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Aqueous seed extract of *Cola acuminata* ameliorated high fat diet-induced hyperlipidaemia in rats

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ABSTRACT: Hyperlipidaemia is a medical condition characterized by an elevation of any or all lipid profiles and/or lipoproteins in the blood. It has been well established that nutrition plays a vital role in the aetiology of hyperlipidaemia and cardiovascular diseases. The antihyperlipidaemic potential and toxicological assessment of aqueous seed extract of *Cola acuminata* in high-fat diet-induced hyperlipidaemic rats were investigated in this study. Twenty-four albino rats were grouped into six of four animals per group. Group 1 (control) was fed formulated feed without high fat. Group 2 was fed a high-fat diet (HFD) but untreated. Group 3 was fed HFD for eight weeks but was treated with atorvastatin from week 5 to week 8 (RFD). Group 4 was fed HFD for eight weeks but was treated with extract 10.71 mg/kg bw from week 5 to week 8. Group 5 was fed HFD for eight weeks but was treated with extract 21.42 mg/kg bw from week 5 to week 8. Group 6 was fed HFD for eight weeks but was treated with extract 42.84 mg/kg bw. The results showed that rats in group 2 (HFD) presented significantly ($p<0.05$) higher levels of blood lipids, Atherogenic Index (AI) and Coronary Disease (CHD) risk ratio considerably higher than in the healthy control rats ($p<0.05$). Group 3 (RFD) rats showed significantly ($p<0.05$) reduced blood lipid profile compared to the HFD but similar to that of the reasonable control. The AI and CHD risk ratios were also not significantly different from that of the control. The ALP, ALT activities of RFD Group, were also not significantly ($p<0.05$) separate from the control except the AST activity that significantly ($p<0.05$) increased. The groups treated with 10.71, 21.42 and 42.84 mg/kg bw extract presented reduced serum level of lipids and ALP, ALTand AST activities considerably. AI and CHD risk factors were significantly ($p<0.05$) decreased, and the reduction was dependent on the dose of the extract. Histopathological assessment of the heart, kidney and liver tissues of the experimental rats presented no significant changes and no sign of acute or chronic injury. However, the HFD group showed with overlying pericardial and coronary artery fat. In the liver, there were mild lymphocytic infiltrations. Therefore, from this study, it is concluded that aqueous extract of *Cola acuminata* was able to improve HFD-induced hyperlipidaemia and caused no significant damage to the organs (heart, kidney, and liver of the rats).

Keywords: Hyperlipidaemia, high-fat diet, *Cola acuminata*.

Introduction

Hyperlipidaemia is a heterogeneous group of disorders characterized by an excess of lipids in the bloodstream (Johnson, 2005). This condition is also called hypercholesterolaemia or hyperlipoproteinaemia (Amit, 2011). The human body is a sophisticated machine for maintaining the homeostasis of various organs and systems. An unfavourable change often disturbs the balance resulting

in the diseased state (Ankur *et al.*, 2012). Excess lipids cause hyperlipidaemia in the diet or by abnormal fat and lipoprotein metabolism in the body (Harikumar, 2011). Hyperlipidaemia is a significant health problem in Nigeria and other developing countries (Chukwu, 2011), and it is considered one of the major risk factors causing cardiovascular diseases (CVDs). CVDs account for one-third of total deaths around the world and are often thought to be a major cause of death and disability World-wide by the year 2020 (Ginghina *et al.*, 2011; Jorgenson *et al.*, 2013). Atherosclerosis (a process of arteries hardening of cholesterol in the arterial wall which causes narrowing of the arteries) and associated atherosclerosis disorders like coronary, cerebrovascular and peripheral vascular diseases are accelerated by the presence of hyperlipidaemia (Wells *et al*., 2007). Prolonged hyperlipidaemia can also lead to non-alcoholic fatty liver disease-a situation whereby cholesterol accumulates in the liver, causing congestion (Hall, 2011). The leading cause of hyperlipidaemia are changes in lifestyle habits, a risk factor being mainly poor diet, i.e. with a fat intake more significant than 40 per cent of total calories, saturated fat intake greater than 10 per cent of total calories; and cholesterol intake higher than 300 milligrams per day or treatable medical conditions (Durrington,1995). The abnormally high cholesterol levels are the result of an unhealthy lifestyle, including taking a high-fat diet and other factors like being overweight, smoking, heavy alcohol use and lack of exercise. Other factors include diabetes, kidney disease, pregnancy, and an underactive thyroid gland (Kelly, 2010).

Herbal medicines are being used by about 80 per cent of the world population, primarily in developing countries. They have stood the test of time for their safety, efficacy, cultural acceptability and low side effects. The chemical constituents present in them are a part of the physiological functions of living flora, and hence they are believed to have better compatibility with the human body (Kambooj, 2000). More than 70 medicinal plants have been documented to have significant hypolipidaemic action (Dahlia *et al.*, 2013). During the last decade, an increase in the use of medicinal plants has been observed in metropolitan areas of developed countries. Medicinal plants play a significant role in the hypolipidaemic activity. The advantages of herbal medicines reported are effectiveness, safety, affordability, and acceptability (Dahlia *et al.*, 2013). There are so many medicinal plants extracts that have recently been reported to have antihyperlipidaemic property. These include *Moringa oleifera* (Onwe *et al.*, 2015), extracts of *Solanum melongena* (Kateregga *et al.*, 2015), *Salvadora oleoides* (Deepak, 2012), *Brassica oleracea* (cabbage) based diet (Oloyede *et al.*, 2015) among others. This research was carried out to study the hypolipidaemic activity of aqueous extract of *Cola acuminata* in high-fat diet-induced hyperlipidaemia.

Materials and Methods

Thirty-six adult female albino rats with an average weight of 122.56 ± 4.32 g were obtained from a reputable source. They were housed in plastic cages at room temperature and 12h light-dark cycle. The animals were randomly divided into six groups (n=6animals per group). The animals were acclimatized for one week before the commencement of the experiment. They were grouped and fed with different dietary formula, as shown in Table 1 and given water *ad libitum.* The extract was gavaged to experimental groups at three dose levels 10.71, 21.42 and 42.84 mg/kg) equivalent to 13.5, 27 and 54 g kola nut per 70 kg man daily for 30 days. Group 1 served as the control group and was fed with a control diet (NC). Group 2 was the hyperlipidaemic group (HFD) and was fed a high-fat diet for eight weeks. Group 3 was fed a high-fat diet for eight weeks but was treated with atorvastatin from week five. Group 4 was fed a high-fat diet for eight weeks but was treated with extract 10.71 mg/kg b.w from week five equivalent to the consumption of half kola nut weighing 13.5 g (half standard) by a 70 kg man per day. Group 5 was fed a high-fat diet for eight weeks but was treated with extract 21.42 mg/kg b.w from week five equivalent to the consumption of one kola nut weighing 27 g (standard) by a 70 kg man per day. Group 6 was fed a high-fat diet for eight weeks but was treated with extract 42.84 mg/kg b.w from week five equivalent to the consumption of 2 kola nuts both weighing 54 g (double standard) by a 70 kg man per day.

Assay Kits and Reagents

Reagent kits were products of Randox Laboratory Limited. Sucrose solution, formalin solution, and other reagents were of analytical grade prepared using distilled water.

Biochemical analysis

The proximate analyses for control and high-fat diet were determined according to the methods of AOAC (2005). After eight weeks, the animals were sacrificed by jugular puncturing under anaesthesia using diethyl ether; blood was collected inside centrifuge tubes and centrifuged at 300 rpm for 20 mins. The clear serum was carefully pipetted into plain sample bottles and kept frozen until needed for analysis. High-density lipoprotein cholesterol (HDL-c) was determined by the methods of Bachorik (1996). The low-density lipoprotein cholesterol (LDL-c) was determined using the method of Williams *et al.* (1979). The purposes of Tiez (1990) were employed in the determination of Triglycerides. The cardiovascular disease risk was calculated as described by Mannien *et al.*, *(*1992) and Atherogenic Index (AI) was calculated as described by Nwagha *et al.*, *(*2005). The method described by Reitman and Frankel (1957) was used in the assay for the activity of alanine aminotransferase and aspartate aminotransferase. The technique described by Wright *et al.* (1972) was employed in the test for the activity of alkaline phosphatase. Bilirubin was determined using the method described by Jendrassik and Grof (1938). The technique used for the determination of urea in the serum of the animals was as described by Veniamin and Vakirtzi (1970). Serum uric acid was determined according to the method described by Tietz (1995). Serum creatinine was measured using the technique described by Bartels and Bohmer (1972).

Statistical Analysis

Values were expressed as mean ± SEM of 4 replicates (n = 4). Statistical analysis was conducted using the SPSS software (version 21). Collected data were subjected to one-way Analysis of Variance (ANOVA), followed by Duncan Multiple Range test for comparisons. The significant differences between the means were determined at $P<0.05$ (95 % confidence interval).

Results

Table 1 presents the proximate composition of the control and high-fat diets; from the table, it could be observed that the crude lipid content of the high-fat diet was significantly ($P<0.05$) higher than the control diet. The caloric value of the high-fat diet was also significantly ($P<0.05$) higher than the control.

Table 1: Proximate Composition of Control and High Fat Diet

Proximate Composition (%)	NC	HFD
Moisture	7.32 ± 0.22^{a}	1.81 ± 0.53^{b}
Ash	3.46 ± 0.33^{a}	2.25 ± 0.08^{a}
Carbohydrate	54.47 ± 0.34^{a}	25.23 ± 0.28^{b}
Caloric Value	1344.1 ± 4.23^{a}	2225.4 ± 2.62^{b}
Crude protein	17.14 ± 0.00^{a}	16.28 ± 0.28^{a}
Crude lipids	3.88 ± 0.26^{a}	36.85 ± 0.03^{b}
Crude fibre	5.65 ± 0.06^{a}	5.58 ± 0.08^{a}

Results are mean of 4 determinations ± SEM. Mean along the same column with different superscript letters are significantly different ($p<0.05$).

NC = Control, HFD = High-fat diet group, RFD = Reference drug group

Table 2: Secondary Metabolites in Aqueous Seed Extract of *Cola acuminata*

Phytochemicals	Concentration (**mg/100g)**
Saponin	0.21 ± 0.00
Phenolics	6.57 ± 0.12
Steroids	51.18 ± 0.17
Flavonoids	60.92 ± 0.16
Anthocyanin	2.00 ± 0.00
Terpenoids	16.43 ± 0.27
Glycosides	8.67 ± 0.04
Triterpenes	74.93 ± 1.75
Alkaloids	10.14 ± 0.70

Table 3 shows the serum and hepatic lipids of rats fed with a high-fat diet and treated with *Cola acuminata* aqueous seed extract. The serum and hepatic lipids of rats fed with high-fat diet were significantly ($P<0.05$) higher than the control and other groups except for HDL which was significantly ($P<0.05$) lower while the hepatic lipids of the reference drug group were not significantly ($P<0.05$) different from the treated groups.

Table 3: Serum Lipid Profile and Hepatic Lipids of Rats Fed with High-Fat Diet and Treated with Aqueous Seed Extract of *Cola acuminate*

Serum lipid profile(mg/dl)					Liver Lipids (mg/dl)	
Groups	CHOL	TRIG	HDL	LDL	CHOL	TRIG
NC	81.68 ± 1.60^{a}	25.90 ± 0.44^{a}	75.97 ± 6.44^{a}	2.03 ± 0.05^{a}	146.18 ± 8.56^{c}	88.75 ± 1.77^{a}
HFD	106.91 ± 1.03^{c}	43.24 ± 0.56^{c}	48.39 ± 1.41^{b}	24.77 ± 2.56^{c}	216.41 ± 4.56^{b}	172.78 ± 3.74^{c}
RFD	82.41 ± 0.64^{a}	24.53 ± 0.09^{a}	82.85 ± 0.61^{a}	2.50 ± 0.04^{a}	154.76 ± 1.34^{c}	102.99 ± 2.99^{b}
10.71mg/kg extract (half standard)	88.35 ± 0.67^{b}	32.26 ± 0.59^{b}	68.47 ± 14.93^{c}	7.49 ± 0.13^{b}	171.35 ± 7.26^{a}	103.32 ± 3.83^{b}
21.42mg/kg extract (standard)	86.95 ± 2.54^{b}	29.38 ± 1.44^{b}	75.44 ± 8.34^{a}	4.61 ± 0.27^{a}	174.75 ± 3.45^{a}	101.77 ± 2.21^{b}
42.85mg/kg extract (double standard)	83.08 ± 0.52^{a}	25.05 ± 0.20^{a}	79.45 ± 7.59^{a}	3.33 ± 0.56^{a}	168.19 ± 3.78^{a}	101.91 ± 3.77^{b}

Results are mean of 4 determinations ± SEM. Mean along the same column with different superscript letters are significantly different ($p<0.05$).
NC=control, HFD = High-fat diet group, RFD = Reference drug group

Table 4 shows the Atherogenic Index (AI) and Coronary Heart Disease (CHD) risk ratio of rats fed with a high-fat diet and treated with aqueous seed extract of *Cola acuminata*. From the table, it is observed that the AI and CHD risk ratio of the rats fed on a high-fat diet were significantly ($p<0.05$) higher compared with the control and other groups.

Table 4: Artherogenic Index and Coronary Heart Disease (CHD) Risk Ratio of Rats Fed with High-Fat Diet and Treated with Aqueous Seed Extract of *Cola acuminate*

Groups	AI Index ($x10^{-1}$)	CHD Risk ratio
NC	0.19 ± 0.01^{b}	1.06 ± 0.01^{a}
HFD	0.36 ± 0.50^{d}	2.23 ± 0.03^{d}
RFD	0.17 ± 0.03^{a}	1.05 ± 0.01^{a}
10.71mg/kg extract	0.20 ± 0.00^{c}	1.12 ± 0.05^{c}
21.42mg/kg extract	0.19 ± 0.08^{b}	1.09 ± 0.03^{b}
42.85mg/kg extract	0.18 ± 0.02^{b}	1.05 ± 0.02^{b}

Results are mean of 4 determinations ± SEM. Mean along the same column with different superscript letters are significantly different ($p<0.05$).
NC = Control, HFD = High-fat diet group, RFD = Reference drug group, AI = Atherogenic Index, CHD = Coronary Heart Disease.

Table 5 shows the specific enzyme activities of ALP, ALT, and AST in the serum of animals fed on High-Fat diet and treated with aqueous seed extract of *Cola acuminata*. The specific activities of ALP, ALT, and AST in the serum of animals fed on High-Fat diet (HFD) were significantly ($P<0.05$) higher than the control and other groups while the specific activities of ALP, ALT, and AST of the treated groups were not significantly ($P<0.05$) different from the control and reference drug group except for AST which was significantly ($P<0.05$) higher in the reference group than the control.

Table 5: Specific Enzyme Activity in the Serum of Rats Fed with High-Fat Diet and Treated with Aqueous Seed Extract of *Cola acuminate*

Groups	Specific Enzyme Activity (nmol min^{-1} mg $protein^{-1}$)		
	ALP	ALT	AST
NC	85.56 ± 2.88^{a}	25.57 ± 0.98^{a}	62.56 ± 2.33^{a}
HFD	101.70 ± 3.04^{b}	35.85 ± 0.87^{b}	85.41 ± 2.68^{c}
RFD	91.46 ± 4.37^{a}	27.04 ± 0.78^{a}	73.27 ± 0.41^{b}
10.71mg/kg extract	91.35 ± 3.85^{a}	25.67 ± 0.86^{a}	63.70 ± 1.42^{a}
21.42mg/kg extract	87.16 ± 7.03^{a}	24.46 ± 0.86^{a}	60.27 ± 1.97^{a}
42.85mg/kg extract	83.95 ± 3.76^{a}	26.89±1.34	61.30 ± 5.40^{a}

Results are mean of 4 determinations ± SEM. Mean along the same column with different superscript letters are significantly different ($p<0.05$).
ALP = Alanine aminotransferase, AST = Aspartate aminotransferase, ALP = Alkaline Phosphatase, NC = Control, HFD = high-fat diet group, RFD = Reference drug group.

Table 6 shows the serum urea, uric acid and creatinine concentrations of rats fed with a high-fat diet and treated with aqueous seed extract of *Cola acuminata.* The levels of urea, uric acid and creatinine were not significantly ($p<0.05$) different in the experimental and control groups.

Table 6: Effect of Aqueous Seed Extract of *Cola acuminata* on the Kidney Function Indices in the Serum of Rats Fed with High-Fat Diet

Groups	Urea(mg/dl)	Uric acid(mg/dl)	Creatinine(mg/dl)
NC	12.16 ± 1.71[a]	1.90 ± 0.09[a]	2.52 ± 0.32[a]
HFD	13.04 ± 0.79[a]	1.69 ± 0.67[a]	2.60 ± 0.11[a]
RFD	12.11 ± 0.00[a]	1.56 ± 0.08[a]	2.78 ± 0.5[b]
10.71mg/kg extract)	12.93 ± 1.03[a]	1.53 ± 0.09[a]	2.39 ± 0.27[a]
21.42mg/kg extract	13.06 ± 0.04[a]	1.68 ± 0.04[a]	2.35 ± 0.54[a]
42.85mg/kg extract	12.13 ± 0.56[a]	1.79 ± 0.02[a]	2.56 ± 0.53[a]

Results are mean of 4 determinations ± SEM. Mean along the same column with different superscript letters are significantly different ($p<0.05$),
NC = Control, HFD = High-fat diet group, RFD = Reference drug group, C Bil = Conjugated Bilirubin, T Bil = Total Bilirubin

Table 7 shows the serum total and conjugated bilirubin concentrations of rats fed with a high-fat diet and treated with aqueous seed extract of C*ola acuminata.* It shows from the table that the concentrations of conjugated and total bilirubin of rats fed with a high-fat diet were significantly ($p<0.05$) higher than the control and other groups.

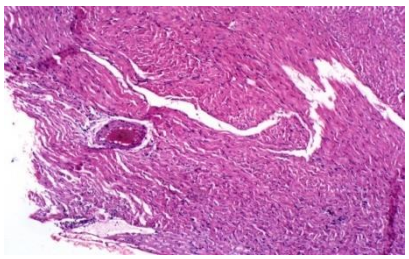
Table 7: Effect of Aqueous Seed Extract of *Cola acuminata* on the Liver Function Indices in the Serum of Rats Fed with High-Fat Diet

Groups	C Bil (mg/dl)	T Bil (mg/dl)
NC	25.44 ± 1.12[a]	65.83 ± 2.54[a]
HFD	32.90 ± 1.09[b]	75.86 ± 1.35[b]
RFD	26.00 ± 0.90[a]	64.03 ± 2.92[a]
10.71 mg/kg extract	27.12 ± 2.64a	65.72 ± 2.61[a]
21.42 mg/kg extract	24.72 ± 2.27[a]	62.86 ± 2.50[a]
42.85 mg/kg extract	26.25 ± 2.56[a]	66.38 ± 2.56[a]

Results are mean of 4 determinations ± SEM. Mean along the same column with different superscript letters are significantly different ($p<0.05$),
NC = Control, HFD = High-fat diet group, RFD = Reference drug group, C Bil = Conjugated Bilirubin, T Bil = Total Bilirubin

Effect of Aqueous Extract of *Cola acuminat*a on the Heart Histoarchitecture of High- Fat Diet-Induced Hyperlipidaemic Rats

Results of the histopathology of the heart of both the experimental and control rats show myocardial tissue composed of a syncytium of cardiac muscle cells and vascular channels (Figs. 1 – 3). There was no significant hypertrophy, infarction or inflammation seen in the control and other groups except for HFD which shows myocardial tissue with overlying pericardial and coronary artery fat but also presented no significant hypertrophy, infarction or inflammation. This is suggestive of the fact that prolonged consumption of a High-Fat Diet could cause atherosclerosis which is a risk factor for Coronary Heart Disease.



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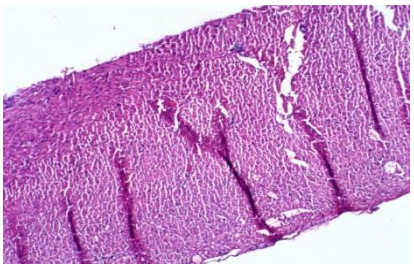

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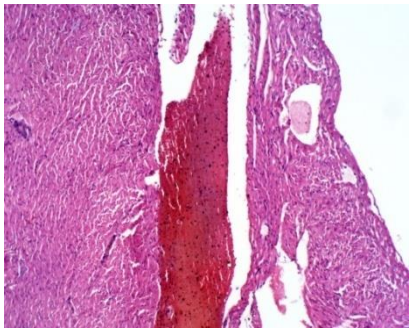

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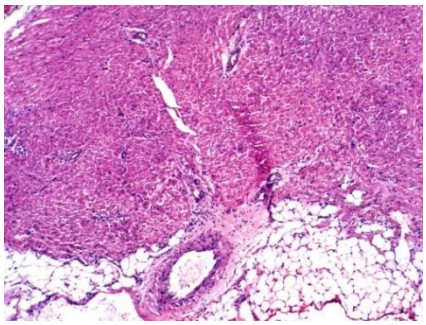

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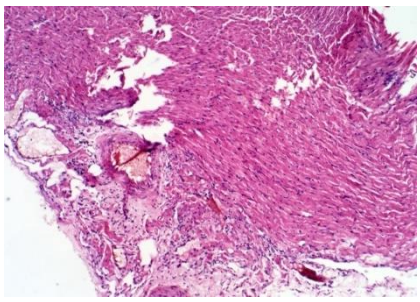
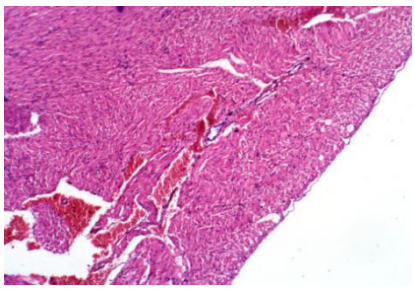


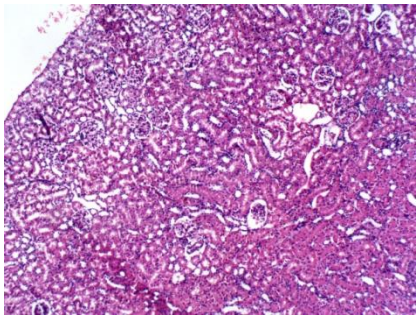
21.42 mg/kg b.w.



42.84 mg/kg b.w.

Fig. 1: Histoarchitecture of the Hearts of control and experimental rats.

Effect of Aqueous Extract of *Cola acuminata* on the Kidney Histoarchitecture of High- Fat Diet-Induced Hyperlipidaemic Rats



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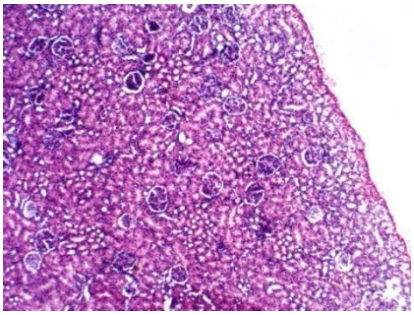

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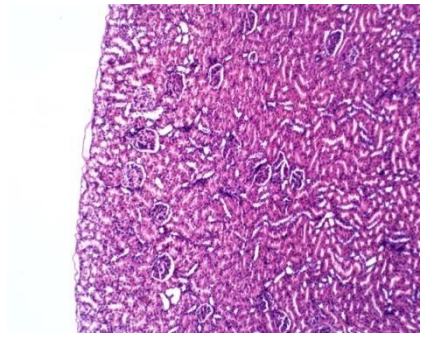

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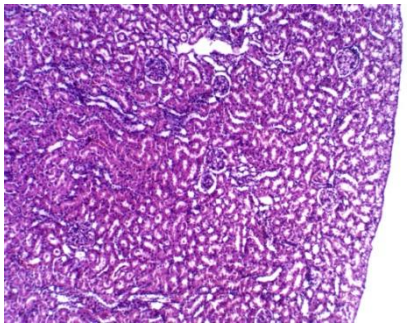
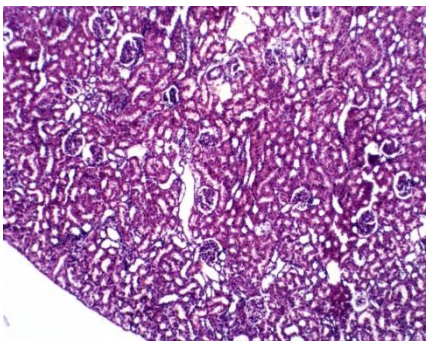
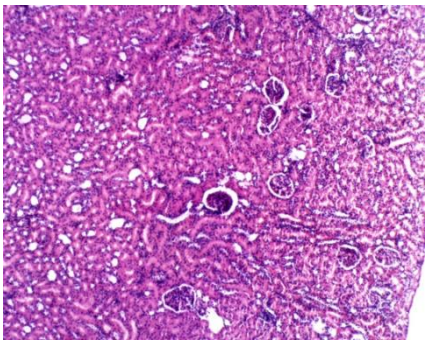


10.71 mg/kg b.w.



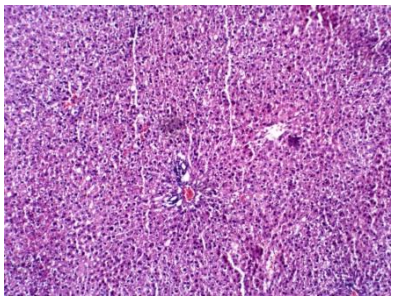
21.42 mg/kg b.w.



42.84 mg/kg b.w.

Fig. 2: Histoarchitecture of the Kidney of the control and experimental rats.
The histopathological examination of the kidneys of control and experimental rats shows kidney tissues with preserved architecture comprising normal glomeruli tubules with no features of acute or chronic damage. There was no significant difference in the kidney histopathology of all groups.

Effect of Aqueous Extract of *Cola acuminat*a on the Liver Histoarchitecture of High-Fat Diet-Induced Hyperlipidaemic Rats



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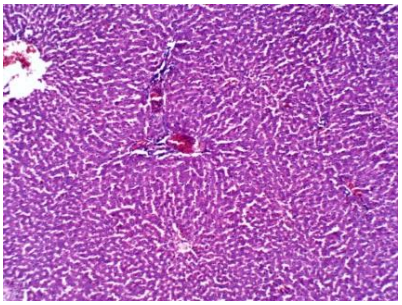

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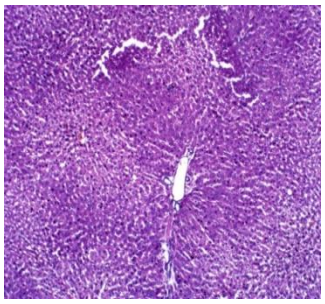
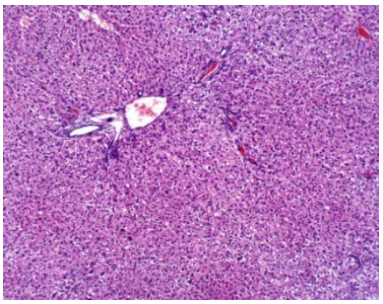
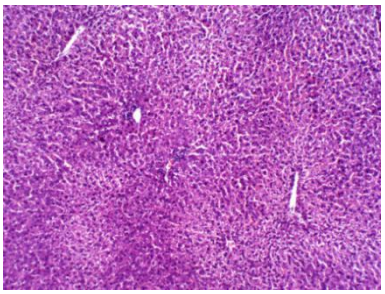


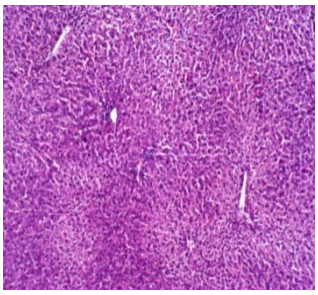
RFD



10.71 mg/kg b.w.



21.42 mg/kg b.w.



42.84 mg/kg b.w.

Fig. 3: Histoarchitecture of the Liver of the control and experimental rats

The histopathological examination of the Liver of control and experimental rats shows liver tissue with preserved architecture, composed of hepatocytes with mild cytoplasmic accumulations (Glycogen accumulation-normal). The portal tract shows mild lymphocytic infiltration in the High-Fat diet group which may be due to the membrane leakage, but there are no features of acute/chronic injury.

Discussion

Africans, especially Nigerians, eat a lot of fatty meats which expose them to risks associated with a high-fat diet. Intake of a high amount of saturated and unsaturated fatty acids have been implicated in the cause of hyperlipidaemia (Varsha *et al.,* 2010) and could be said to be responsible for the induction of hyperlipidaemia in rats (Harikumar *et al.,* 2013).

A high-fat diet prepared with animal fat was rich in saturated and unsaturated fatty acids (Table 5). The crude fat content of the high-fat diet was significantly ($P<0.05$) higher than the control diet (Table 5). Intake of a High-fat diet has been known to induce hyperlipidaemia in previous studies (Monike *et al.,* 2011; Oloyede *et al.,* 2015; Karam *et al.,* 2018). Administration of high-fat diet demonstrated a significant increase in total cholesterol, low- density lipoprotein and triglycerides with a decrease in high-density lipoprotein cholesterol when compared with the control (Table 7).

Kola nuts have been reported to have lipolytic (fat-burning) properties (Arun, 2012; Salawu *et al.,* unpublished 2018). Thus the use of *Cola acuminata* extract at varying concentrations was carried out in this study of the effectiveness of kola nut, in ameliorating high-fat diet-induced hyperlipidaemia. The serum and hepatic lipids of the untreated high-fat diet group were found to be significantly ($P<0.05$) higher than the control and other groups. The serum lipid profile of the extract-treated groups was found not to be significantly ($P<0.05$) different from the control and RFD group, except the 42.84mg/kg bw extract group presented the least values for lipid profile parameters thus, could be assumed to be the most effective dose in ameliorating high-fat diet-induced hyperlipidaemia in the rats. This is consistence with a recent study by Nku *et al.,* (2014) that high consumption of kola nut does reduce the risk of coronary heart disease and another previous research has also shown that chronic administration of kola nut significantly decreased body weight (Hwu and Lin 2010).

Hyperlipidaemia is associated with heart diseases. Coronary heart disease is the leading cause of death in developed countries. This alarming statistic is partly attributable to lifestyle, and partly due to the genetic factors that make humans highly susceptible to atherosclerotic vascular disease. The principal metabolic causes of atherosclerosis include hyperlipidaemia, hypertension, obesity, and diabetes mellitus (Dhandapani, 2007).

The atherogenic index is a direct pointer to exposure to atherosclerosis which is a precursor of all cardiovascular diseases. The high atherogenic index may imply that atherosclerotic plaques have been deposited on the walls of the arteries (Kaushik *et al.,* 2014). These plaques are caused primarily by deposition of low-density lipoproteins (LDL) on the walls of the arteries. They may lead to partial or complete blockage of the flow of blood in the arteries (Harikumar *et al.,* 2013). The result of this study showed that the atherogenic index (AI) of the HFD untreated group was significantly ($P<0.05$) higher than the control and other groups which means that there is high probability that atherosclerotic plaque has started forming in the arterial walls of the rats of which prolonged exposure to the high-fat diet may later result to atherosclerosis. In contrast, the AI of the extract-treated groups reduced but not to the level of the reference drug (atorvastatin) (Table 8). However, long term treatment with aqueous extract of *Cola acuminata* might give a better result.

Cardiovascular disease (CVD) risk ratio is a reliable marker for predicting the risk of coronary heart diseases like heart attack, myocardial infarction, atherosclerosis, etc. CVDs account for one-third of total deaths around the world, and it is believed that it will turn out to be the leading cause of death and disability World-wide by the year 2020 (Ginghina *et al.,* 2011; Jorgenson *et al.,* 2013). The CVD risk ratio of the HFD untreated group was significantly ($P<0.05$) higher than the control and other groups, suggesting that the chance of developing CVDs is high in the HFD untreated group, agreeing with the report by Wells *et al.* (2007) that the presence of hyperlipidaemia accelerates atherosclerosis and other CVDs. On the other hand, the CVD risk ratio of the extract-treated groups significantly ($P<0.05$) reduced but not to the level of the reference drug. This also implies that long term treatment with the extract may give a better result.

Results from the study indicate the presence of saponins, phenolics, terpenoids, flavonoids, and alkaloid in the aqueous extract seed extract of *Cola acuminata,* which is in agreement with a report by Dewole *et al*., (2013). The concentration of phenolics and flavonoids might have contributed to the reduction of oxidative stress and hence improving the hyperlipidemic activity. Phenolics and flavonoids, as reported by El-Tantawy *et al.,* (205) have the potential for lowering the hyperlipidaemia.

Alaninet aminotransferase and aspartate aminotransferase (ALT and AST) are two closely related enzymes of clinical importance (Huncrantz *et al*., 1986), especially in the assessment of liver and kidney functions. Both enzymes increase in many disorders related to liver damage; hence they have been proven to be sensitive indicators of liver-cell injury (Pratt and Kaplan 2000). ALT is more elevated than AST in various necro-inflammatory conditions of the liver, reflecting its greater efficiency as a liver disease marker (Rosenthal and Haight 1989). The activities of ALT and AST in the serum of the untreated animals (HFD) were found to increase significantly ($P<0.05$) and this may be due to damage to the membranes of the liver leading to leakage of the enzymes out of the liver, and this is consistent with the finding of Oloyede *et al.,* (2015) that high-fat diet formulated with goat fat caused damage to the membranes of heart and liver while the increase in the activity of AST in the reference drug group (RFD) suggests localized system of toxicity of the reference drug (Table 9).

There was also a significant ($P<0.05$) increase in the serum activity of ALP in the untreated group (Table 5), too suggestive of damage to the membranes in the organs of the rats. ALP is a biomarker of the plasma membrane and is widely used in the assessment of liver injury, an increase in serum activity of ALP indicates altered membrane integrity (Saukkonen *et al*., 2006).

Urea is the end product of protein catabolism. Amino acid deamination takes place in the liver which is also the site of the urea cycle where ammonia is converted into urea that is excreted through the urine (Amadi *et al.,* 2012). Urea varies directly with protein intake and inversely with the rate of excretion(Adebayo *et al.,* 2003). The functional capacity of the kidney can be assessed by determining the serum electrolyte, urea, uric acid, and creatinine concentrations. In this study, the serum urea, uric acid and creatinine concentrations of the experimental rats were not significantly ($P<0.05$) different from that of the control. This indicated that the administration of aqueous extract of *Cola acuminata* did not alter glomeruli and tubular functions of the experimental rats. Biu et al. reported *a similar result.,* (2009) who said that *Cola nitida* extract caused no significant changes in the plasma creatinine level and also in consistence with Salawu *et al.,* unpublished (2018), that the administration of aqueous extract of the two varieties of *Cola nitida* did not cause any significant ($P<0.05$) changes in the creatinine and urea levels in the serum.

The level of conjugated and total bilirubin can be used to monitor the excretory function of the liver (Yakubu *et al*., 2003). Increase ($P<0.05$) in total and direct bilirubin concentrations of the untreated group as compared to other groups might be a result of haemolysis of red blood cells. It has been reported that there is a relationship between serum lipids and erythrocyte membrane fragility (Cooper, 1977) and that increasing hyperlipidaemia (Particularly hypertriglyceridaemia) is associated with increased haemolysis. It is, therefore, possible, that increased lipid concentrations alter the composition of the erythrocyte membrane leading to increased fragility of the membrane and subsequent leakage of cellular content such as haemoglobin. It is the breakdown of haemoglobin that produces bilirubin.

Results of the histopathology of the heart of both the experimental and control rats show myocardial tissue composed of a syncytium of cardiac muscle cells and vascular channels. There was no significant hypertrophy, infarction or inflammation seen in the control and other groups except for HFD which shows myocardial tissue with overlying pericardial and coronary artery fat but also presented no significant hypertrophy, infarction or inflammation.

This is suggestive of the fact that prolonged consumption of a High-Fat Diet could cause atherosclerosis which is a risk factor for Coronary Heart Disease.

The histopathological examination of the kidneys of control and experimental rats shows kidney tissues with preserved architecture comprising normal glomeruli tubules with no features of acute or chronic damage. There was no significant difference in the kidney histopathological examination of all groups.

The histopathological examination of the Liver of control and experimental rats shows liver tissue with preserved architecture, composed of hepatocytes with mild cytoplasmic accumulations (Glycogen accumulation-normal). The portal tract shows mild lymphocytic infiltration in the High-Fat diet group, but there are no features of acute/chronic injury. There was no significant difference in the kidney histopathological examination of all groups.

Conclusion

The result of this study shows that a high-fat diet formulated with goat fat was able to induce hyperlipidaemia and caused membrane lipid damage to the liver. *Cola acuminata* extract of varying

concentrations was able to reduce blood lipids to almost normal levels. The histopathological assessment of the heart, kidney, and liver of the experimental and control animals presented no significant changes in the biochemistry of the rats.

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