guided from similar research with minor modifications made. The conduction of the methodology and compilation of content were both guided by Professor Raymond Jagessar which contributes to the validity of the research.

Reliability: To ensure consistency of the results obtained, three guinea pigs were placed in different cages and further separated within their respective cages during the experiment.

Results

(Tables 1-5)

Table 1: Fasting Blood Glucose for *A. bilimbi* Treated Groups.

Blood Glucose (mg/dl)								
Group	Day 0	Day 3	Day 6	Day 9	Day 12	Day 15	Day 18	Day 21
Controlled								
A	99	95	91	84	113	99	90	115
B	116	100	103	120	120	114	102	103
C	102	90	101	97	96	105	96	97
Mean ± Standard deviation	105.67±7.41	95.00±4.08	98.33±5.25	100.33±14.88	109.67±10.08	106.00±6.16	96.00±4.90	105.00±7.48
Confidence Level 95%	3.75	2.07	2.66	7.53	5.1	3.12	2.48	3.79
A. Bilimbi								
A	141	98	94	95	110	106	100	94
B	128	87	91	103	95	108	105	114
C	176	111	99	93	105	99	108	105
Mean±Standard deviation	148.33± 20.77	98.67±9.81	94.67±3.30	97.00± 4.32	103.33± 6.24	104.33± 3.86	104.33± 3.30	104.33± 8.18
Confidence Level 95%	10.26	4.96	1.67	2.19	3.16	1.95	1.67	4.14
Glibenclamide Treatment								
A	176	78	90	78	110	111	102	123
B	88	94	97	94	105	100	101	103
C	116	96	103	96	86	108	99	110
Mean±Standard deviation	126.67± 36.71	89.33±8.06	96.67±5.31	89.33± 8,06	100.33± 10.34	106.33± 4.64	100.67± 1.25	112.00 ± 8,29
Confidence Level 95%	18.58	4.08	2.69	4.08	5.23	2.35	0.63	4.19

Table 2: Body Weight for *A. bilimbi* Treated Groups.

Body Weight(kg)								
Group	Day 0	Day 3	Day 6	Day9	Day 12	Day 15	Day 18	Day 21
Control Group								
A	0.64	0.64	0.64	0.64	0.72	0.72	0.8	0.72
B	0.6	0.62	0.62	0.62	0.6	0.64	0.66	0.66
C	0.68	0.7	0.72	0.7	0.74	0.72	0.74	0.74
Mean± Standard deviation	0.64± 0.04	0.65± 0.04	0.66± 0.05	0.65± 0.04	0.69 ± 0.08	0.69± 0.05	0.73± 0.07	0.71± 0.04
Confidence Level 95%	0.02	0.02	0.03	0.02	0.04	0.02	0.04	0.02
A. bilimbi Treatment								
A	0.88	0.9	0.88	0.88	0.88	0.94	1	0.98
B	0.64	0.64	0.64	0.68	0.74	0.7	0.74	0.72
C	0.58	0.6	0.6	0.61	0.61	0.64	0.66	0.6
Mean±Standard deviation	0.70 ± 0.16	0.71± 0.16	0.71± 0.15	0.72± 0.14	0.74± 0.14	0.76± 0.16	0.80± 0.18	0.77± 0.19
Confidence Level 95%	0.08	0.08	0.08	0.07	0.07	0.08	0.09	0.1
Glibencamide Treatment								
A	0.6	0.68	0.66	0.68	0.72	0.68	0.76	0.74
B	0.68	0.62	0.66	0.62	0.68	0.66	0.66	0.66
C	0.6	0.6	0.6	0.6	0.61	0.64	0.66	0.64
Mean±Standard deviation	0.63± 0.05	0.63± 0.04	0.64± 0.03	0.63± 0.04	0.67± 0.06	0.66± 0.02	0.69± 0.06	0.68± 0.05
Confidence Level 95%	0.02	0.02	0.02	0.02	0.03	0.01	0.03	0.03

Table 3: Fasting Blood Glucose for *P. acidus* Treated Groups.

Blood Glucose (mg/dl)								
Group	Day 0	Day 3	Day 6	Day9	Day 12	Day 15	Day 18	Day 21
Control								
A	99	95	91	84	113	99	90	115
B	116	100	103	120	120	114	102	103
C	102	90	101	97	96	105	96	97
Mean ± Standard deviation	105.67± 7.41	95.00± 4.08	98.33± 5.25	100.33± 14.88	109.67± 10.08	106.00± 6.16	96.00± 4.90	105.00± 7.48
Confidence Level 95%	3.75	2.07	2.66	7.53	5.1	3.12	2.48	3.79
Glibencamide Treatment								
A	176	78	90	78	110	111	102	123
B	88	94	97	94	105	100	101	103
C	116	96	103	96	86	108	99	110
Mean ± Standard deviation	126.67± 36.1	89.33± 8.06	96.67± 5.31	89.33± 8.06	100.33± 10.34	106.33± 4.64	100.67± 1.25	112.00± 8.29
Confidence Level 95%	18.58	4.08	2.69	4.08	5.23	2.35	0.63	4.19
Pacidus Treatment								
A	128	79	90	79	108	95	98	95
B	104	100	97	100	99	101	101	104
C	128	86	88	86	95	100	100	99
Mean ± Standard deviation	120.00± 11.31	88.33 ± 8.73	91.67± 3.86	88.33± 8.73	100.67± 5.44	98.67± 2.62	99.67± 1.25	99.33± 3.68
Confidence Level 95%	5.73	4.42	1.95	4.42	2.75	1.33	0.63	1.86

Table 4: Body Weight for *P. acidus* Treated Groups.

Group	Day 0	Day 3	Day 6	Day 9	Day 12	Day 15	Day 18	Day 21
Control Group								
A	0.64	0.64	0.64	0.64	0.72	0.72	0.8	0.72
B	0.6	0.62	0.62	0.62	0.6	0.64	0.66	0.66
C	0.68	0.7	0.72	0.7	0.74	0.72	0.74	0.74
Mean± Standard deviation	0.64± 0.04	0.65± 0.04	0.66± 0.05	0.65± 0.04	0.69± 0.08	0.69± 0.05	0.73± 0.07	0.71± 0.04
Confidence Level 95%	0.02	0.02	0.03	0.02	0.04	0.02	0.04	0.02
Phyllantus Acidus Treatment								
A	0.76	0.72	0.72	0.72	0.76	0.78	0.78	0.76
B	0.62	0.62	0.64	0.62	0.61	0.64	0.72	0.72
C	0.52	0.56	0.56	0.56	0.6	0.59	0.6	0.56
Mean ± Standard deviation	0.63± 0.12	0.63± 0.08	0.64± 0.08	0.63± 0.08	0.66± 0.09	0.67± 0.1	0.70± 0.09	0.68± 0.11
Confidence Level 95%	0.06	0.04	0.04	0.04	0.05	0.05	0.05	0.05
Glibencamide Treatment								
A	0.6	0.68	0.66	0.68	0.72	0.68	0.76	0.74
B	0.68	0.62	0.66	0.62	0.68	0.66	0.66	0.66
C	0.6	0.6	0.6	0.6	0.61	0.64	0.66	0.64
Mean± Standard deviation	0.63± 0.05	0.63± 0.04	0.64± 0.03	0.63± 0.04	0.67± 0.06	0.66± 0.02	0.69± 0.06	0.68± 0.05
Confidence Level 95%	0.02	0.02	0.02	0.02	0.03	0.01	0.03	0.03

Table 5: Fasting Blood Glucose for Controlled VS No Treatment Diabetic Group.

Blood Glucose (mg/dl)								
Group	Day 0	Day 3	Day 6	Day 9	Day 12	Day 15	Day 18	Day 21
Control								
A	99	95	91	84	113	99	90	115
B	116	100	103	120	120	114	102	103
C	102	90	101	97	96	105	96	97
Mean ± Standard deviation	105.67± 7.41	95.00± 4.08	98.33± 5.25	100.33± 14.88	109.67± 10.08	106.00± 6.16	96.00± 4.90	105.00± 7.48
Confidence Level 95%	3.75	2.07	2.66	7.53	5.1	3.12	2.48	3.79
Glibencamide Treatment								
A	176	78	90	78	110	111	102	123
B	88	94	97	94	105	100	101	103
C	116	96	103	96	86	108	99	110
Mean ± Standard deviation	126.67± 36.71	89.33± 8.06	96.67± 5.31	89.33± 8.06	100.33± 10.34	106.33± 4.64	100.67± 1.25	112.00± 8.29
Confidence Level 95%	18.58	4.08	2.69	4.08	5.23	2.35	0.63	4.19
No Treatment								
A	155	116	127	91	116	128	127	131
B	100	110	103	91	140	104	116	133
C	104	120	111	145	121	117	130	136
Mean ± Standard deviation	119.67± 25.04	115.33± 4.11	113.67± 9.98	109.00± 25.46	125.67± 10.34	116.33± 9.81	124.33± 6.02	133.33± 2.05
Confidence Level 95%	12.67	2.08	5.05	12.88	5.23	4.96	3.05	1.04

Anova Analyses

(Tables 6-17 & Graphs 1-6)

Table 6: Fasting Blood Glucose for Controlled VS *A. bilimbi* Treated Groups.

		F	Sig.
Day_0	Between Groups	7.817	0.049
	Within Groups		
	Total		
Day_3	Between Groups	0.238	0.651
	Within Groups		
	Total		
Day_6	Between Groups	0.699	0.450
	Within Groups		
	Total		
Day_9	Between Groups	0.093	0.776
	Within Groups		
	Total		
Day_12	Between Groups	0.571	0.492
	Within Groups		
	Total		
Day_15	Between Groups	0.105	0.762
	Within Groups		
	Total		
Day_18	Between Groups	3.981	0.117
	Within Groups		
	Total		
Day_21	Between Groups	0.007	0.936
	Within Groups		
	Total		

Table 7: Fasting Blood Glucose for Controlled VS Glibenclamide Treated Groups.

		F	Sig.
Day_0	Between Groups	0.629	0.472
	Within Groups		
	Total		
Day_3	Between Groups	0.787	0.425
	Within Groups		
	Total		
Day_6	Between Groups	0.100	0.768
	Within Groups		
	Total		
Day_9	Between Groups	0.845	0.410
	Within Groups		
	Total		
Day_12	Between Groups	0.836	0.412
	Within Groups		
	Total		
Day_15	Between Groups	0.004	0.954
	Within Groups		
	Total		

Day_18	Between Groups	1.704	0.262
	Within Groups		
	Total		
Day_21	Between Groups	0.786	0.425
	Within Groups		
	Total		

Table 8: Body Weight for Controlled VS *A. bilimbi* Treated Groups.

		F	Sig.
Day_0	Between Groups	0.403	0.560
	Within Groups		
	Total		
Day_3	Between Groups	0.382	0.570
	Within Groups		
	Total		
Day_6	Between Groups	0.254	0.641
	Within Groups		
	Total		
Day_9	Between Groups	0.688	0.453
	Within Groups		
	Total		
Day_12	Between Groups	0.402	0.561
	Within Groups		
	Total		
Day_15	Between Groups	0.488	0.523
	Within Groups		
	Total		
Day_18	Between Groups	0.365	0.578
	Within Groups		
	Total		
Day_21	Between Groups	0.274	0.629
	Within Groups		
	Total		

Table 9: Body Weight for Controlled VS Glibencamide Treated Groups.

		F	Sig.
Day_0	Between Groups	0.143	0.725
	Within Groups		
	Total		
Day_3	Between Groups	0.346	0.588
	Within Groups		
	Total		
Day_6	Between Groups	0.300	0.613
	Within Groups		
	Total		

Day_9	Between Groups	0.346	0.588
	Within Groups		
	Total		
Day_12	Between Groups	0.094	0.774
	Within Groups		
	Total		
Day_15	Between Groups	1.316	0.315
	Within Groups		
	Total		
Day_18	Between Groups	0.58	0.489
	Within Groups		
	Total		
Day_21	Between Groups	0.471	0.530
	Within Groups		
	Total		

Table 10: Fasting Blood Glucose for Controlled VS *P. acidus* Treated Groups.

		F	Sig.
Day_0	Between Groups	2.247	0.208
	Within Groups		
	Total		
Day_3	Between Groups	0.957	0.383
	Within Groups		
	Total		
Day_6	Between Groups	2.094	0.221
	Within Groups		
	Total		
Day_9	Between Groups	0.967	0.381
	Within Groups		
	Total		
Day_12	Between Groups	1.236	0.329
	Within Groups		
	Total		
Day_15	Between Groups	2.396	0.197
	Within Groups		
	Total		
Day_18	Between Groups	1.052	0.363
	Within Groups		
	Total		
Day_21	Between Groups	0.923	0.391
	Within Groups		
	Total		

Table 11: Fasting Blood Glucose for Controlled VS Glibencamide Treated Groups.

		F	Sig.
Day_0	Between Groups	0.629	0.472
	Within Groups		
	Total		
Day_3	Between Groups	0.787	0.425
	Within Groups		
	Total		
Day_6	Between Groups	0.100	0.768
	Within Groups		
	Total		
Day_9	Between Groups	0.845	0.410
	Within Groups		
	Total		
Day_12	Between Groups	0.836	0.412
	Within Groups		
	Total		
Day_15	Between Groups	0.004	0.954
	Within Groups		
	Total		
Day_18	Between Groups	1.704	0.262
	Within Groups		
	Total		
Day_21	Between Groups	0.786	0.425
	Within Groups		
	Total		

Table 12: Body weight for Controlled VS *P. acidus* treated groups.

		F	Sig.
Day_0	Between Groups	0.08	0.932
	Within Groups		
	Total		
Day_3	Between Groups	0.145	0.723
	Within Groups		
	Total		
Day_6	Between Groups	0.130	0.736
	Within Groups		
	Total		
Day_9	Between Groups	0.145	0.723
	Within Groups		
	Total		
Day_12	Between Groups	0.196	0.681
	Within Groups		
	Total		

Day_15	Between Groups	0.138	0.729
	Within Groups		
	Total		
Day_18	Between Groups	0.250	0.643
	Within Groups		
	Total		
Day_21	Between Groups	0.165	0.705
	Within Groups		
	Total		

Table 13: Body Weight for Controlled VS Glibenamide Treated Groups.

		F	Sig.
Day_0	Between Groups	0.143	0.725
	Within Groups		
	Total		
Day_3	Between Groups	0.346	0.588
	Within Groups		
	Total		
Day_6	Between Groups	0.300	0.613
	Within Groups		
	Total		
Day_9	Between Groups	0.346	0.588
	Within Groups		
	Total		
Day_12	Between Groups	0.094	0.774
	Within Groups		
	Total		
Day_15	Between Groups	1.316	0.315
	Within Groups		
	Total		
Day_18	Between Groups	0.581	0.489
	Within Groups		
	Total		
Day_21	Between Groups	0.471	0.530
	Within Groups		
	Total		

Table 14: Fasting Blood Glucose for Controlled VS No treatment Diabetic Group.

		F	Sig.
Day_0	Between Groups	0.575	0.491
	Within Groups		
	Total		
Day_3	Between Groups	24.642	0.008
	Within Groups		
	Total		

Day_6	Between Groups	3.699	0.127
	Within Groups		
	Total		
Day_9	Between Groups	0.173	0.699
	Within Groups		
	Total		
Day_12	Between Groups	2.456	0.192
	Within Groups		
	Total		
Day_15	Between Groups	1.591	0.276
	Within Groups		
	Total		
Day_18	Between Groups	26.661	0.007
	Within Groups		
	Total		
Day_21	Between Groups	26.661	0.007
	Within Groups		
	Total		

Table 15: Fasting Blood Glucose for Controlled VS Glibencamide Treated Groups.

		F	Sig.
Day_0	Between Groups	0.629	0.472
	Within Groups		
	Total		
Day_3	Between Groups	0.787	0.425
	Within Groups		
	Total		
Day_6	Between Groups	0.100	0.768
	Within Groups		
	Total		
Day_9	Between Groups	0.845	0.410
	Within Groups		
	Total		
Day_12	Between Groups	0.836	0.412
	Within Groups		
	Total		
Day_15	Between Groups	0.004	0.954
	Within Groups		
	Total		
Day_18	Between Groups	1.704	0.262
	Within Groups		
	Total		
Day_21	Between Groups	0.786	0.425
	Within Groups		
	Total		

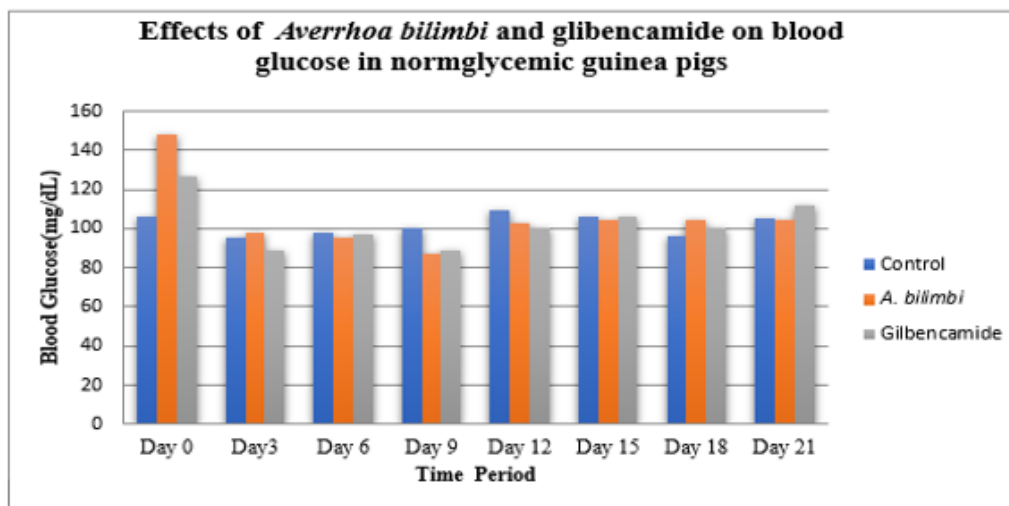
Table 16: Body Weight for Controlled VS No Treatment Diabetic Group.

		F	Sig.
Day_0	Between Groups	0.471	0.530
	Within Groups		
	Total		
Day_3	Between Groups	1.077	0.358
	Within Groups		
	Total		
Day_6	Between Groups	0.876	0.402
	Within Groups		
	Total		
Day_9	Between Groups	2.628	0.180
	Within Groups		
	Total		
Day_12	Between Groups	0.920	0.392
	Within Groups		
	Total		
Day_15	Between Groups	2.314	0.203
	Within Groups		
	Total		
Day_18	Between Groups	1.414	0.300
	Within Groups		
	Total		
Day_21	Between Groups	2.124	0.219
	Within Groups		
	Total		

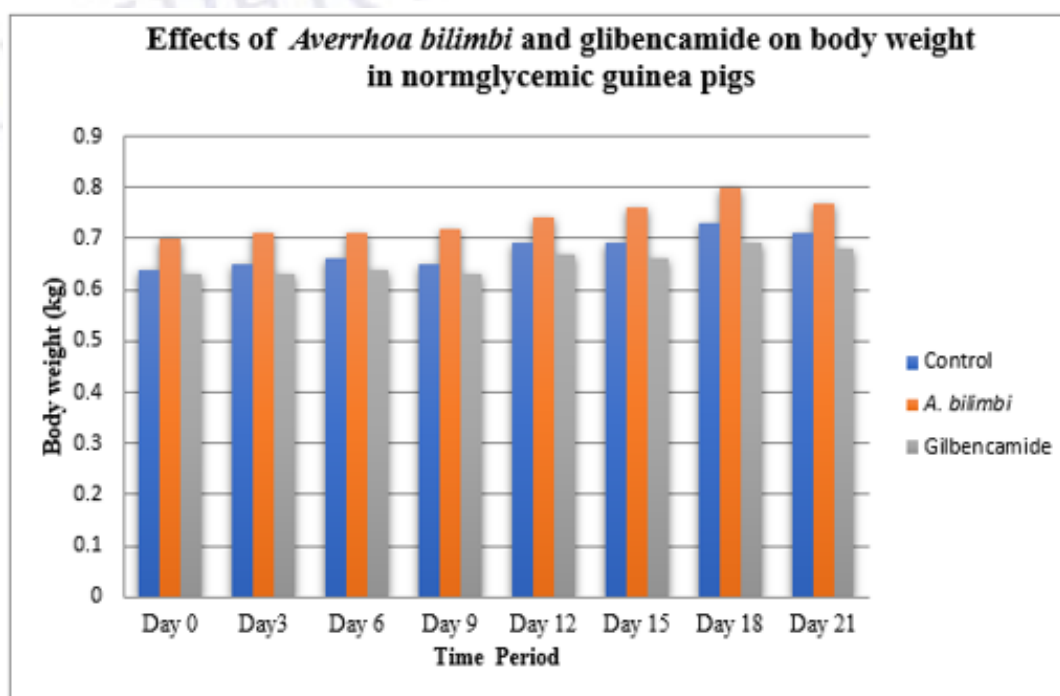
Table 17: Body Weight for Controlled VS Glibenclamide Treated Groups.

		F	Sig.
Day_0	Between Groups	0.143	0.725
	Within Groups		
	Total		
Day_3	Between Groups	0.346	0.588
	Within Groups		
	Total		
Day_6	Between Groups	0.300	0.613
	Within Groups		
	Total		
Day_9	Between Groups	0.35	0.588
	Within Groups		
	Total		
Day_12	Between Groups	0.094	0.774
	Within Groups		
	Total		

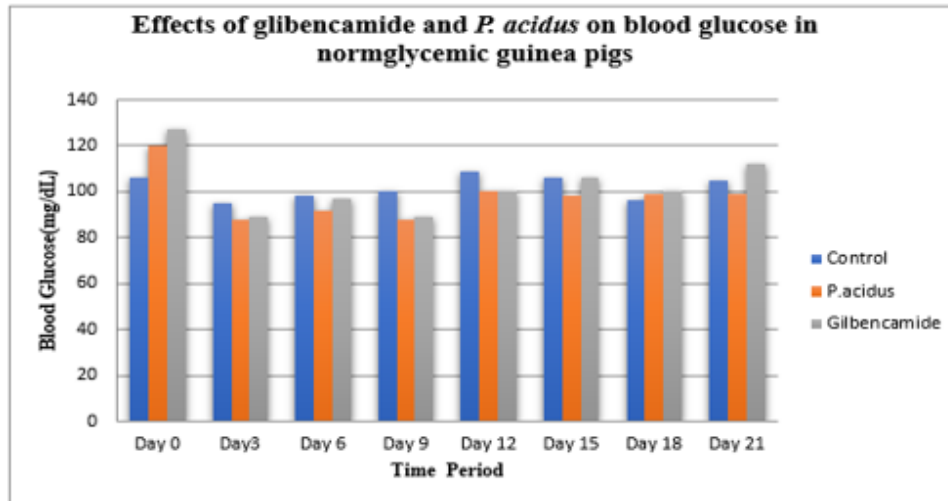
Day_15	Between Groups	1.316	0.315
	Within Groups		
	Total		
Day_18	Between Groups	0.581	0.489
	Within Groups		
	Total		
Day_21	Between Groups	0.471	0.530
	Within Groups		
	Total		



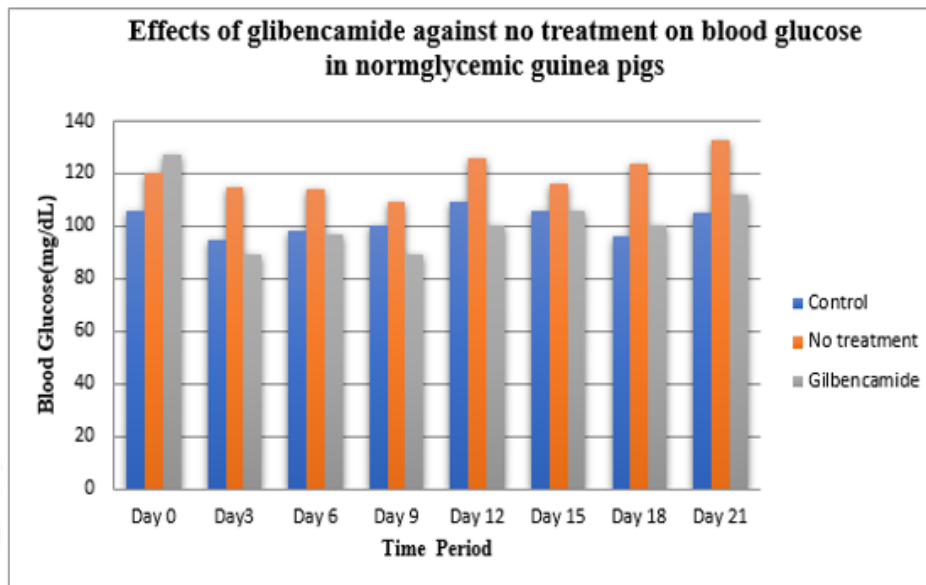
Graph 1: The Effect of Aqueous Extract of *Averrhoa bilimbi* Fruit and Glibenclamide on Blood Glucose Levels in Normoglycemic Guinea Pigs as compared to the Controlled Group.



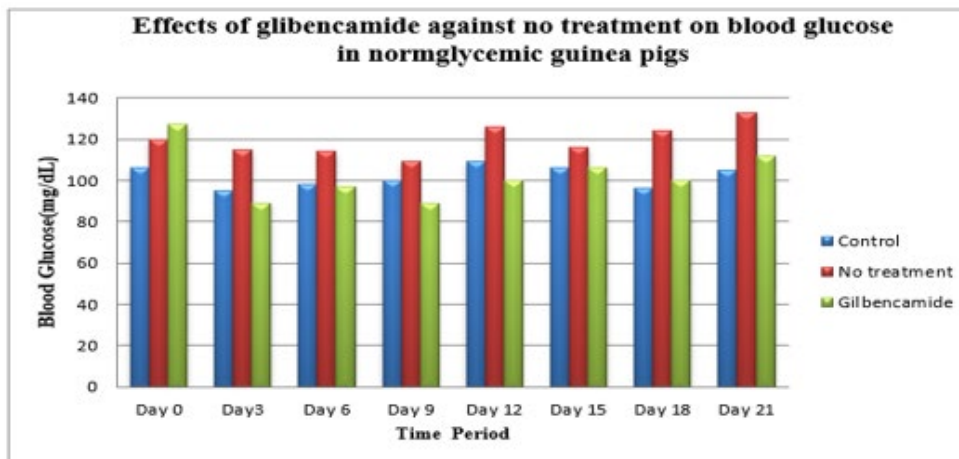
Graph 2: The Effect of Aqueous extract of *Averrhoa bilimbi* Fruit and Glibenclamide on Body Weight of Guinea Pigs as compared to the Controlled Group.



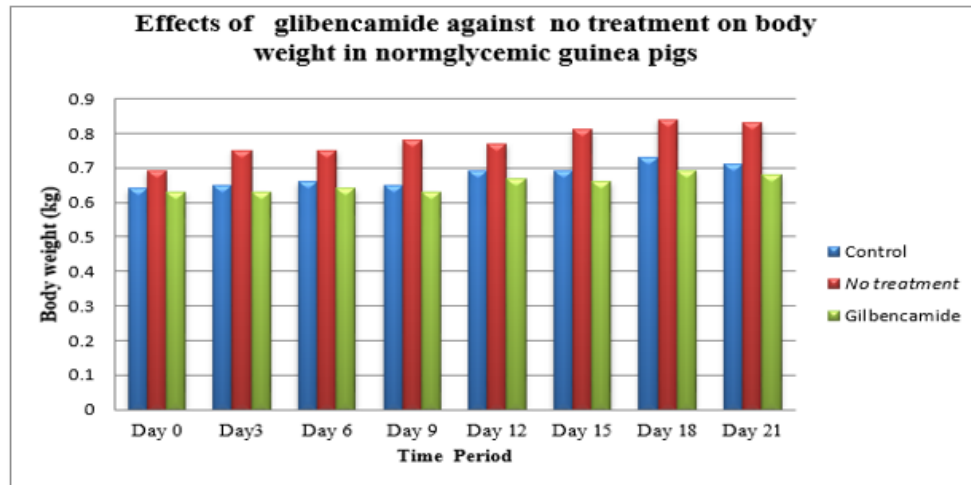
Graph 3: Effects of Glibenclamide and *P. acidus* on Blood Glucose in Normoglycemic Guinea Pigs.



Graph 4: Effects of *Phyllanthus acidus* and Glibenclamide on Blood Glucose in Normoglycemic Guinea Pigs.



Graph 5: Effects of Glibenclamide Against No Treatment on Blood Glucose in Normoglycemic Guinea Pigs.



Graph 6: The Effect of Glibenclamide Against No Treatment on Body Weight in Normoglycemic Guinea Pigs as Compared to the Controlled Group.

Discussion

Fasting Blood Glucose (FBG) of the guinea pigs, Baseline Body Weight (BW) were tested. During the experiments, there were no signs of intoxication observed, including restraint of animals, chills, hesitation, rustling hairs, anuria and finally death. The hypoglycemic potential of *A. bilimbi* & *P. acidus* was tested over 21 days period, alongside reference drug, Glibenclamide to determine whether the blood glucose lowering effect was comparable to that of Glibenclamide. Results were recorded at three days intervals, after first establishing fasting blood glucose (FBG) values for each group. In addition, controlled experiments were done. On the third day of treatment, there was a significant decrease (33.48%) in the FBG level for the *A. bilimbi* treated group (from 148.33±20.77mg/dl to 98.67±9.81 mg/dl), compared with 29.47% decrease (from 126.67±36.71mg/dl to 89.33±8.06mg/dl) for the Glibenclamide treated group. For the controlled group, there was 10.09% (from 105.67±7.41mg/dl to 95.00±4.08mg/dl). On the 9th day of treatment, the further hypoglycemic effect of *A. bilimbi* extract is noted. A 34.6% reduction in the FBG level (from 148.33±20.77 mg/dl to 97.00±4.32mg/dl) was noted. Glibenclamide induced 29.48% reduction in FBG level (from 126.67± to 89.33±8.06), For the controlled group, a corresponding reduction of 5.05% (from 105.67±7.41mg/dl to 100.33±14.88mg/dl) was observed. On the 21st day of treatment, *A. bilimbi* induced a 29.66% reduction in FBG level (from 148.33±20.77 mg/dl to 104.33±8.18mg/dl) whereas Glibenclamide induced 11.58% reduction (from 126.67±36.71 mg/dl to 112.0±8.29mg/dl). The controlled group showed 0.63% reduction (from 105.67±7.41 mg/dl to 105.00±7.48mg/dl), for the 21 days period.

Body weight can be an indicator of obesity and later diabetes. Thus, the body weight of the guinea pigs were taken over the period of conduct of the experiment. On the 3rd day of treatment, *A. bilimbi* treated group showed (1.43%) reduction in BW (kg) (from 0.70±0.16 mg/dl to 0.71±0.16 mg/dl). The Glibenclamide treated group showed 0 % reduction in BW (kg) (from 0.63±0.05mg/dl to 0.63±0.04mg/dl). The controlled group showed 1.58 % in reduction (from 0.64±0.04 mg/dl to 0.65±0.04mg/dl) in BW (kg). On the 9th day of treatment, *A. bilimbi* treated group showed an increase in BW of 2.86% (from 0.70±0.16 mg/dl to 0.72±0.14mg/dl) after the 9th day. Glibenclamide induced no % increase in BW (from 0.63±0.05 mg/dl to 0.63± 0.04mg/dl), The controlled group showed 1.56% increase in BW (kg) (from 0.64±0.04 mg/dl to 0.65±0.04mg/dl). On the 21st day of treatment, the *A. bilimbi* treated group showed 10% increase in BW (kg) (from 0.70±0.16 mg/dl to 0.77±0.19mg/dl). The Glibenclamide treated group showed 7.94% increase in BW (kg) (from 0.63±0.05 mg/dl to 0.68±0.05mg/dl). The controlled group showed 10.94% increase in BW (kg) (from 0.64±0.04 mg/dl to 0.71±0.04mg/dl).

Table 3 shows the FBG level for the *P. acidus* treated group over the 21 days interval. For the *P. acidus* treated group, the extract on the 3rd day of treatment, induced a 26.39 % reduction in FBG values (from 120.00±11.31mg/dl to 88.33±8.73mg/dl). The Glibenclamide treated group showed 29.48 % reduction FBG level (from 126.67±36.1 mg/dl to 89.33±8.06mg/dl). The controlled group showed 10.09% reduction in FBG level (from 105.67±7.41 mg/dl to 95.00±4.08mg/dl). On the 9th day of treatment, *P. acidus* extract induced 26.39 % reduction in FBG level (from 120.00±11.31 mg/dl to 88.33±8.73mg/dl). The Glibenclamide treated group showed a decrease in FBG level of 29.48% (from 126.67±36.1 mg/dl to 89.33±8.06mg/dl) after the 9th day. The controlled group also showed a hypoglycemic effect of 5.05 % (from 105.67±7.41 mg/dl to 100.33±14.88mg/dl). On the 21st day of treatment, *A. bilimbi* extract induced a FBG level reduction of 17.23% (from 120.00±11.31 mg/dl to 99.33±3.68 mg/dl). Glibenclamide induced 11.58% reduction in FBG level (from 126.67±36.1 mg/dl to 112±8.29mg/dl). The controlled group showed 0.63 % reduction in FBG level (from 105.67±7.41 mg/dl to 105.00±7.48mg/dl).

Table 4 shows the BW (kg) of the guinea pigs, subjected to *P. acidus* and glibenclamide treatments. On the 3rd day, animals that were treated with *P. acidus* extracts showed 0 % reduction (from 0.63±0.12kg to 0.63±0.08kg). The Glibenclamide treated group also showed 0% reduction in BW (from 0.63±0.05kg to 0.63±0.04kg). The control group, however, showed an increase of 1.56 % in BW (from 0.64±0.04kg to 0.65±0.04kg).

On the 9th day of treatment, the *P. acidus* extract induced 0% increase in BW (from 0.63±0.12kg to 0.63±0.08kg). The Glibenclamide treated group showed 0% reduction in BW (from 0.63±0.05kg to 0.63±0.04kg). The controlled group continued to show an increase in BW of 1.56 % (from 0.64±0.04kg to 0.65±0.04kg). On the 21st day of treatment, the *P. acidus* extract induced 7.94 % increase in BW (from 0.63±0.12 kg to 0.68±0.11kg). The Glibenclamide treated group also induced an increase in BW of 7.94 % (from 0.63±0.05kg to 0.68±0.05kg). The control group showed an increase of 10.94 % in BW (from 0.64±0.04kg to 0.71±0.04kg).

Table 5 shows the Fasting Blood Glucose (FBG) for controlled vs. Glibenclamide treated and non-treatment group. For the NO treatment group, there was a progressive increase in the blood glucose level from Day 0 to Day 21. This range from (119.67±25.04 mg/dl to 133.33±2.05 mg/dl) i.e 11.41% increase. For the control group, there was variation. It decreases from an initial value of 105.67±7.41 mg/dl to 100.33±14.88 mg/dl on day 9th and then increases again to (105.00±7.48 mg/dl) on the 21st day. For the Glibenclamide treated group, there was progressive decrease from 126.67±36.71 mg/dl to 112.00±8.29 on the 21st day i.e a 11.58% reduction.

Graph 1 shows the effects of Aqueous Extract of *Averrhoa bilimbi* fruit and Glibenclamide on the Blood Glucose Levels in Normoglycemic Guinea Pigs as compared to the Controlled Group over the 21 days period. As can be seen, there is a general decrease in blood glucose level (mg/dl) on administering both the aqueous *Averrhoa bilimbi* extract & Glibenclamide. However, Glibenclamide administration was seen to be greater on Day 1, Day 3, Day 12 and Day 18. In both cases, there seem to be a decrease from Day 3 to Day 9, then and increase from Day 12 to Day 21. Graph 2 shows the effects of *Averrhoa bilimbi* extract & Glibenclamide on the body weight in normoglycemic guinea pigs. For the Glibenclamide, treated group, the body weight was more or less constant from Day 0 to Day 9. However, from Day 12 to Day 21, there was an increase in Body weight. *A. bilimbi* extract on the other hand, induced a progressive increase in Body weight from Day 12 to Day 18 and a decrease on Day 21.

For the control group, there was an increase in Body Weight to Day 18 and then a decrease on day 21st. Graph 3 shows the effect of Glibenclamide and *P. acidus* extract on blood glucose level in normoglycemic guinea pigs. As seen, there is an overall decrease in blood glucose level (mg/dl) from Day 1 to Day 21 for both groups. For both groups, there is a decrease in Blood Glucose level from Day 1 to Day 9, then an increase from Day 12 to Day 21. For the Control Group, there was an increase in Blood Glucose Level up to Day 12 and a general decrease to Day 21. Graph 4 shows the effect of *Phyllanthus acidus* extract and Glibenclamide on the Body weight in normoglycemic guinea pigs. It was found that the administration of both, over the 21 days period, resulted in an increase in body weight of the normoglycemic guinea pigs. This was also the case for the control experiment. According to Graph 5, Glibenclamide induced general decrease in blood glucose level from Day 1 to Day 21. There was a decrease from Day 0 to Day 9, then a general increase from Day 12 to Day 21.00. The same goes for the NO treatment group. For the control group, the opposite was observed. There was a general increase in body weight from Day 1 to Day 12, then a decrease from Day 12 to Day 21. According to Graph 6, Glibenclamide induced a general increase in body weight in normoglycemic guinea pigs. There was a general increase in body weight to Day 18th and then a decrease on Day 21. For the NO treatment group, there was a general increase in body weight from Day 0 to Day 21. The NO control group showed a general increase in body weight to Day 18th and then a decrease to Day 21.0

Anova analyses were done to see whether there was any significant differences in the Fasting Blood Glucose Level and Body Weight (BW) between and within groups for the 21 days period, for the various treatments. According to Table 6, there wasn't any significant difference in the values for the FBG level for controlled vs. *A. bilimbi* treated groups. All values were statistically ≥ 0.05 . Table 7 shows the FBG levels for Controlled vs. Glibenclamide treated group. Accordingly, all P values were statistically > 0.05 , indicating no significant statistical differences in the values. Table 8 shows that there wasn't any significant statistical difference in the body weight for the Controlled vs. *A. bilimbi* treated groups. The P-values range from (0.560 to 0.629) and are > 0.05 . Table 9 shows that there wasn't any significant statistical differences between the body weight (BW) for Controlled vs. Glibenclamide treated groups. The P-values were all > 0.05 . It ranges from 0.315 to 0.774. Table 10, shows that there wasn't any significant differences for the FBG levels for controlled vs. *P. acidus* treated groups. The P-values are all ≥ 0.05 and range from 0.197 to 0.391. Table 11 shows the FBG levels for Controlled vs. Glibenclamide treated groups. All values were > 0.05 , indicating no significant differences. These values range from 0.262 to 0.954. Table 12 shows the F and P values for the BW for Controlled vs. *P. acidus* treated groups. All values are > 0.05 , indicating that there are no significant differences. The P-values range from 0.643 to 0.932.

Table 13 shows the BW for Controlled vs. Glibenclamide treated groups. The P-values were all $>$ than 0.05, indicating no significant differences. The P-values range from 0.315 to 0.725. Table 14 shows the FBG level for Controlled vs. No treatment Diabetic group. As seen, only on Day 3, Day 18 and Day 21, the P-values were < 0.05 , indicating statistically significant differences. Table 15 shows the FBG levels for Controlled vs. Glibenclamide treated groups. No P value was less than 0.05, indicating that there wasn't any statistical differences between groups for the two treatments, from 0.262 to 0.954. Table 16 shows the P-values for the BW measurements for Controlled vs. No treatments diabetic group. All P values are greater than 0.05, ranging from (0.18 to 0.3), indicating no significant differences. Table 17, shows the P-values for the BW measurements for Controlled vs. Glibenclamide treated groups. All these values are > 0.05 , ranging from (0.315 to 0.725), indicating no significant differences in the value.

Conclusion

In conclusion, the anti-diabetic activity of the aqueous extract of fruits of *Averrhoa bilimbi* and *Phyllanthus acidus* in Normoglycemic Guinea Pigs was investigated. Twelve guinea pigs were divided into five groups of three: Control group, *A. bilimbi* treated group, *P. acidus* treated group

and Glibenclamide treatment group and Non-diabetic treated group. Glibenclamide was used as the reference drug. The *A. bilimbi* extract did induced an hypoglycemic effect over the 21 days period. There was a 29.66% (148.33±20.77 to 104.33±8.18 mg/dl) reduction in the Fasting Blood Glucose (FBG) level compared to 14.67% (126.67±36.71 to 112.00±8.29). Glibenclamide showed 14.67 % reduction in blood glucose level from (126.67±36.71 to 112.00±8.29 mg/dl). The *P. acidus* treated group showed 17.23% in reduction in Blood Glucose level. With regards to the effect on Body weight, *A. bilimbi* extract showed 10% increase in the body weight (0.70±0.16 to 0.77±0.19 kg) compared to the 20% increase in body weight (BW) induced by *Pacidus* extract from (0.63±0.12 kg to 0.68±0.11 kg). The Glibenclamide treated group showed a 5% increase in body weight (0.63±0.05 to 0.68±0.05 kg). Thus, the increasing order of induction of hypoglycemic effect is *A. bilimbi* > *P. acidus* > Glibenclamide. In terms of body weight, the increasing order of induction is: Glibenclamide > *A. bilimbi* > *Pacidus*. Thus, both *A. bilimbi* and *P. acidus* extracts are hypoglycemic agents.

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5.5

mmol / L

3

10