Effect of Ethanoic Leaf Extracts of *Carica Papaya* and *New Bouldia Laevis* on Lipid Profile of Diabetic Wistar Rats

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***Abstract*:- Objective: This study was carried out to investigate the effect of the ethanolic leaf extracts of *Carica papaya (C. papaya)* and *Newbouldia laevis (N. laevis)* on the lipid profile of alloxan-induced Wistar rats.**

Methodology: Forty (40) male wistar rats weighing 130-150g were procured and acclimatized for two weeks, after which they were divided into eight (8) groups of five (5) rats each, and were housed in cages. The groups were designated as groups A, B, C, D, E, F, G and H. Groups B - H were induced with diabetes using alloxan. Group A served as the control group and received only distilled water; group B diabetic received only distilled water only, while groups C – H diabetic received 400mg/kg of *C. papaya*, 600mg/kg of *C. papaya*, 400mg/kg of *N. laevis*, 600mg/kg of *N. laevis*, 200mg/kg of *C. papaya* + 200mg/kg of *N. laevis* and 300mg/kg of *C. papaya* + 300mg/kg of *N. laevis* respectively for 21 days through oral route with the aid of oral gastric tube. On the 22nd day, the animals were sacrificed by chloroform inhalation, and blood samples were obtained through cardiac puncture for lipid profile parameters' assays. Data obtained were analyzed using SPSS version 25 and (P<0.05) was considered significant.

Result: There was significant increase in the plasma total cholesterol, triglycerides, low density lipoprotein (LDL) with a decrease in plasma high density lipoprotein (HDL) of the animals in group B when compared with the control group. These effects were ameliorated in Groups C - H that received the variable doses of the ethanolic leaf extracts *C. papaya* and *N. laevis* with more positive effects on the groups that received the combined ethanolic leaf extracts.

Conclusion: The leaf extracts of *C. papaya* and *N. laevis* have ameliorative effects on the lipid profile alloxan-induced diabetic Wistar rats.

***Keywords: Carica papaya, Newbouldia laevis,* total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL)**

I. INTRODUCTION

About 422 million people worldwide have diabetes, the majority living in low-and middle-income countries, and 1.6 million deaths are directly attributed to diabetes each year [1]. Both the number of cases and the prevalence of diabetes have been steadily increasing over the past few decades [1]. Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves [1]. The most common is type 2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or does not make enough insulin [1]. In the past three decades the prevalence of type 2 diabetes has risen dramatically in countries of all income levels [1]. Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition in which the pancreas produces little or no insulin by itself. For people living with diabetes, access to affordable treatment, including insulin, is critical to their survival. There is a globally agreed target to halt the rise in diabetes and obesity by 2025 [1].

DM is a major risk factor for coronary artery disease (CAD), stroke, peripheral arterial disease (PAD), cardiomyopathy, diabetic nephropathy, diabetic retinopathy, and central as well as peripheral neuropathy [2, 3]. Studies have attempted to correlate blood glucose levels with serum lipid profile parameters [4, 5], and research findings have showed that it is mainly body fat that is responsible for increase in prevalence of diabetic disease among the body composition components [6, 7, and 8]. Diabetes is characterized by chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism, and widespread lipid abnormalities in the course of diabetes triggered dyslipidemia as hypercholesterolemia, hypertriglyceridemia, elevated LDL and decreased HDL [9]. Dyslipidemia is considered to be a risk factor for the development of Type 2 DM [10, 11]. Diabetic dyslipidaemia comprises of elevated triglyceride levels as well as decreased HDL cholesterol levels [12]. LDL cholesterol is quantitatively not significantly different from non-diabetic subjects; however, there is a preponderance of small dense LDL particles with a greater susceptibility to oxidation [12]. Epidemiological studies have shown that patients with type-2 diabetes mellitus with no history of cardiovascular disease have the same risk for cardiac events as non-diabetic patients

with preexisting coronary disease have [12]. The increased incidence of cardiovascular disease (CVD) in diabetes, the greater case fatality and 1-year mortality in patients with myocardial infarction strongly suggest that preventive lipid lowering therapy is of great importance [12]. Patients with cardiovascular diseases and diabetes mellitus should strictly controlled their lipid profiles to reduce mortality and complications [13]. Thus, the basic goal in the treatment of diabetes is to lower blood glucose concentrations to levels that approximate those representing normal range and its maintenance thereof [14]. This helps to reduce the progression of the disease process and its complications with emphasis on hypertension control and correction of dyslipidemia [15].

Medicinal plants are plants that possess therapeutic properties or exert beneficial pharmacological effect on the human or animal body [16]. Several medicinal plants have been investigated to ameliorate abnormalities in lipid metabolism arising from diabetes metabolic disorder in many institutions located in different regions of the world [17, 18]. Examples of such medical plants widely used in traditional treatment system iiclude the *Carica payaya* and the *Newbouldia*.

Carica papaya is one of the 22 accepted species in the genus *Carica* of the family *Caricaceae* that originate in the tropics of the Americas, perhaps from Central America and southern Mexico [19]. It is a small, sparsely branched tree, usually with a single stem growing from 5 to 10 m (16 to 33 ft) tall, with spirally arranged leaves confined to the top of the trunk [20]. The lower trunk is conspicuously scarred where leaves and fruit are borne, and the leaves are large, 50–70 cm (20–28 in) in diameter, deeply palmately lobed, with seven lobes [20]. In traditional medicine, papaya leaves have been used as a treatment for malaria [21], an abortifacient, a purgative, or smoked to relieve asthma [19]. *C. papaya* leaves reduce symptoms of asthma, worming and dysentery [22, 23] and have long been used as remedy for cancer and infectious diseases [23]. Its leaf extract accelerates wound healing [24, 25], exhibits vasodilating and antioxidant effects, both being associated with cardiovascular risk reduction [22] and useful in the treatment of diabetes in Nigeria [26]. According to Gray *et al*, [27] the reduced glucose levels in alloxan induced diabetes suggests that *Carica papaya* leaves might exert insulin-like effect on peripheral tissues by either promoting glucose uptake metabolism. Besides their hypoglycemic properties [25], different parts of *C. papay*a are used in Mexican folk medicine to treat various diseases such as diarrhea, inflammation and diabetes [25, 28]. *C. papaya* has also been attributed to the following properties - antioxidant activity, immunomodulatory, hypoglycemia and hypolipidemic [29] and hepatoprotective [30, 31]. *C. papaya* leaf extract may be beneficial to diabetic patients and helpful in the prevention of diabetic complications by dyslipidemia improvement [32].

Newbouldia laevis is a fast-growing evergreen shrub or small tree that can only reaches a height of 3 - 8 metres in the west of its range, but can attain a height of up to 20 metres in the east [33, 34, and 35]. The bole can be up to 90cm in diameter, but is usually less [35]. *N. laevis* is a medium sized angiosperm in the *Bignoniaceae* family and is native to tropical Africa and grows to a height of about 10 m with a cauliferous habit. It is ever green, though its leaves turn somewhat dark purple during the cold seasons [36], and is popularly known as the tree of life or fertility tree in Nigeria. Its local Nigerian names include Akoko (Yoruba), Aduruku (Hausa), Kontor (Tiv), Ikhimi (Bini), Ogirisi (Igbo) and Ogiriki (Urhobo). It is used in folkloric medicine to treat a number of diseases. Some of which include the following: the leaves and roots are boiled and used to treat earaches, sore foot, chest pain, fever, convulsion and epilepsy in children [35, 37] and diarrhea [38]. The roots are used to treat arthritis, malaria and general malady and worms [39]. The leaves are used as decoction for eye wash in conjunctivitis. The leaves are also used as chieftaincy leaf in Yoruba land [39]. The stem bark is used for toothache, febrifuge, stomach and skin infections [35, 39]. Recently, the flowers and leaves have been used in the treatment of diabetes respectively [37, 38, 40, and 41]. It is also used to stop vaginal bleeding in threatened abortion [39] and had shown strong antioxidant activity [42]. According to Chinyelu *et al*, [43] *N. laevis* leaf possesses the ability of managing hyperglycemia, improve haematological and biochemical derrangements in alloxan induced-diabetic rats. It can also control muscle wasting and induce adipogenesis [43]. *N. laevis* leaf and stem have anti-diabetic properties [44]. Anaduaka *et al*, [45] reported that the ethanol extracts of the leaves and stem of *N. laevis* possess hepatoprotective properties for curbing oxidative stress complication. Kolawole *et al*, [40] in their research reported that the ethanolic extract of the leaves of *Newbouldia laevis* possesses anti-diabetic properties and that it can prevent the complications of diabetes that result from glycation of hemoglobin and lipid peroxidation. The leaf extract of the *N. laevis* was also reported to lower blood glucose level in diabetic rats [38].

Therefore, this research study was carried out to investigate the effect of the ethanolic leaf extracts of *C. papaya* and *N. laevis* on the lipid profile of alloxan-induced Wistar rats since no work has been carried out on this.

II. MATERIALS AND METHODS

2.1 Animal procurement, care and treatment

Forty (40) male wistar rats weighing between 130g to 130g were procured and housed at the Animal house of the Department Physiology, Nnamdi Azikiwe University, Nnewi Campus with wire gauze cages in a well-ventilated area. They were fed with standard commercial pellet diet and water *ad libitum*. There were acclimatized for two weeks before the experiment. Their health statuses were closely monitored before and during the experiment. All procedures were carried out in strict accordance with the Institutional guidelines on the care and use of experimental animals.

2.2 Collection, identification and preparation of plant material

Fresh leaves of *C. papaya* and *N. laevis* were harvested from a local settlement in Okofia in Nnewi, Anambra State. The leaves were properly washed with water to remove sand and other impurities, and were authenticated at the herbarium Unit, Botany Department, Nnamdi Azikiwe University, Anambra State. They were air dried and crushed using laboratory blender. Extraction was done using ethanol. The crude ethanol extracts were filtered into a stainless basin with a white cloth and placed in a water bath so as to dry up the ethanol. Then 200mg, 300mg, 400mg and 600mg of these extracts per kg body weight were dissolved in 100mls of distilled water and were administered to the animals in each group respectively.

2.3 Induction of diabetes

The rats were divided into non-diabetic control group and experimental groups. The baseline blood glucose level of the experimental group to be inducted was determined before the induction of diabetes. The rats were allowed to fast over night prior to injection of alloxan and diabetes was induced by intra-peritoneal administration of 150mg of alloxan per kg body weight of rat (150mg/kg body weight) [46]. After the induction, the rats were allowed to have free access to the same feed and water. After 72 hours, blood samples obtained through tail tip puncture of the rats were used to confirm diabetes in the rats by testing for hyperglycemia using Glucometer. Diabetes was confirmed at fasting blood glucose levels greater than 200mg/dl [47].

2.4 Experimental protocol

The animals were grouped into eight (8) groups of five (5) rats each. Different doses of the leaf extracts were administered via oral route with the aid of oral gastric tube as shown below:

Group A (The Control group) distilled water.

Group B (Diabetic group) distilled water.

Group C Diabetic + 400mg/kg of *C. papaya* leaf extract.

Group D Diabetic + 400mg/kg of *N. laevis* leaf extract.

Group E Diabetic + 600mg/kg of *C. papya* leaf extract.

Group F Diabetic + 600mg/kg of *N. laevis* leaf extract

Group G Diabetic + 200mg/kg of *C. papaya* + 200mg/kg of *N. laevis* leaf extracts.

Group H Diabetic + 300mg/kg of *C. papaya* + 300mg/kg of *N. laevis* leaf extracts.

2.5 Sample collection and analysis

The extracts were administered for twenty one (21) days. On the 22nd day, the animals were sacrificed by anaestethizing under chloroform vapour and blood samples were collected from each of the rats by cardiac puncture for hormonal assays. Thus serum levels of total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) were analyzed using Cholestech LDX analyser.

2.6 Statistical Analysis

All data were tabulated and statistically analyzed using SPSS version 25.0. Results were expressed as Mean ± standard error of mean (SEM). Comparative analysis amongst groups was done using one-way analysis of variance (ANOVA). A post-hoc analysis using Bonferoni multiple comparative tests was performed to identify significant groups. $P<0.05$ was taken as statistically significant.

III. RESULTS

Table 1: Effect of ethanoic leaf extracts of *C. Papaya* and *N. laevis* on the serum level of total cholesterol (TC).

Groups	Dosage of extract	Total Cholesterol (TC) (mmol/L)
A	Control (Distilled water)	2.43±0.08
B	Diabetic (Distilled water)	3.37±0.17*
C	400mg/kg of *C. papaya*	2.87±0.21
D	400mg/kg of *N. laevis*	3.00±0.22
E	600mg/kg of *C. papaya*	1.45±0.23*
F	600mg/kg of *N. laevis*	1.41±0.23*
G	200mg/kg of *C. papaya* + 200mg/kg *N. laevis*	1.76±0.19
H	300mg/kg of *C. papaya* + 300mg/kg *N. laevis*	0.75±0.18*

(Data are presented as mean ± standard error of mean and values are considered significant at $P< 0.05$, where * = $P<0.05$)

Result of the table above showed a significant increase ($P<0.05$) on the serum level of TC of the animals in group B (diabetic without treatment) when compared with the serum level of TC in group A (Control), and significant decreases ($P<0.05$) on the serum level of TC of the animals in groups E, F and H that received 600mg/kg of *C. papaya*, 600mg/kg of *N. laevis* and 300mg/kg of *C. papaya* + 300mg/kg of *N. laevis* of the ethanoic leaf extracts respectively when compared with the serum level of TC of the animals in group A (Control). However, there was no significant change ($P<0.05$) on the serum level of TC of the animals in groups C, D and G that received 400mg/kg of *C. papaya*, 400mg/kg of *N. laevis and* 200mg/kg of *C. papaya* + 200mg/kg *N. laevis* of the ethanoic leaf extracts respectively when compared with the serum level of TC of the animals in group A (Control).

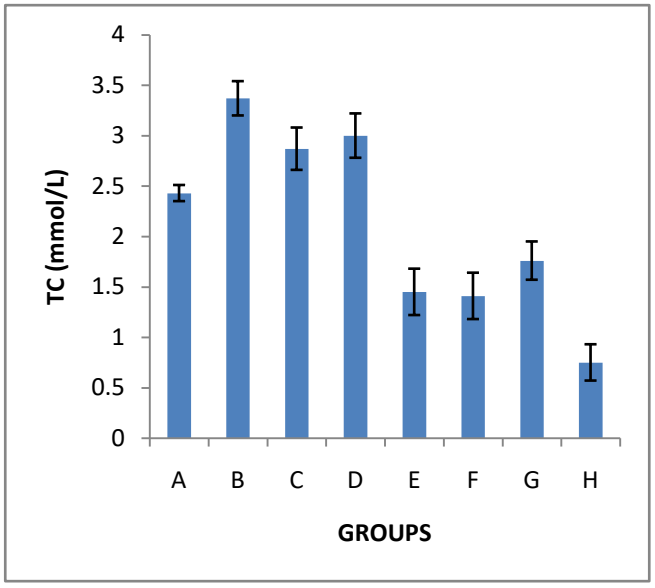

Figure 1: Effect of ethanoic leaf extracts of *C. Papaya* and *N. laevis* on the serum level of total cholesterol (TC) of alloxan-induced wistar rat.

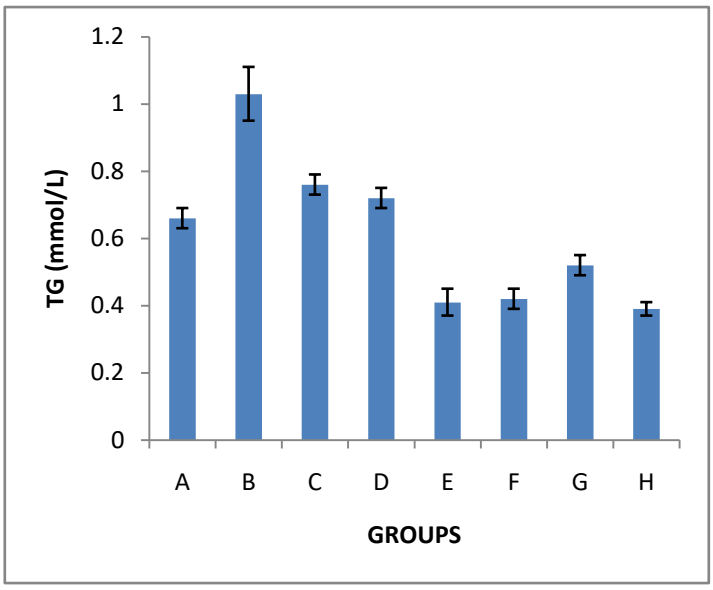

Figure 2: Effect of ethanoic leaf extracts of *C. Papaya* and *N. laevis* on the serum level of triglyceride (TG) of alloxan-induced wistar rat.

Table 2: Effect of ethanoic leaf extracts of *C. Papaya* and *N. laevis* on the serum level of Triglyceride (TG)

Groups	Dosage of extract	Triglyceride (TG) (mmol/L)
A	Control (Distilled water)	0.66±0.03
B	Diabetic (Distilled water)	1.03±0.08*
C	400mg/kg of *C. papaya*	0.76±0.03
D	400mg/kg of *N. laevis*	0.72±0.03
E	600mg/kg of *C. papaya*	0.41±0.04*
F	600mg/kg of *N. laevis*	0.42±0.03*
G	200mg/kg of *C. papaya* + 200mg/kg *N. laevis*	0.52±0.03
H	300mg/kg of *C. papaya* + 300mg/kg *N. laevis*	0.39±0.02*

(Data are presented as mean ± standard error of mean and values are considered significant at P< 0.05, where * = P<0.05)

Table 2 showed a significant increase (P<0.05) on the serum level of TG of the animals in group B (diabetic without treatment) when compared with the serum level of TG of the animals in group A (Control), and significant decreases (P<0.05) on the serum level of TG of the animals in groups E, F and H that received 600mg/kg of *C. papaya*, 600mg/kg of *N. laevis* and 300mg/kg of *C. papaya* + 300mg/kg of *N. laevis* of the ethanoic leaf extracts respectively when compared with the serum level of TG of the animals in group A (Control). However, there was no significant change (P<0.05) on the serum level of TG of the animals in groups C, D and G that received 400mg/kg of *C. papaya*, 400mg/kg of *N. laevis and* 200mg/kg of *C. papaya* + 200mg/kg *N. laevis* of the ethanoic leaf extracts respectively when compared with the serum level of TG of the animals in group A (Control).

Table 3: Effect of ethanoic leaf extracts of *C. Papaya* and *N. laevis* on the serum level of Low Density Lipoprotein (LDL)

Groups	Dosage of extract	LDL (mmol/L)
A	Control (Distilled water)	1.52±0.07
B	Diabetic (Distilled water)	2.24±0.17*
C	400mg/kg of *C. papaya*	1.61±0.04
D	400mg/kg of *N. laevis*	1.58±0.05
E	600mg/kg of *C. papaya*	0.67±0.17*
F	600mg/kg of *N. laevis*	0.68±0.16*
G	200mg/kg of *C. papaya* + 200mg/kg *N. laevis*	1.36±0.23
H	300mg/kg of *C. papaya* + 300mg/kg *N. laevis*	0.83±0.10*

(Data are presented as mean ± standard error of mean and values are considered significant at P< 0.05, where * = P<0.05)

Result of Table 3 showed a significant increase (P<0.05) on the serum level of LDL of the animals in group B (diabetic without treatment) when compared with the serum level of LDL of the animals in group A (Control), and significant decreases (P<0.05) on the serum level of LDL the animals in groups E, F and H that received 600mg/kg of *C. papaya*, 600mg/kg of *N. laevis* and 300mg/kg of *C. papaya* + 300mg/kg of *N. laevis* of the ethanoic leaf extracts respectively when compared with the serum level of LDL of the animals in group A (Control). However, there was no significant change (P<0.05) on the serum level of LDL of the animals in groups C, D and G that received 400mg/kg of *C. papaya*, 400mg/kg of *N. laevis and* 200mg/kg of *C. papaya* + 200mg/kg *N. laevis* of the ethanoic leaf extracts respectively when compared with the serum level of LDL of the animals in group A (Control).

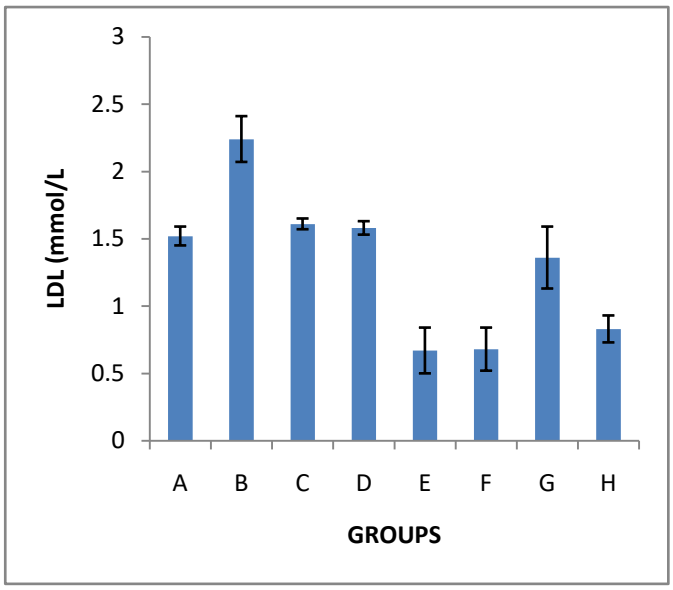

Figure 3: Effect of ethanoic leaf extracts of *C. Papaya* and *N. laevis* on the serum level of low density lipoprotein (LDL) of alloxan-induced wistar rat.

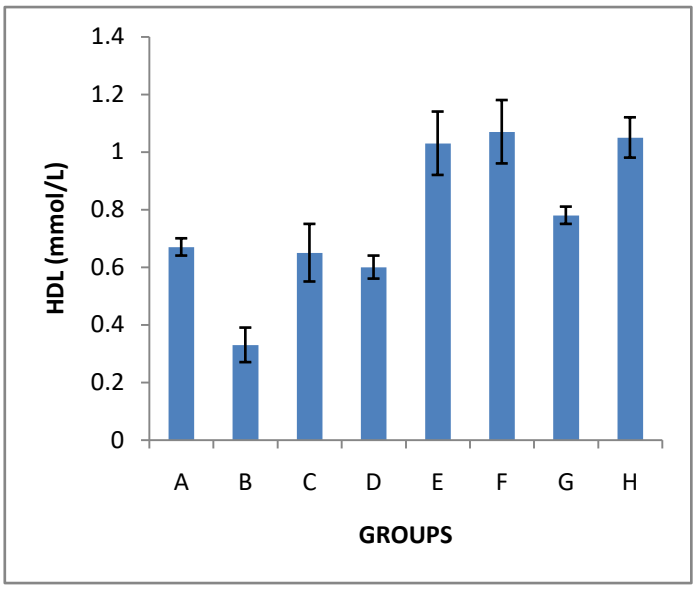

Figure 4: Effect of ethanoic leaf extracts of *C. Papaya* and *N. laevis* on the serum level of high density lipoprotein (HDL) of alloxan-induced wistar rat.

Table 4: Effect of ethanoic leaf extracts of *C. Papaya* and *N. laevis* on the serum level of High Density Lipoprotein (HDL)

Groups	Dosage of extract	HDL (mmol/L)
A	Control (Distilled water)	0.67±0.03
B	Diabetic (Distilled water)	0.33±0.06*
C	400mg/kg of *C. papaya*	0.65±0.10
D	400mg/kg of *N. laevis*	0.60±0.04
E	600mg/kg of *C. papaya*	1.03±0.11*
F	600mg/kg of *N. laevis*	1.07±0.11*
G	200mg/kg of *C. papaya* + 200mg/kg *N. laevis*	0.78±0.03
H	300mg/kg of *C. papaya* + 300mg/kg *N. laevis*	1.05±0.07*

(Data are presented as mean ± standard error of mean and values are considered significant at P< 0.05, where * = P<0.05)

In Table 4, there was a significant decrease (P<0.05) on the serum level of HDL of the animals in group B (diabetic without treatment) when compared with the serum level of HDL of the animals in group A (Control), and significant increases (P<0.05) on the serum level of HDL of the animals in groups E, F and H that received 600mg/kg of *C. papaya*, 600mg/kg of *N. laevis* and 300mg/kg of *C. papaya* + 300mg/kg of *N. laevis* of the ethanoic leaf extracts respectively when compared with the serum level of HDL of the animals in group A (Control). However, there was no significant change (P<0.05) on the serum level of HDL of the animals in groups C, D and G that received 400mg/kg of *C. papaya*, 400mg/kg of *N. laevis and* 200mg/kg of *C. papaya* + 200mg/kg *N. laevis* of the ethanoic leaf extracts respectively when compared with the serum level of HDL of the animals in group A (Control).

IV. DISCUSSION

According to Aronson and Edelman [48] DM and its related cardiovascular complications are major public health challenges worldwide, and individuals with type 2 DM have two- to four-fold increased risk of coronary artery disease (CAD), the leading cause of death among people with type 2 DM. Dyslipidemia and hypertension are major modifiable risk factors for T2DM and related CAD, which account for more than 87% of disability in low- and middle-income countries [49, 50], and it has also been revealed that Diabetic dyslipidemia is often characterized by high TC, high TG, low HDL cholesterol, and increased level of LDL [51, 52].

The significant increase (P<0.05) on the serum level of TC, TG and LDL and significant decrease (P<0.05) on the serum level of HDL of the animals in group B (diabetic without treatment) in tables 1-4/figures1-4 when compared with the serum level of TC, TG, LDL and HDL in group A (Control) could be due the toxic effect of the induced alloxan on the pancreas leading to diabetes "Diabetic dyslipidemia". Research has shown that alloxan selectively kills the insulin-producing beta-cells found in the pancreas thereby inducing diabetes in laboratory animals [53, 54]. This occurs most likely because of selective uptake of the compound due to its structural similarity to glucose as well as the beta-cell's highly efficient uptake mechanism (GLUT2). Also alloxan has a high affinity to SH-containing cellular compounds, thus, reduces glutathione content and inhibits glucokinase, a SH-containing protein essential for insulin secretion induced by glucose [46]. Diabetic dyslipidemia has been shown to often been characterized by high TC, high TG, low HDL cholesterol, and increased level of LDL [51, 52]. Also the increased serum levels of TC, TG, and LDL, and deceased serum level of HDL in group B could be due to inhibitive

action of insulin due to its deficiency or absence caused by the induced-alloxan to the beta cells of the pancreas. Thus, the hormone-sensitive lipase in adipose tissue which is known to convert triglycerides to free fatty acids and glycerol is inhibited by insulin deficiency leading to increase in serum level of free fatty acids. In the liver, the free fatty acids are catabolized to acetyl CoA, and the excess acetyl CoA is converted to cholesterol, triglyceride and ketone bodies resulting in ketosis [55].

The significant decreases (P<0.05) on the serum level of TC, TG and LDL, and the significant increases (P<0.05) on the serum level HDL of the animals in groups E, F and H that received 600mg/kg of *C. papaya*, 600mg/kg of *N. laevis* and 300mg/kg of *C. papaya* + 300mg/kg of *N. laevis* of the ethanoic leaf extracts respectively in tables 1- 4/figures 1- 4 when compared with the serum level of TC,TG, LDL and HDL of the animals in group A (Control) could be duo to the anti-diabetic and ameliorating activities of *C. papaya* and *N. laevis* to the diabetic wistar rats at that given dosages. Studies have revealed that *C. papaya* leaf extract accelerates wound healing [24, 25], exhibits vasodilating and antioxidant effects, both being associated with cardiovascular risk reduction [22] and treatment of diabetes in Nigeria [26], reduces glucose levels in alloxan induced diabetes [27], exhibits hypoglycemic properties [25], is being used to treat various diseases such as diarrhea, inflammation and diabetes [25, 28], exhibits antioxidant activity, immunomodulatory, hypoglycemia and hypolipidemic [29] and hepatoprotective properties [30, 31], may be beneficial to diabetic patients and helpful in the prevention of diabetic complications by dyslipidemia improvement [32]. Likewise *N. laevis* leaf has been shown to possess the ability to manage hyperglycemia, improves haematological and biochemical derrangements in alloxan induced-diabetic rats [43], control muscle wasting and induces adipogenesis [43], has anti-diabetic properties [44], possesses hepatoprotective properties for curbing oxidative stress complication [45, 31] possesses anti-diabetic properties and prevents complications of diabetes resulting from glycation of hemoglobin and lipid peroxidation [40] and lowers blood glucose level in diabetic rats [38].

However, the no significant change (P<0.05) on the serum level of TC, TG, LDL and HDL of the animals in groups C, D and G that received 400mg/kg of *C. papaya*, 400mg/kg of *N. laevis and* 200mg/kg of *C. papaya* + 200mg/kg *N. laevis* of the ethanoic leaf extracts respectively as shown in tables 1 – 4/figures 1 - 4 when compared with the serum level of TC, TG, LDL, HDL of the animals in group A (Control) could due because the doses of the leaf extracts administered could not produced significant healing/ameliorative effect when compared to the control group A.

V. CONCLUSION

This study has shown that ethanolic leaf extract of *C. papaya and N. laevis* extracts have ameliorative effects not just on diabetes mellitus but also on the lipid profile of alloxan-induced diabetic wistar rats. It also confirms that the ameliorative effects are more enhanced in the co-administration of the extracts than in the individual administration. Hence, the combination of the two leaf extracts could be more beneficial in the treatment of diabetes mellitus.

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Ethical Approval: Approved by Institutional ethical approval.

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