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Modulatory effect of aqueous leaf extract of *Terminalia catappa* on dyslipidemia in alloxan induced diabetic rats

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Abstract

Dyslipidemia is a major cause of cardiovascular complications in diabetes mellitus. This study was carried out to evaluate the modulatory effect of *Terminalia catappa* leaf extract on dyslipidemia in diabetic rats. Twenty-five (25) male wistar rats weighting 150-200 g were divided randomly into five groups with five rats each for the study. Group 1 was control administered 5 ml/kg body weight of distilled water orally. Group 2 was treated with aqueous leaf extract of *T. catappa* at 130 mg/kg body weight orally while Group 3 was diabetic group orally administered with distilled water, 5ml/kg body weight. Groups 4 and 5 were diabetic rats treated respectively with 130 mg/kg body weight of aqueous leaf extract of *Terminalia catappa* and subcutaneous administration of insulin, 0.75 U/Kg body weight. Diabetes was induced with alloxan; 150 mg/kg body weight. The results showed significant ($p < 0.05$) increase in TC, TG, HDL, LDL and VLDL in diabetic untreated group. These were all reduced significantly ($p < 0.05$) in the *Terminalia catappa* leaf extract treated group. There was significant ($p< 0.05$) reduction in Fasting blood glucose and increase in insulin levels. These changes were observed to be similar in diabetic insulin administered group. Therefore, the aqueous leaf extract of *T. catappa* modulates hyperglycemia induced dyslipidemia suggesting its potency in managing dyslipidemia in type 1 diabetes mellitus and may be used to ameliorate diabetes associated cardiovascular complications.

Keywords: Dyslipidemia; *Terminalia catappa*; Insulin; Cardiovascular Complication; Diabetes Mellitus.

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder considered as a growing non-infectious worldwide health challenge [1] in both developed and developing countries. It is specially characterized by hyperglycaemia due to defective insulin secretion, inaction or both [2]. This consequently leads to increased hepatic glucose production [3,4]. The complications of diabetes mellitus are associated with numerous hyperglycemia related injuries. There is an increased prevalence of DM globally with a projection of 500 million adults to be affected with diabetes mellitus by 2030 [5].The risk of developing cardiovascular disease (CVD) is high in diabetic individuals [6] and CVD is the primary cause of death in people with either type 1 or type 2 diabetes [7,8]. It is reported that, CVD accounts for the high health care demand and expenditures in people with diabetes. [8,9]. Diabetes mellitus is associated with atherosclerotic cardiovascular diseases (ASCVD) complications. Atherosclerotic cardiovascular disease composes of coronary heart disease (CHD) [10,11], myocardial infarction [12], cerebrovascular disease and peripheral arterial disease with atherosclerotic origin [13]. The ASCVD constitutes the leading cause of morbidity and mortality for individuals with diabetes [13]. The increased risk of ASCVD stimulates aggressive investigation for therapeutic regimes that can achieve prevention of these complications [8].

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Targeting of blood lipid concentration in diabetes becomes necessary. Studies have shown that lipid-lowering agents such as statins and fibric acid derivative decreases macrovascular disease in patients with diabetes mellitus [14]. These drugs are effective for both primary and secondary prevention of CVD [15]. Several studies have shown the efficacy of controlling individual cardiovascular risk factors in preventing or slowing ASCVD in people with diabetes. It has been advocated that natural medicinal substances be investigated with the aim of discovering alternative pattern of treatment by WHO [16]. This study seeks to evaluate the potentials of *Terminalia catappa* leaf extract on diabetic dyslipidemia in alloxan induced diabetes.

2. Materials and methods

2.1. Preparation of Plant Extract

Fresh leaves of *Terminalia catappa* were collected at the premises of the University of Uyo and the area was free of pesticides and other contaminants. The leaves were authenticated by a botanist at the Department of Botany and Ecological studies, University of Uyo and with herbarium number UUPH 22(a). The leaves were then washed with clean water to remove debris. The water was blotted out and kept overnight at room temperature to dry up. The clean leaves were pulverized and 5000 g of the pulverized leaves were soaked in 5 litres of deionised water for 18 hours. The mixture was filtered using muslin cloth and evaporated to dryness using thermostatic water bath at 45 ^{o}C until a semi solid paste of 204.18 g of the extract was obtained after evaporation representing a percentage yield of 4.08 %. The extract was stored in refrigerator for later use.

2.2. Preparation of Experimental Animal

Healthy adult male albino Wister rats weighting between 150-200 g were used for the study. The animals were procured from the animal house, Department of Physiology, Faculty of Basic Medical Sciences, University of Uyo. The animals were housed in a well-ventilated cage in the animal house and they were allowed to acclimatize for two weeks and maintained in a 24-hour dark and light cycle. The animals were fed with standard pellets (from Guinea Feeds, Plc Nigeria) and have access to water *ad libitum*.

2.3. Induction of diabetes

Diabetes was induced by intraperitoneal injection of alloxan monohydrate at a dose of 150 mg/Kg body weight [17,18,19]. The animals were assessed for development of diabetes after 72 hours [20] by obtaining blood sample from the tip of the tail. The blood sample was dropped into glucose strip to measure the glucose level using a glucometer (One Touch Ultra, Life Scan Inc, U.S.A). Blood glucose of ≥200 mg/dl was considered diabetic (normal range of blood glucose in rat is 80 – 120mg/dl) and were used for the experiments [18,20]

2.4. Experimental Design

The experimental animals were randomly distributed into five (5) groups of five (n=5) rats per group as follows:

- **Group 1:** Control group administered with only distilled water orally at a dose of 5 ml/kg body weight.
- **Group 2:** Normal rats with only aqueous leaf extract of *Terminalia catappa* at a dose of 130 mg/kg body weight administered orally.
- **Group 3:** Diabetic group administered with only distilled water orally at a dose of 5 ml/Kg body weight.
- **Group 4:** Diabetic group treated with *Terminalia catappa* leaf extract at a dose of 130 mg/Kg body weight by oral administration.
- **Group 5:** Diabetic group treated with exogenous Insulin at a dose of 0.75 U/Kg body weight by subcutaneous administration.

2.5. Determination of lipid profile

The total cholesterol, triglyceride and high-density lipoprotein was estimated by spectrophotometric method using standard analysis kits by Biotech (China) following the manufacturer's procedures. 1.0ml of reagent was prepared into all sample tubes labelled blank, standard, control and samples and pre-warmed at 37 ^{o}C for at least 2 minutes. 10ul of samples were added to respective tubes and mixed. The mixture was incubated for 10minutes at 37 ^{o}C and the absorbance was read at 520 nm. Low density lipoprotein and very low-density lipoprotein were determined by calculation using a mathematical formula by Friedewald et al [21] as follows;

Low density Lipoprotein (LDL, mg/dL) = Total cholesterol (TC, mg/dL) –High density Lipoprotein (HDL) mg/dL

2.6. Very low-density Lipoprotein (VLDL, mg/dL) = Triglyceride (TG)/5 mg/dL.

Assessment of Cardiovascular Risk Indices in Normal and Diabetic groups

Cardiovascular risk of the *T. catappa* was calculated using various indices to assess the cardiovascular disease index and coronary heart disease index.

(a) Atheroginic Index of Plasma (AIP) was calculated as:

AIP = Log (TG/HDL-c)

(b). Castelli's risk Index-I (CRI-I) and Castelli's Index-II (CRI-II) were calculated as follows:

CRI-I = TC/HDL-c and CRI-II = LDL-c/HDL-c

where: TG is Triglyceride, HDL-c is High density lipoprotein-cholesterol, LDL- c is Low density lipoprotein-cholesterol and TC is Total cholesterol

2.7. Measurement of fasting blood glucose

Fasting blood glucose (FBG) was measured in the animals after overnight fast (about 14 hours) and the blood sample was obtained by pricking the tip of the tail. Measurement of blood glucose was done using glucometer (One Touch, Life Scan USA) on day 1, 4 and 14 [22].

2.8. Determination of serum insulin level

Serum insulin level was analysed using enzyme-linked immunosorbent assay (ELISA) method. Commercial analysis kits for rat insulin (Biotech, China) was used following the manufacture's procedure. The absorbance or optical density was obtained at 450 nm using a microtiter plate reader

2.9. Statistical analysis

The data obtained from the result was subjected to statistical testing using GraphPad Prism 5.0 software. One-way analysis of variance (ANOVA) with post hoc Turkey test was carried out. The result was presented as mean + standard error of mean (SEM) and the values with $p<0.05$ were considered significant.

3. Results

3.1. Serum Total Cholesterol (TC) level

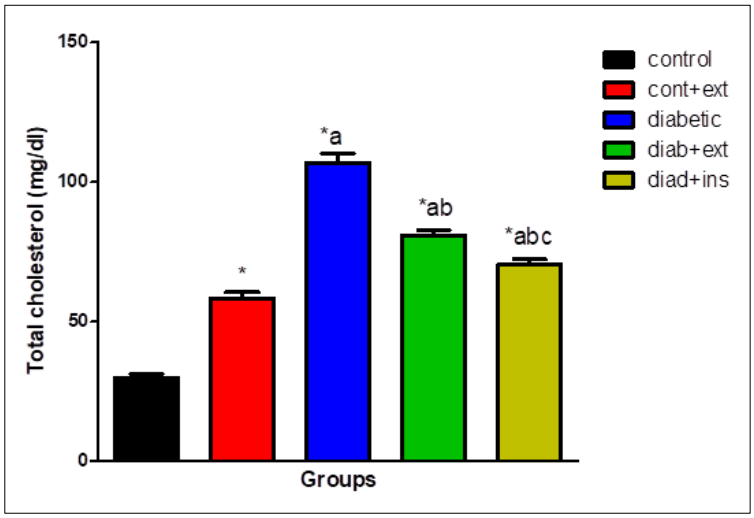

Figure 1 Serum Total cholesterol levels in normal and diabetic treated groups. Values are in mean ± SEM, $p<0.05$. *= test vs control, a= test vs control+extract, b= test vs diabetic group, c= test vs diabetic+extract.

The results of Total cholesterol are represented in figure 1. The serum total cholesterol level was 28.80±1.43 mg/dl in the control group, 58.20±2.29 mg/dl in control+extract group and 107.0±3.11 mg/dl in diabetic group. The diabetic group presented with a significantly ($p < 0.05$) raised TC level compared with the control group. The TC level was seen to reduce significantly ($p < 0.05$) in the diabetic+extract group to a mean value of 80.80±1.96 mg/dl compared with the diabetic group but this value was still higher than the control group value. In diabetic insulin treated group, there was also a significant ($p < 0.05$) reduction to mean value of 70.40±1.83 mg/dl when compared with diabetic group but not with the control group.

3.2. Serum Triglyceride (TG) Level

The results of Triglyceride (TG) are represented in figure 2. The value of triglyceride in the control group was 23.00±1.05 mg/dl, the control+extract was 29.20±1.46 mg/dl while diabetic group was 65.40±2.68 mg/dl. the TG of the diabetic group was significantly ($p < 0.05$) higher than the control group. The diabetic group treated with *T. catappa* leaf extract and insulin showed significant ($p < 0.05$) reduction to a mean value of 46.40±2.21 mg/dl and 47.0±3.03 mg/dl respectively when compared with diabetic group but was however significantly higher than the control group value.

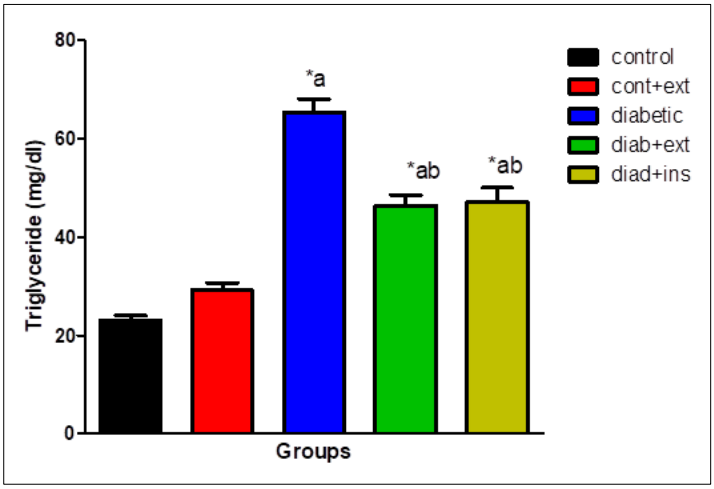

Figure 2 Serum Triglyceride levels in normal and diabetic treated groups. Values are in mean ± SEM, $p<0.05$. *= test vs control, a= test vs control+extract, b= test vs diabetic group.

3.3. Serum High Density Lipoprotein Cholesterol (HDL-c) Level

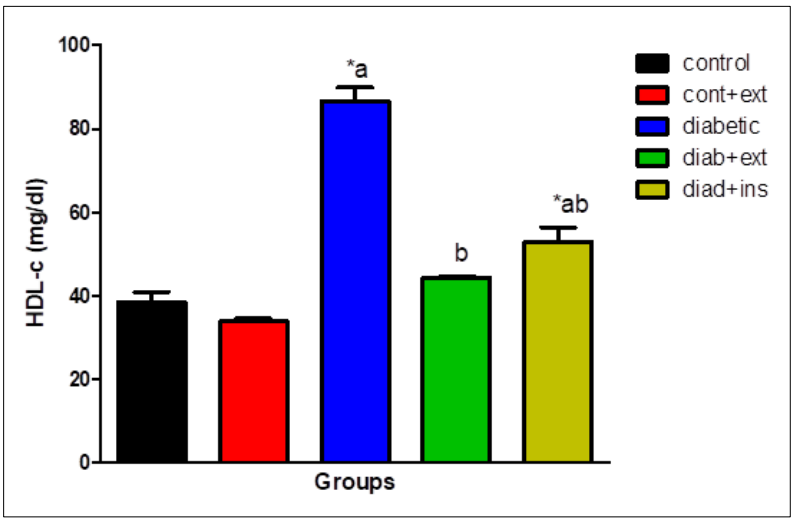

Figure 3 Serum High density lipoprotein-cholesterol levels in normal and diabetic treated groups. Values are in mean ± SEM, $p<0.05$. *= test vs control, a= test vs control+extract, b= test vs diabetic group.

In figure 3, the results of high-density lipoprotein (HDL-c) are represented. The serum levels of HDL for control, control+extract and diabetic groups were 38.40±2.54 mg/dl, 33.80±0.80 mg/dl and 86.60±3.23 mg/dl respectively. Comparing the results, the HDL-c of diabetic group was significantly ($p < 0.05$) higher than the control group while the control+extract group showed no significant change on the HDL-c. The HDL-c in diabetic group treated with extract was 44.20±0.49 mg/dl and insulin treated group was 52.80±3.56 mg/dl. The observed reductions were significant ($p < 0.05$) when compared with the diabetic group but not the control group.

3.4. Serum Low Density Lipoprotein Cholesterol (LDL-C) Level

The results of Low-density lipoprotein are represented in figure 4. The serum low density lipoprotein level was 55.60±1.97 mg/dl in the control group, 71.00±2.95 mg/dl in control+extract group and 141.60±4.01 mg/dl in diabetic group. But in diabetic group treated with extract, the value significantly ($p<0.05$) reduced to 64.00±2.45 compared to the diabetic group although it was still higher than the control group value. Diabetic+insulin group also showed significant ($p < 0.05$) reduction to mean value of 59.80±0.92 mg/dl.

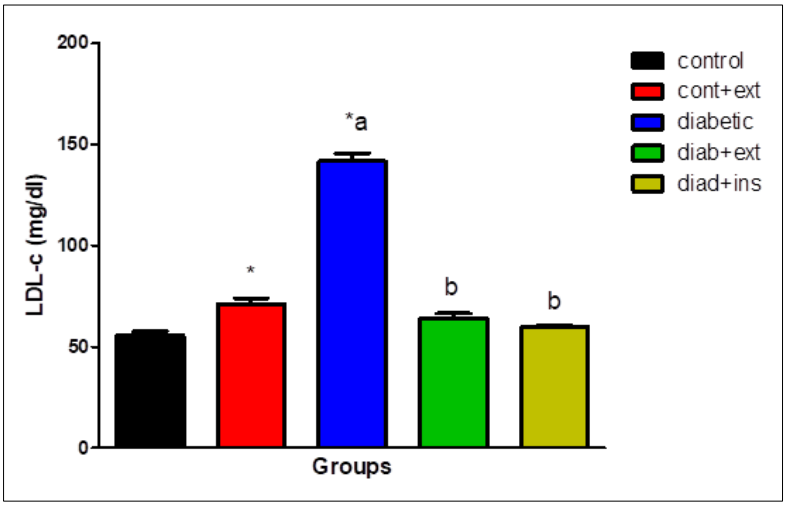

Figure 4 Serum Low density lipoprotein-cholesterol levels in normal and diabetic treated groups. Values are in mean ± SEM, $p<0.05$. *= test vs control, a= test vs control+extract, b= test vs diabetic group.

3.5. Serum Very Low-Density Lipoprotein Cholesterol (VLDL-C) Level

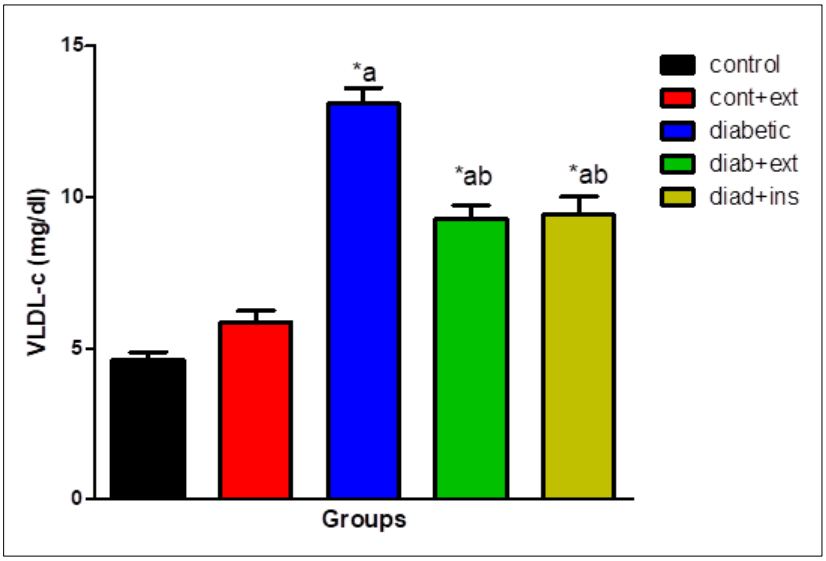

Figure 5 Serum Very low density lipoprotein-cholesterol levels in normal and diabetic treated groups. Values are in mean ± SEM, $p<0.05$. *= test vs control, a= test vs control+extract, b= test vs diabetic group.

The results of very low-density lipoproteins are represented in figure 5. The serum level of very low-density lipoprotein was 4.60±0.27 mg/dl in the control group, 5.84±0.41 mg/dl in control+extract group and 13.08±0.54 mg/dl in diabetic group. The diabetic+extract and diabetic+insulin groups showed significant ($p<0.05$) reductions to mean values of 9.28±0.44 mg/dl and 9.40±0.61 mg/dl respectively compared to the diabetic group. These were higher than the control group value.

3.6. Fasting Blood Glucose (FBG) Level on Different Days

The results of the fasting blood glucose (FBG) levels in different days within the group is presented in table 1. The result in control group showed slight changes on day 1, 4 and 14 which had no significant difference within the days. But there was significant ($p < 0.05$) reduction on day 4 FBG in control+extract group when compared with its day 1 and this may be attributed to the effect of the extract. In the diabetic group, the glucose level significantly ($p < 0.05$) increased on day 4 and 14 respectively compared with day 1 and this was attributed to the alloxan effect. Groups administered with extract and insulin showed significant ($p < 0.05$) reductions on day 14 compared to their respective values on day 4 after diabetes induction.

Moreover, the fasting blood glucose level across all the groups on different days are shown in figures 6a, 6b and 6c. The FBG on day 1 in all the groups were not different significantly. Day 4 showed significant ($p < 0.05$) increase in the diabetic induced groups (diabetic group, diabetic+extract group, diabetic+insulin group) compared with day 4 glucose level in control group. On day 14 there was significant ($p < 0.05$) decrease in FBG levels of extract and insulin treated groups (diabetic+extract and diabetic+insulin) compared with diabetic group but significantly ($p < 0.05$) higher than control group.

Table 1 Changes on Fasting Glucose Level between days in each group

GROUPS	**FASTING BLOOD GLUCOSE (g/ml)**			**% Relative Change from**	
	Day 1	Day 4	Day 14	Day 1-4	Day 4-14
Control	59.3 ± 9.9	68.3 ± 5.7	86.3 ± 3.95	-15.2	-26.4
Non-diabetic+ Extract	61.4 ± 2.6	50.4 ± 2.4[a]	59.6 ± 2.54	+17.9	-18.3
Diabetic Control	52.2 ± 7.2	216.6 ± 11.4[a]	264.6 ± 5.9[a]	-314.9	-22.2
Diabetic + Extract	42.8 ± 4.2	295.0 ± 31.9[a]	104.4 ± 2.3[ab]	-589.3	+64.6
Diabetic + Insulin	44.5 ± 1.8[b]	303.0 ± 14.5[a]	139.8 ± 5.7[ab]	-603.4	+57.2

N= 5; a Significant change compared to day 1 ($p<0.05$); b Significant change compared to day 4 ($p<0.05$)

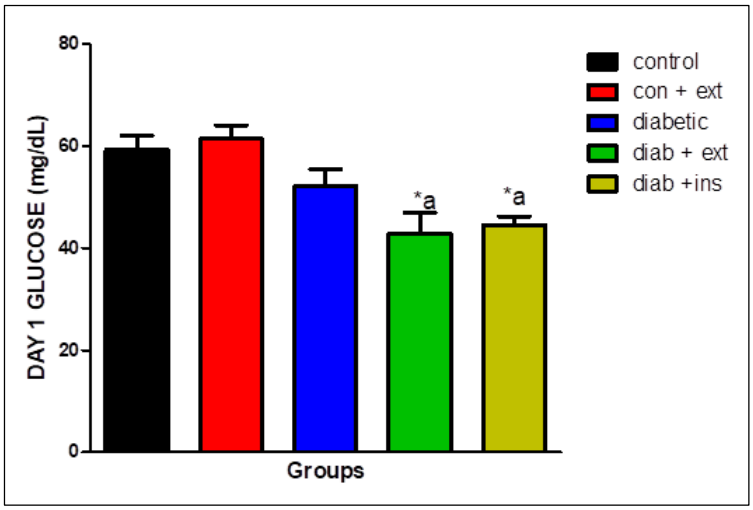

Figure 6a Day 1 fasting blood glucose levels in normal and diabetic treated groups. Values are in mean ± SEM, $p<0.05$. *= test vs control, a= test vs control+extract.

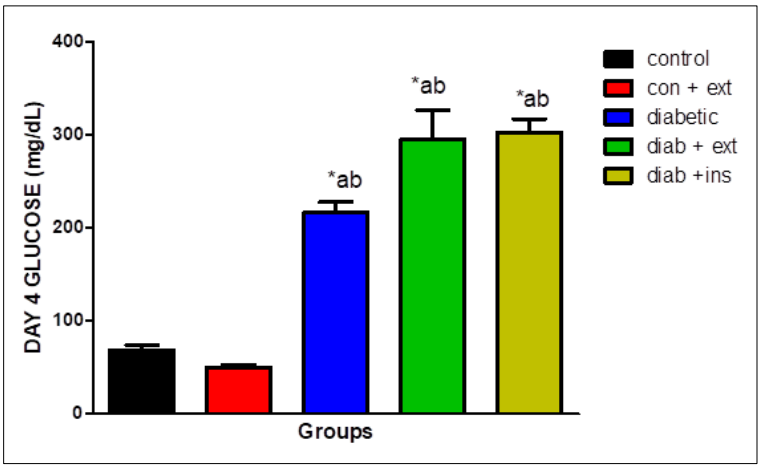

Figure 6b Day 4 fasting blood glucose levels in normal and diabetic treated groups. Values are in mean ± SEM, p<0.05. *= test vs control, a= test vs control+extract, b= test vs diabetic group.

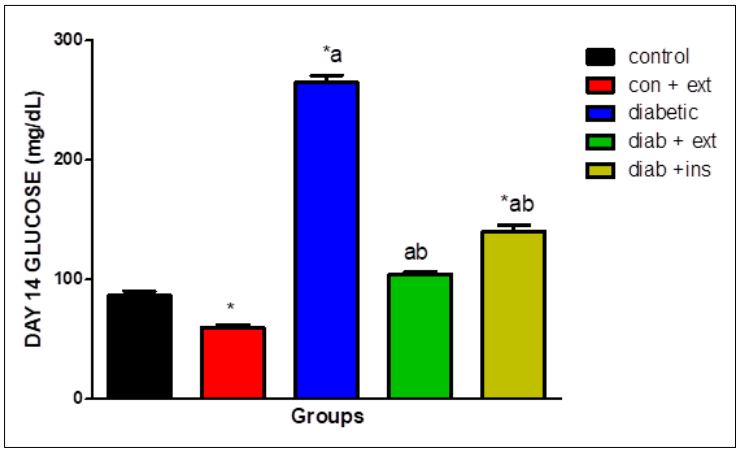

Figure 6c Day 14 fasting blood glucose levels in normal and diabetic treated groups. Values are in mean ± SEM, p<0.05. *= test vs control, a= test vs control+extract, b= test vs diabetic group.

3.7. Serum Insulin level in diabetic and non-diabetic groups

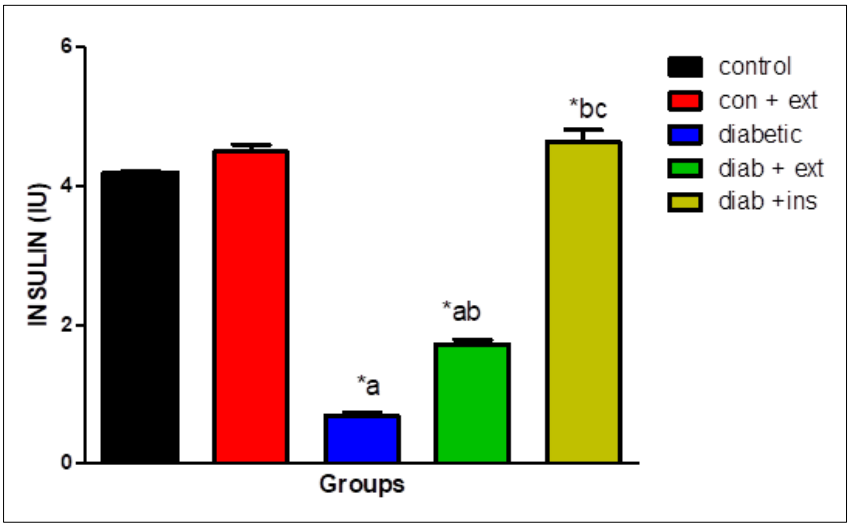

Figure 7 Serum insulin levels in normal and diabetic treated groups. Values are in mean ± SEM, p<0.05. *= test vs control, a= test vs control+extract, b= test vs diabetic group, c= test vs diabetic+extract.

The changes in the serum levels of insulin is represented in figure 7. The result showed that control group had insulin level of 4.20±0.22 U/mL and a slight increase in control+extract group to 4.49±0.11 U/mL. The insulin level decreased significantly ($p<0.05$) to mean value of 0.68±0.6 U/mL in the diabetic group compared with control. In the diabetic treated with extract, there was a significant ($p<0.05$) increase in serum insulin level up to 1.72±0.06 U/mL compared with diabetic group. This value was however significantly ($p < 0.05$) lower than the control group. Similarly, the insulin treated diabetic group had insulin level of 4.63±0018 U/mL which was significantly ($p<0.05$) increased when compared with diabetic group and diabetic+extract groups but marginally higher than the value of the control group.

3.8. Cardiovascular risk assessment

The cardiovascular risk assessment was calculated using Atherogenic Index of Plasma (AIP) and Castelli's Index 1 and 2 (CRI-I & CRI-II) as represented in table 2. The results showed that extract treated groups had low values of AIP compared with the control and diabetic groups. On the other hand, the CRI-I value was higher in extract treated groups compared to control and diabetic groups but the CRI-II was higher in control+extract treated group but reduced in diabetic group treated with the extract.

Table 2 Assessment of Cardiovascular Risk Indices in Normal and Diabetic groups

Risk Indices	Control	Control + Extract	Diabetic	Diabetic + Extract	Diabetic + Insulin
AIP	-0.22	-0.06	-0.12	-0.04	-0.05
CRI-I	0.78	1.72	1.24	1.83	1.33
CRI-II	1.45	2.1	1.64	1.45	1.13

AIP: Atherogenic Index of Plasma, CRI-I: Castelli's Risk Index-1, CRI-II: Castelli's Risk Index-II

4. Discussion

Dyslipideamia is one of the common abnormalities associated with diabetes mellitus [23,24,25]. Primary therapeutic target for diabetes mellitus is to achieve tight glycemic control. This however may not achieve total correction of the changes in lipid status and its related effects [26]. Therefore, adjunct therapy has been advocated in managing diabetes to address both glycemic and lipidemic status to forestall some associated cardiovascular disorders [23]. This study was carried out to evaluate the modulating effect of aqueous leaf extract of *Terminalia catappa* on dyslipidemia in diabetic rats. The result of lipid profile showed that total cholesterol (TC), triglyceride (TG), high density lipoprotein-cholesterol (HDL-c), low density lipoprotein-cholesterol (LDL-c) and very low density lipoprotein- cholesterol (VLDL-c) were increased significantly in the diabetic untreated group compared with the control group. The results of TC and TG agrees with previous reports by other researchers associating diabetes mellitus with increased synthesis of cholesterol [27,28] and increased triglyceride [29,27,28]. This may be due to higher rate of hepatic production of cholesterol and triglyceride rich VLDL-c [30] and decreased removal of TG by peripheral tissues such as adipose tissues and muscles [31]. In diabetes mellitus, the inability of the cells to takeup glucose affects the cellular energy metabolism [32] and changes in triglyceride is associated with changes in energy metabolism. Insulin deficiency leads to high TG production as well as inability of the body to utilize triglyceride for energy [33]. It is reported that high TG level has strong association with inadequate glycemic control in humans [34] and complex relationship between TG and glucose metabolism may be influenced by antidiabetic drugs such as insulin and metformin [35]. The result showed that insulin treated group TG significantly decrease compared with the untreated diabetic group. The chronic action of dyslipidemia is associated cardiovascular complications [36,37] while the glycemic control constitutes the acute effect [38]. Therefore, handling of TG can invariably address both acute and chronic disorders. Comparing with diabetic group administered with leaf extract of *Terminalia catappa*, there was similar trend of reduction. It is speculated that atherogenic tendency of hypertriglyceridemia could be attenuated by treating of hypertriglyceridemia [39]. This reduction in hypertriglyceridemia following extract treatment can attenuate potential atherogenic tendency, improve insulin sensitivity, enhance glucose uptake and utilization by peripheral tissues.

Moreover, abnormal HDL-c metabolism as a risk factor in cardiovascular disorders have been established. Documented evidence had shown that HDL-cholesterol level is reduced in type 2 diabetes mellitus [40] but raised in type 1 diabetes mellitus [41]. It was observed that the HDL-c level was significantly increased in diabetic group compared with control group. This is contrary to the report of Pandhare et al [42] but corroborates with the findings of Gourgari et al [43], Orchard et al [41] and supported by research report of [44] that low HDL is not common in type I diabetes mellitus. High incidence of cardiovascular heart disease (CHD) reported in type 1 diabetes mellitus [45,46,47] is attributed to associated dyslipidemia [48,49,50] in which HDL-c have been implicated. It is generally known that HDL-c possesses a

cardioprotective potential cholesterol exchange capacity (CEC) through reverse transport of cholesterol from LDL-c to the liver for excretion [51,52] anti-inflammatory [53,54,55] and anti-oxidative functions [56,57]. Contrary to previous believes that increased HDL-c protect against cardiovascular disease, studies have shown that abnormally raised HDL-c does not protect against coronary heart disease (CHD) [58]. There is increasing evidence on failure of increased circulating HDL-c to protect against coronary heart disease [59,60]. Biological activities of HDL-c may be altered in various pathological conditions resulting in lose of protective properties. In a poorly control diabetes, hyperglycemia induced covalent modification of apolipoprotein major HDL particles such apo-AI alters metabolism and funtions of HDL-c [61,62,63]. Following increased oxidative stress, glycoxidation of HDL proteins [64,65] and peroxidation of HDL lipid [66] occur. Since the functionality of HDL-c can be affected in diseased condition like diabetes mellitus, the increased level of HDL-c may indicate abnormalities associated with HDL-c sub-fractions, protein contents or size [67]. Such alterations in HDL-c protein content results in a dysfunctionality of HDL-c particles and reduces the protecting capability against cardiovascular disease. The observed reduction of HDL-c level towards the control value by extract of *Terminalia catappa* on HDL-c was considered beneficial. It is reported that some affected HDL-c protein may be corrected by obtaining good glycemic control while some proteins are not. Thus, the use of therapeutic agent capable of modulating the HDL-c proteins becomes necessary option to enhance the cardioprotective function of HDL-c. Therefore, the leaf extract of *Terminalia catappa* modulates abnormal HDL-c changes in diabetes mellitus. Although there is need to evaluate the specific manner in which the HDL-c is affected by the extract, it could be speculated that the extract may interfere with changes in either the HDL-c sub-fractions or HDL-c protein content or improved cholesterol efflux capacity [63]. The reduction of HDL-c levels in extract and insulin treated groups were similar when compared with the diabetic untreated group but not as low as the control group.

Futher more, raised LDL-cholesterol as cardiovascular risk is well established. In the diabetic untreated group, the level of LDL was significantly increased. The result is in line with many research reports [68,69] but does not agree with a reports that LDL-c is normal in diabetic condition [49] However, the administration of extract in diabetic+extract group reduced the LDL-c to level not different from control. The observed reduction is consistent with [70,71,72]. The importance of maintaining low LDL-c in diabeties mellitus have been stressed [73] because increased LDL-c is a major risk factor in development of atherosclerosis [74] and associated macrovascular complications in diabetes mellitus [75]. The result of this study implies that the extract of *T. catappa* leaves can reduce LDL-c in diabetes mellitus thus mitigating the process of developing atherosclerotic cardiovascular disorders (ASCVD). Assessing cardiovascular risk showed a reduced atherogenic index of plasma (AIP) in both normal and diabetic groups treated with aqueous extract of *T. catappa* compared with control and diabetic groups respectively. However, assessing coronary risk by Castelli's Risk Index (CRI-1 and CRI-11) reflects increased index value in extract treated nondiabetic and diabetic groups compared with control and non-treated diabetic group. This suggest the extract potency in reducing risk of developing cardiovascular disease (CVD) while prevention of coronary heart disease (CHD) may be questionable in diabetes mellitus and unattainable in non-diabetic state.

With regards to hyperglycemic control, fasting blood glucose in this study showed significant decrease in the extract treated group on day 14 compared with the fasting blood glucose on day 4 after alloxan administration in diabetic untreated, diabetic+extract and diabetic+insulin groups. Administration of insulin also significantly reduced the fasting blood glucose compared with the diabetic untreated group on day 14. The serum insulin level was significantly elevated in extract treated group though not as much as the elevation in insulin treated group. Research has reported that decrease in blood glucose is a major pathway in correcting dyslipidemia [76]. Therefore, the extract may function indirectly by its ability to improve glycemia and enhance insulin secretion as observed in this study. Therapeutically targetting dyslipidemia has been reported to be advantagous [77] and co-administration of lipid drugs had been recommended in the management regimes of diabetes mellitus. The observed extract anti-dyslipidemic function may be activated through pathways other than glycemic control and insulin secretion in the modulation of dyslipidemia.

5. Conclusion

In conclusion, the aqueous leaf extract of *T. catappa* modulates hyperglycemia induced dyslipidemia suggesting its potency in managing dyslipidemia in type 1 diabetes mellitus and may be used to ameliorate diabetes associated cardiovascular complications, hence possessing a cardioprotective function against atherosclerotic cardiovascular disorders in diabetic condition.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The experimental protocol received full ethical approval from Faculty Animal Research Ethics committee - Faculty of Basic Medical Sciences (FAREC-FBMS) with approval number 021PY30417

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