

Hypolipidemic Activity of Solvents Extracts of *Khaya senegalensis* Stem Bark in Diet Induced Hyperlipidemic Rats

A. J. Alhassan^{1*} I. U. Muhammad¹ M. A. Dangambo¹ A. Idi¹ A.M. Gadanya¹ A. Mohammed²
S.M. Adamu³

1.Department of Biochemistry, Faculty of Basic Science, Bayero University, P.M.B. 3011, Kano, Nigeria

2.Department of Biochemistry, College of Medical Sciences, Abubakar Tafawa Balewa University, Bauchi, Nigeria

3.Pathology Department, National Orthopedic Hospital Dala-Kano

Abstract

Introduction: Hyperlipidemia is a modifiable risk factor of an important killer disease “cardiovascular diseases”, which account for as much mortality as infectious disease, nutritional deficiency and maternal and prenatal disease combined together. **Aim:** To investigate the effect of oral administration of Aqueous-methanol stem bark extract of *Khaya senegalensis* and its solvents (hexane, chloroform and ethyl acetate) extracts on lipid profile of hyperlipidemic rats. **Methodology:** Hyperlipidemia was induced in rats via feeding on high lipid diet (HLD) for 6 weeks. A total of fifty five (55) rats were divided into two phases: For phase one, twenty five (25) rats were placed into five groups (GI - GV) of five rats each. GI served as normal control, GII serves as hyperlipidemic control group, while GIII, GIV and GV were hyperlipidemic and administered with crude extract (E1) at a dose of 250mg/kg, 350mg/kg and 450mg/kg body weight respectively for two weeks. For the second phase, thirty (30) rats were placed into six (6) groups of five (5) rats. GI served as normal control, GII served as hyperlipidemic control group, while GIII, GIV GV and GVI were hyperlipidemic and administered with hexane extract (E2), chloroform extract (E3), ethyl acetate extract (E4) and the residue (E5) at a dose of 250mg/kg body weight respectively for two weeks. The animals from each group were euthanized and serum was collected for analysis lipid profile (Total Cholesterol, LDL-Cholesterol, HDL-Cholesterol and Triglyceride). **Results:** The research found that aqueous methanol extract of *Khaya senegalensis* possess hypolipidemic ability with the ethyl acetate extract showing the highest potency with a significant ($p < 0.01$) decrease in serum total cholesterol, triglyceride and LDL-cholesterol level when compared to hyperlipidemic control. **Conclusion:** The present study demonstrated that the ethyl acetate extract from the crude extract possesses the highest hypolipidemic activity.

Keywords: High lipid diets; hyperlipidemia; lipid profile; *Khaya senegalensis*; sequential extraction.

1. Introduction

Hyperlipidemia is the presence of elevated levels of lipids and/or lipoproteins fractions (LDL-cholesterol, Total cholesterol and Triglyceride) in the blood. Hyperlipidemia is classified into two; familial (also called primary hyperlipidemia) caused by specific genetic abnormalities or acquired (also called secondary hyperlipidemia) when resulting from another underlying disorder that lead to alterations in plasma lipids and lipoprotein metabolism (Chait and Brunzell, 1990). Hyperlipidemia has a diverse and complex etiology consisting of genetic, lifestyle, and environmental factors, It is not a disease but a metabolic derangement that can lead to many diseases, most notably cardiovascular diseases (Durrington, 2003).

Significant ethnic differences exist in the prevalence and types of lipid disorders. While elevated serum Total-cholesterol and LDL-cholesterol are the main concern in Western populations, in other countries hypertriglyceridemia and low HDL-cholesterol are more prevalent (Bell *et al.*, 1997). The escalating trend of obesity, as well as changes in lifestyle and environmental factors have make lipid disorders a global medical and public health threat (Telmo Pereira, 2012). Elevated levels of LDL-cholesterol and lower level of HDL-Cholesterol are regarded as atherogenic (prone to cause atherosclerosis) (Lewington, 2007). This disease process leads to myocardial infraction, stroke and peripheral vascular diseases (Brunzell, 2008). LDL particles are often termed “bad cholesterol” because they have been linked to atheroma formation. On the other hand, high concentration of functional HDL, which can remove cholesterol from cells and atheroma, offer protection and are sometimes referred to colloquially as “good cholesterol”. If these postulations were correct, then lowering blood lipid (Total-cholesterol Triglycerides and LDL-cholesterol) concentration should reduce mortality and morbidity from diseases associated with high lipid concentration, most notably cardiovascular diseases.

Khaya senegalensis A. Juss (Meliaceae) is commonly called the dry zone mahogany or African mahogany. The specific name means ‘of Senegal’, which is where the type specimen was collected and regarded as the most popular medicinal meliaceous plant in African traditional remedies (Danquah *et al.*, 2012). The bitter bark extract have been used as a folk medicine for treatment of diabetes (Kolawole *et al.*, 2012), kidney diseases (El Badwi *et al.*, 2012), jaundice (Muhammad *et al.*, 2015) and malaria (Bickii *et al.*, 2010). The bark extract has been used as an astringent for wounds and used occasionally for tanning because of the rich red color it provides. Roots are applied topically against stomach-ache, oedema and amenorrhoea, young twigs and roots are used as

chewing sticks, and Fruits extracts have been shown to exhibit Antioxidative and hypolipidemic properties (Ijeoma *et al.*, 1997, Kalpana and Pugalendi, 2011).

2. Materials and methods

2.1 Study animals

Fifty (50) male and female albino rats of three to four months weighting 80-120 g were purchased from the department of Biological Science, Bayero University Kano, they were housed in aluminum cages with saw dust at the bottom of the cage at an ambient temperature (temperature 25-30°C, photo period 12 hours natural light and 12 hours dark). The animals had free access to standard palletized grower feed and drinking water. The rats were allowed to acclimatize for one week prior to the experiment. Principle of laboratory animal care (NIH, 1996). Ethical guidelines for investigation of experimental pain in conscious animals were observed during experimentation (Zimmermann, 1983).

2.2 Plant material

Khaya senegalensis stem barks were collected from Bayero University Kano (located in the ancient city of Kano, North West of Nigeria). The plant was identified and authenticated at the Herbarium of Plant Biology Department, Bayero University Kano and was given a voucher number of (BUK/HAN/0116). The stem bark was shade dried and ground to powder.

2.3 Extract preparation

Five hundred gram of the powder was weighed and soaked in two liters of 1:1 distilled water-methanol, the solution was shaken vigorously and left to stand at room temperature for 24 hours. The mixture was filtered by passing through Whatman's Filter No.1. The filtrate thus obtained was concentrated by complete evaporation of solvent using rotary evaporator to yield the crude aqueous-methanol extract labelled E1.

2.3.1 Fractionation of crude extract

The solvent free aqueous-methanol crude extract (50g) was suspended in distilled water (500 mL). The suspension was transferred into a separatory funnel. Then it was extracted successively with equal volume of different organic solvent with increasing polarity viz-a-viz hexane, chloroform and ethyl acetate. The extraction procedure was repeated twice for all solvent for complete extraction and then filtered. The combined extracts were concentrated and evaporated using rotary evaporator and dried under water bath, hexane extract was labelled E2, chloroform extract labelled E3, ethyl acetate extract labelled E4 and the residue labelled E5.

The volume to be administered to animals was calculated according to the method of (Muhammad and Alhassan, 2016).

2.4 Induction of hyperlipidemia

A modified method of Vesselinitch *et al* 1980 was used to induce hyperlipidemia. The rats were exposed to the high lipid diet formulation for a period of six weeks. The diet was formulated by mixing pure cholesterol, palm oil and grower mash feed in a percentage ratio of 2:20:78 by mass.

A total of sixty (60) rats were placed into five (5) groups of twelve (12) rats each. Group one was feed on normal grower mash while the rest were feed on high lipid diet. Body weight gain of rats were recorded weekly. Segregation into hyperlipidemic induced rats was performed based on the weight gained by the rats. Rats with the highest body weight gain (Upper one-third, weight gained >66.67%) were considered to be hyperlipidemic.

2.5 Experimental protocol

The research was divided into two phases. Phase one investigate the effect of the crude extract while phase two investigates the effect of various solvents extracts from the crude extract. For the first phase, Thirty (25) albino rats were placed into six groups of five rats each. Extract was administered to animals for a period of two weeks

Group I: Normal control

Group II: hyperlipidemic control

Group III: hyperlipidemic, administered with crude extract (E1) at a dose of 250 mg/kg.

Group IV: hyperlipidemic, administered with crude extract (E1) at a dose of 350 mg/kg.

Group V: hyperlipidemic, administered with crude extract (E1) at a dose of 450 mg/kg.

At the end of experimental period the animals were euthanized. The blood of each rat was collected into a labelled centrifuge tube and centrifuged to obtain serum for lipid profile analysis.

For the second phase, Thirty five (30) rats were grouped into six (6) groups of five (5) rats each. Extracts was administered to the animals for a period of two weeks, hyperlipidemia was induced using the method describe previously for the crude extract.

Group I: Normal control

Group II: hyperlipidemic control

Group III: hyperlipidemic, administered with 250 mg/kg of hexane extract (E2)

Group IV: hyperlipidemic, administered with 250 mg/kg of chloroform extract (E3)

Group V: hyperlipidemic, administered with 250 mg/kg of ethyl acetate extract (E4)

Group VI: hyperlipidemic, administered with 250 mg/kg of residue after ethyl acetate extraction (E5)

At the end of experimental period, the animals were euthanized. The blood of each rat was collected into a labelled centrifuge tube after which it was centrifuged and the serum obtained for analysis of lipid profile.

2.6 Estimation of Parameters

Serum HDL and LDL-Cholesterol were assayed by the method of Friedwald *et al* (1972), Triglycerides and Total Cholesterol by the method of Trinder (1969). The Artherogenic indices were estimated using lipid profile parameters as described below:

I- Cardio Risk Ratio (CRR) = $TCh / HDL-C$ (Martirosyan *et al.*, 2007).

II- Artherogenic Coefficient (AC) = $(TCh - HDL-C) / HDL-C$ (Brehm *et al.*, 2004).

III- Artherogenic Index of Plasma (AIP) = $\log (TG / HDL-C)$ (Dobiasova *et al.*, 2001).

2.7 Statistical Analysis

Results were expressed as mean \pm standard deviation and analyzed using ANOVA, with p value <0.05 considered significant followed by Tukey's post hoc test. A component of GraphPad Instat3 Software version 3.05 by GraphPadInc was used to analyze the data (GraphPad, 2000).

3. Results

Table 1a shows the percent yield and total yield of *Khaya senegalensis* aqueous methanol extract (crude extract) while Table 1b shows the Percent yield and total yield from sequential extraction of the crude extract using solvents of increasing polarity.

Table 1a: Percent yield and total yield of *Khaya senegalensis* aqueous methanol extract

Plant	Yield (%)	Total yield (g)
Aqueous methanol extract	10.91	54.55

Table 1b: Percent yield and total yield of sequential extraction of the aqueous methanol extract of *Khaya senegalensis* stem bark using solvents of increasing polarity

Solvents	Yield (%)	Total yield (g)
Hexane	6.65	3.325
Chloroform	2.91	1.455
Ethyl acetate	10.82	5.41
Residue	79.62	39.81

Table 2 presents the body weight in gram of rats feed with normal grower mash (G I) and those feed with the high lipid diet (G II- G V). Body weight gain in rats feed with high lipid diet was significantly ($p < 0.05$) higher than weight gain in normal control rats even at week four. At week six, significant increase in body weigh was observed at ($p < 0.01$). While table 3 and 4 present the effect of administration of crude and solvents extract respectively.

Table 2: average weight gain of rats feed on standard feed and high lipid diet for six weeks

Period Groups	Initial weight	One week	Two weeks	Three weeks	four weeks	five weeks	Six weeks
G I	97.00 ± 13.52	100.33 ± 15.50	104.67 ± 15.50	108.33 ± 13.50	111.67 ± 12.58	115.00 ± 11.79	117.67 ± 11.24
G II	105.00 ± 15.00 ^{a,b,c}	118.67 ± 9.01	126.33 ± 10.40	134.67 ± 6.42	143.67 ± 10.01 ^a	150.00 ± 8.54 ^b	162.33 ± 7.50 ^c
G III	100.00 ± 21.79 ^{a,b,c}	115.67 ± 20.40	130.67 ± 16.86	141.67 ± 18.77	155.00 ± 13.22 ^a	166.00 ± 10.58 ^b	184.33 ± 5.85 ^c
G IV	91.66 ± 16.07 ^{a,b,c}	103.00 ± 14.17	114.67 ± 13.50	128.33 ± 10.06	143.00 ± 10.81 ^a	159.00 ± 8.18 ^b	173.00 ± 8.18 ^c
G V	108.33 ± 12.58 ^{a,b,c} _d	120.00 ± 13.52	131.33 ± 15.27	140.67 ± 9.01 ^a	153.33 ± 10.59 ^b	165.00 ± 9.16 ^c	178.33 ± 6.35 ^d

Results are presented as Mean ± standard deviation, (n=12). Value with the same superscripts in a row are significantly (P<0.05) different compared to each other. a, b,c and d: significantly different from initial weight.

Table 3: Effect crude extract (E1) of *Khaya senegalensis* stem bark on body weight of hyperlipidemic rats after one and two weeks of extract administration.

Period Groups	Weight at start of administration	Weight at one week	Weight after two weeks
G I	114.33 ± 6.02 ^a	121.67 ± 3.51	127.67 ± 2.51 ^a
G II	184.33 ± 12.09 ^{a,b}	200.33 ± 10.50 ^a	219.33 ± 5.13 ^b
G III	204.33 ± 6.02	209.33 ± 6.50	212.67 ± 5.03
G IV	174.33 ± 8.14	180.67 ± 6.65	186.33 ± 5.50
G V	183.67 ± 18.03	188.00 ± 17.08	194.00 ± 18.08

Results are presented as Mean ± standard deviation, (n=5). Value with the same superscripts in a column are significantly different compared to each other (P<0.05).

Table 4: Effect of different solvents extract (E2, E3, E4 and E5) on body weight of hyperlipidemic rats after one and two weeks of extract administration.

Period Group	Weight at start of administration	Weight at one week	Weight after two weeks
G I	126.00 ± 7.21	131.67 ± 6.50	138.00 ± 5.29
G II	220.00 ± 13.22	233.67 ± 12.74 ^a	248.67 ± 14.46 ^a
G III	215.00 ± 5.00	229.00 ± 7.00	242.67 ± 6.42
G IV	195.00 ± 15.00	211.00 ± 11.79	225.67 ± 12.01
G V	196.00 ± 11.53	201.00 ± 9.00 ^a	205.67 ± 9.50 ^a
G VI	216.33 ± 5.68	231.00 ± 8.54	246.67 ± 11.06

Results are presented as Mean ± standard deviation, (n=5). Value with the same superscripts in a column are significantly different compared to each other (P<0.05).

Table 5 present the effect of aqueous methanol stem bark extract of *Khaya senegalensis* (E1) on lipid profile (TC, TG, LDL-Chol and HDL-Chol) of hyperlipidemic rats after two weeks of extract administration. The result shows a significant increase ($p < 0.01$) in serum Total Cholesterol, triglyceride and LDL-Cholesterol in hyperlipidemic control group compared to normal control. A non-dose dependent decrease ($p < 0.05$) in total cholesterol, triglyceride and LDL-cholesterol was observed in all test groups (GIII, GIV and GV) compared to hyperlipidemic control. From the table, no significant difference ($p < 0.05$) was observed in HDL-cholesterol between all groups.

Table 5: Effect of crude aqueous-methanol stem bark extract (E1) of *Khaya senegalensis* on lipid profile (HDL-C, LDL-C, TC and TG) of hyperlipidemic rats

parameters groups	TC (mmol/L)	TG(mmol/L)	LDL (mmol/L)	HDL (mmol/L)
G I	3.71± 0.25 ^a	1.46 ± 0.20 ^a	2.00± 0.15 ^a	0.90± 0.08
G II	8.27± 0.79 ^{a,b,c,d}	4.32 ± 0.43 ^{a,b}	4.41± 0.37 ^{a,b,c,d}	1.01± 0.07
G III	4.72± 0.36 ^b	2.23± 0.06 ^b	1.92± 0.10 ^b	1.02± 0.11
G IV	4.75± 0.50 ^c	2.24± 0.22 ^c	1.81± 0.23 ^c	1.14± 0.23
G V	4.63± 0.47 ^d	2.10± 0.10 ^d	1.91± 0.16 ^d	1.12± 0.24

Results are presented as Mean ± standard deviation, (n=5). Value with the same superscripts in a column are significantly different compared to each other ($P < 0.05$). a: significantly different from control group. b,c and d: significantly different from hyperlipidemic group.

Table 6 present the effect of administration of solvents extract from crude aqueous methanol stem bark extract (E1) on lipid profile (TC, TG, LDL-Chol and HDL-Chol) of hyperlipidemic rats. A significant increase ($p < 0.01$) was observed in serum Total Cholesterol, triglyceride and LDL-Cholesterol in hyperlipidemic control group compared to normal control. A significant decrease ($p < 0.01$) in total cholesterol, triglyceride and LDL-cholesterol was observed in in group V (ethyl acetate extract treated group) compared to hyperlipidemic control. A decrease ($p < 0.05$) in triglyceride was also observed in group IV treated with chloroform extract compared to hyperlipidemic control group.

Table 6: Effect of different solvents extract (E2, E3, E4 and E5) of *Khaya senegalensis* stem bark on lipid profile (TC, TG, LDL-C and HDL-C) of hyperlipidemic rats

Parameters Groups	TC (mmol/L)	TG(mmol/L)	LDL (mmol/L)	HDL (mmol/L)
G I	3.75 ± 0.75 ^a	1.78 ± 0.23 ^a	1.89± 0.22 ^a	0.81± 0.17
G II	8.08 ± 0.43 ^{a,b}	4.31 ± 0.23 ^{a,b,c}	4.63± 0.56 ^{a,b}	0.79± 0.10
G III	6.46 ± 1.35	3.68± 0.72	4.53± 1.39	0.63± 0.13
G IV	7.75 ± 0.40	3.00± 0.40 ^b	3.18± 0.32	0.69± 0.10
G V	3.43 ± 0.40 ^b	1.82± 0.17 ^c	1.45± 0.22 ^b	1.03± 0.14
G VI	7.91± 0.24	3.19± 0.46	2.92± 0.12	0.65± 0.05

Results are presented as Mean ± standard deviation, (n=5). Value with the same superscripts in a column are significantly different compared to each other ($P < 0.05$). a: significantly different from control group, b and c: significantly different from hyperlipidemic control.

Table 7 shows the values of atherogenic indices (CRR, AC, and AIP) of rats administered with different doses of crude extract (E1). A significant increase in CRR and AC was observed in hyperlipidemic rats compared to control, on the other hand a significant decrease in CRR and AC was observed between hyperlipidemic control (G II) and test groups (G III, G IV and G V).

Table 7: Artherogenic indices of rats administered with different dosses of crude extract (E1)

Parameters Groups	Cardio Risk Ratio (CRR)	Artherogenic Coefficient (AC)	Artherogenic Index of Plasma (AIP)
G I	4.12± 0.31 ^a	3.12±1.06 ^a	0.61± 0.23
G II	8.18± 1.12 ^{a,b,c,d}	7.18±1.02 ^{a,b,c,d}	0.92± 0.32
G III	4.62± 0.36 ^b	3.62±0.22 ^b	0.66± 0.14
G IV	4.16± 0.22 ^c	3.16±1.17 ^c	0.61± 0.16
G V	4.13± 1.95 ^d	3.13±0.95 ^d	0.62± 0.29

Results are presented as Mean ± standard deviation, (n=5). Values with the same superscripts in a column are significantly different compared to each other (P<0.05). a: significantly different from control group. b,c and d: significantly different from hyperlipidemic group.

Table 8 shows the values of artherogenic indices (CRR, AC, and AIP) of rats administered with different solvents extract from crude extract (E2, E3, E4 and E5). A significant increase in CRR and AC was observed in hyperlipidemic control (G II) and test groups (G III, G IV and GVI) rats compared to control (G I), on the other hand a significant decrease in CRR and AC was observed between hyperlipidemic control (G II) and ethyl acetate extract administered group (G V). No significant difference was observed in the level of AIP between groups.

Table 8: Artherogenic indices of rats administered with different solvents extract (E2, E3, E4 and E5)

Parameters Groups	Cardio Risk Ratio (CRR)	Artherogenic Coefficient (AC)	Artherogenic Index of Plasma (AIP)
G I	4.62± 0.44 ^{a,b,c,d}	3.62 ± 0.34 ^{a,b,c,d}	0.66 ± 0.28
G II	10.22± 0.43 ^{a,e}	9.22 ± 0.23 ^{a,e}	1.00 ± 0.36
G III	10.25 ± 0.10 ^b	9.25 ± 0.93 ^b	1.01 ± 0.41
G IV	11.23 ± 0.40 ^c	10.23 ± 0.30 ^c	1.05 ± 0.36
G V	3.33 ± 0.28 ^e	2.33 ± 0.33 ^e	0.52 ± 0.15
G VI	12.16±0.48 ^d	11.60 ±0.45 ^d	1.08 ±0.31

Results are presented as Mean ± standard deviation, (n=5). Value with the same superscripts in a column are significantly different compared to each other (P<0.05). a,b c and d significantly different from control group, e: significantly different from hyperlipidemic group.

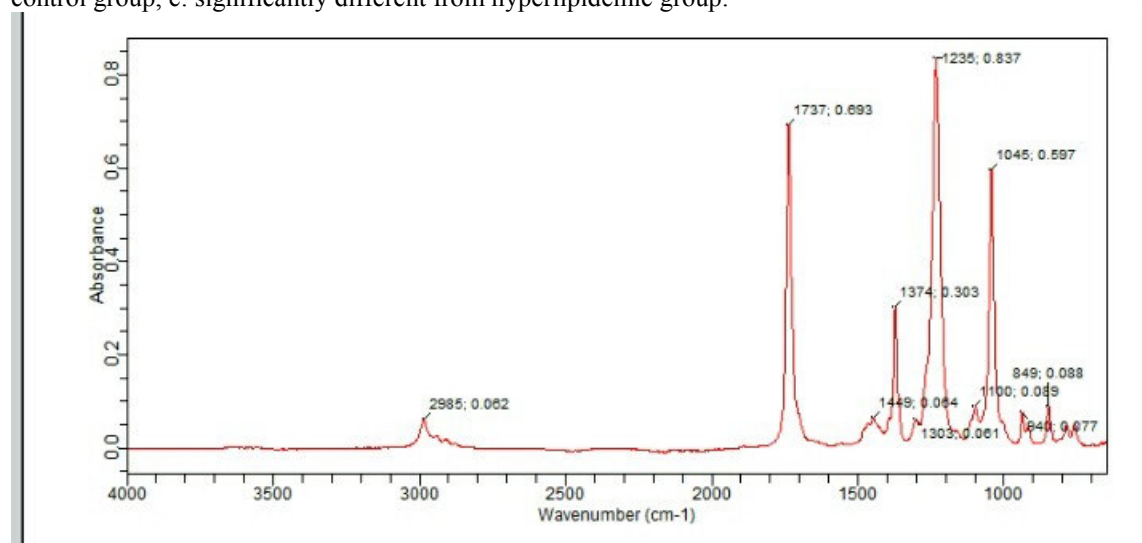


Fig 1: FTIR result showing absorbance of ethyl acetate solvent (E4)

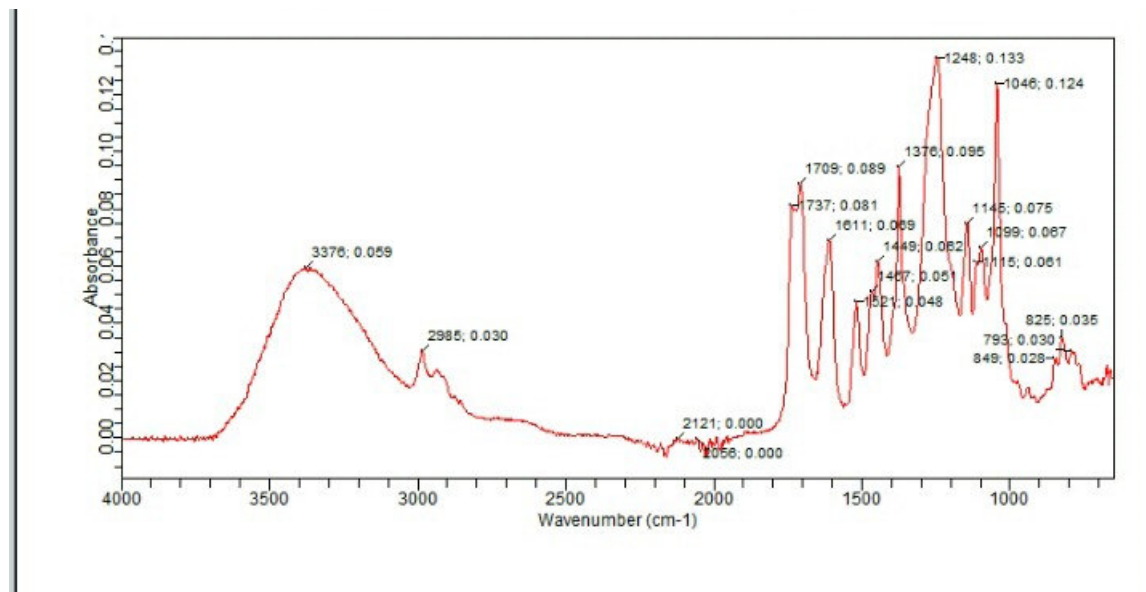


Fig 2: FTIR result showing absorbance of the most potent ethyl acetate extract (E4)

4. Discussion

Body weight gain in hyperlipidemic control rats (Table 2) was significantly ($p < 0.01$) higher than weight gain in normal control rats. This is an indication of successful induction of hyperlipidemia as a result of six weeks feeding on high lipid diet. Significant increase ($p < 0.01$) in serum total cholesterol, triglyceride and LDL-cholesterol of animals fed with high lipid diet was observed when compared to normal control (Table 3 and 4). This is because the intake of high lipid rich food have been positively related to hyperlipidemia and the risk of cardiovascular diseases (Ma *et al.*, 1999). This finding was in line with the findings of Austin 2007 who lamented that hyperlipidemic condition is presented with elevated serum total cholesterol, low density lipoprotein (LDL), very low density lipoprotein (VLDL) cholesterol and reduced high density lipoprotein (HDL) and/or elevated hypertriglyceridemia. Treatment with different concentrations of crude extract E1 (Table 1) reduced weight gain in test groups (G III, G IV and G V) compared to hyperlipidemic control rats (G II). However, significant reduction in weight gain was only observed in ethyl acetate extract treated group (G V) in the second phase of the research. Thus, this might be the reason why *Khaya senegalensis* is used traditionally by obese people to control weight, hence confirming earlier report of the use of *Khaya senegalensis* stem bark extract to regulate body weight gain (Muhammad and Alhassan, 2016).

The effect of oral administration of varying doses of crude extract (E1) on hyperlipidemic rats was shown in table 5. A non-dose dependent anti hyperlipidemic effect was observed. The results for the effects on total cholesterol and triglycerides showed significant decrease in their concentrations in all tests groups treated with the extract for two weeks compared to normal control. Thus it may be suggested that the extract may have affected cholesterol biosynthesis which resulted to reduction in the level of cholesterol in the blood. The low density lipoprotein cholesterol (LDL-Ch.) values obtained like that of cholesterol decreased after two weeks of extract administration. These results are in agreement with the work of 27. Onu *et al.*, 2013 who carried out work on the effect of aqueous stem bark extract of the plant serum lipid levels.

Administration of the solvents extract from sequential fractionation of the crude extract for two weeks shows a significant decrease in serum total cholesterol, triglycerides and LDL-cholesterol only in the ethyl acetate extract treated group (G V), this suggest that the ethyl acetate extract has the highest efficacy and contain the compound(s) responsible for the hypolipidemic activity of the crude extract.

Epidemiologic surveys have shown a continuous linear relationship between cholesterol levels and chronic heart disease events, this was supported by the decrease observed in atherogenic indices of test groups compared to hyperlipidemic control. A similar relationship probably exists relating cholesterol levels to risk of ischaemic stroke (Zhang *et al.*, 2003). A series of trials has been performed to examine whether or not achieving lower levels of LDL-cholesterol translates to increased therapeutic benefit. One recent study have both demonstrated a benefit in lowering LDL-C to levels substantially below 2.0 mmol/L in high-risk patients. A similar conclusion has been reached by the National Cholesterol Education Program who suggested a target LDL-C of 70 mg/dL (1.8 mmol/L) was a very reasonable therapeutic option in very high-risk patients (Grundy *et al.*, 2010).

The atherogenic indices: Cardio Risk Ratio (CRR), Atherogenic Coefficient (AC) and Atherogenic Index of Plasma (AIP) were used to predict the development of Myocardial Infarction (MI) and Ischemic Heart

Disease (IHD). According to Grover *et al.*, 1999, the ratio of LDL-C /HDL-C or TG/HDL-C is a best related predictor of future cardiovascular events, however, TG/HDL-C ratio was shown to be a more accurate predictor of chronic heart disease. The logarithmically transformed ratio of TG /HDL-C correlated closely with the LDL-C particle size and could serve as an indicator of the atherogenic lipoprotein phenotype (Priya *et al.*, 2011).

The Atherogenic Index of plasma (AIP) defined as (TG/HDL-C), has recently been proposed as a marker of atherogenicity because it is increased in people at high risk for chronic heart disease and it is inversely related with LDL-C particles (Meng *et al.*, 2004).

In this research, a significant decrease in CRR and AC was observed between hyperlipidemic control (G II) and test groups (G III, G IV and G V) in the first phase while a significant decrease in CRR, AC and AIP was observed between hyperlipidemic control (G II) and ethyl acetate extract administered group (G V).

FTIR result of the most active ethyl acetate extract revealed the presence of compounds containing carboxylic acids, alcohols and/or phenolic functional groups, with absorbance at 3376cm⁻¹. The exact mechanism of action of this extract on lipid metabolism has not been clarified. One possible mechanism may be *Khaya senegalensis* lowers the plasma and hepatic cholesterol concentrations by suppressing/inhibiting HMG-CoA reductase an enzyme that catalyzes the committed step in cholesterol synthesis (Stensvold *et al.*, 1992). Although phenolics are not similar in structures to statins, they have been shown to inhibit HMG-CoA reductase activity both competitively with HMG-CoA and non-competitively with NADPH (Seenivasan *et al.*, 2011). Another possible mechanism may be through counteracting LDL-cholesterol by promoting the reverse cholesterol transport pathway through inducing an efflux of excess accumulated cellular cholesterol (Assmann and Gotto, 2004). Also, TG lowering effect of the extract may contribute to inhibition of VLDL secretion by the liver and increase VLDL clearance via lipoprotein lipase pathway (Nelson and Cox 2005, Yokozawa *et al.*, 2006).

5. Conclusion

It can be concluded that stem bark extract of *Khaya senegalensis* shows good anti hyperlipidemic action against High lipid diet induced hyperlipidemia, with the ethyl acetate extract possessing the highest hypolipidemic activity. Hence, further studies that aim to isolate the active compound(s) and elucidating the possible mechanism of action(s) of the extract should be encouraged.

References

- Assmann, G. and Gotto, A.M. (2004). HDL cholesterol and protective factors in atherosclerosis. *Circulation*. 109:1118-1148.
- Austin, M. A. (2007). Lipid Profile Automated assays for clinical analyzers to assess the risk of cardiovascular disease. Randox Laboratories Limited, 55 Diamond Road, Crumlin, County Antrim, BT29 4QY, United Kingdom.
- Bell, S.J., Bradley, D., Forse, R.A. and Bistrain, B.R. (1997) the new dietary fats in health and disease. *J. Am. Dietetic Assoc.* 97, 280–286.
- Bickii, J., Njifutie, N., Foyere, J.A., Basco, L.K. and Ringwald, P. (2010). In vitro antimalarial activity of limonoids from *Khaya grandifoliola* C.D.C. (Meliaceae). *J.Ethnopharmacol.* 69: 27–33.
- Brehm, A., Pfeiler, G., Pacini, G., Vierhapper, H. and Roden, M. (2004). Relationship between Serum Lipoprotein Ratios and Insulin Resistance in Obesity. *Clinical Chemistry*. 50: 2316-2322.
- Brunzell, J.D. (2008). Lipoprotein management in patient with cardiometabolic risk. Pubmed. (12): 957-61.
- Chait, A., Brunzell, J.D. (1990). Acquired hyperlipidemia (secondary dyslipoproteinemias). *Endocrinol. Metab. Clin. North Am.* 19(2):259-78.
- Danquah, J.A., Appiah, M. and Pappinen, A. (2012). The effect of African mahogany species on soil chemical properties in degraded dry semideciduous forest ecosystems in Ghana. *International Journal of Agriculture and Biology*. 14:321–328.
- Dobiasova, M. and Frohlich, J. (2001). The plasma parameter log (TG/HDL-C) as an atherogenic index; correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FERHDL). *Clinical Biochemistry*. 34: 583-588.
- Durrington, P. (2003). Dyslipidemia. *Lancet* 362 (9385): 717-731.
- El Badwi, S.M.A., Bakhiet, A.O. and Abdel Gadir, E.H. (2012). Haemato-biochemical effects of aqueous extract of *Khaya senegalensis* stem bark on gentamicin-induced nephrotoxicity in Wister Rats. *Journal of Biological Sciences*. 12:361-366.
- Friedwald, W.T., Levy, R.I. and Fredrickson, D.S. (1972). Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of preparative centrifuge. *Clinical Chemistry*. 18:499-502.
- GraphPad Instat3 Software (2000). Available: www.graphpad.com
- Grover, S.A., Levington, C. and Panquet, S. (1999). Identifying adults at low risk for significant hyperlipidemia:

- a validated clinical index". *Journal of Clinical Epidemiology*. 52: 49-55.
- Grundy, S., Cleeman, J., Merz, C., Brewer, H.J., Clark, L. and Hunninghake, D. (2010). Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation*. 110:227–39.
- Ijeoma, J. U., Idu, M. and Umar, A. H. (1997). Medicinal Plant in use by the Fulani traditional herbalist in Yola North and Yola South L. G. A. of Adamawa State. *Journal of Applied Science*. 1(1): 59 – 63.
- Kalpana, K. and Pugalendi, K.V. (2011). Antioxidative and hypolipidemic efficacy of alcoholic seed extract of *Khaya senegalensis* in streptozotocin diabetic rats. *J. Basic Clin. Physiol. Pharmacol.* 22, 11–21.
- Kolawole, O.T., Kolawole, S.O., Ayankunle, A.A. and Olaniran, O.I. (2012). Anti-hyperglycemic Effect of *Khaya senegalensis* Stem Bark Aqueous Extract in Wistar Rats. *European Journal of Medicinal Plants*. 2(1): 66-73.
- Lewington, S. (2007). Blood cholesterol and vascular mortality by age, sex and blood pressure. *Arm. J clin path* 29:55.
- Ma, A.Z., Ana, B., Henri, G., Paul H. and Jose, A.M. (1999). Alterations in Carbohydrate and Lipid Metabolism Induced by a Diet Rich in Coconut Oil and Cholesterol in a Rat Model. *Journal of the American College of Nutrition*. 18(1): 36–42.
- Martirosyan, D.M., Miroshnichenko, L.A., Kulokawa, S.N., Pogojeva, A.V. and Zoloedov, V.I. (2007). Amaranth oil application for heart disease and hypertension lipid health. *Dis.* 6:1-10.
- Meng, H.T., Don, J. and Bradly, G. (2004). Pioglitazone reduces the atherogenic index of plasma in patient's type 2 diabetes. *Clinical Chemistry*. 50(7): 1184- 1188.
- Muhammad, I. U. and Alhassan, A. J. (2016). Effect of Aqueous Stem Bark Extract of *Khaya senegalensis* (ASBEKS) on Lipid Profile in Diet Induced Hyperlipidemic Rats. *Journal of Advances in Medical and Pharmaceutical Sciences*. 7(3): 1-6.
- Muhammad, I.U., Alhassan, A.J., Wudil, A.M. and Jarumi, I.K. (2015). Toxicological and protective effect of aqueous stem bark extract of *Khaya senegalensis* (ASBEKS) on liver of experimental rat. *British Journal of Applied Science and Technology*. 9(6):600-605.
- Nelson, D.L. and Cox, M.M. (2005). *Lehninger principles of biochemistry*. 4th edition. W.H Freeman and company, New York. 816-820.
- NIH. (1996). Guidelines for the care and use of laboratory animals. National Academic Press, NIH Publication No. 85:23.
- Onu, A., Saidu, Y., Ladan, M.J., Bilbis, L.S., Aleiro, A.A. and Sahabi, M. (2013). Effect of aqueous stem bark extract of *Khaya senegalensis* on some biochemical, haematological and histopathological parameters of rats. *Journal of Toxicology*. 10:803-812.
- Priya, K., Desigamini, K., Kavitha, G. and Rita Mary A. (2011). Coronary Artery Disease. *Journal of Clinical and Diagnostic Research*. 5(3):516-518.
- Seenivasan, A., Panda, T. and Théodore, T. (2011). Characterization, modes of synthesis, and pleiotropic effects of hypocholesterolemic compounds – a review. *Open Enz. Inhibit. J.* 4: 23–32.
- Stensvold, L, Udar, P. and Thurmer, H. (1992). High density lipoprotein cholesterol and coronary, cardiovascular and all-cause mortality among middle age Norwegian men and women. *European Heart Journal*. 13:1155-1163.
- Telmo Pereira (2012). *Dyslipidemia and Cardiovascular Risk: Lipid Ratios as Risk Factors for Cardiovascular Disease, Dyslipidemia - From Prevention to Treatment*, Prof. Roya Kelishadi (Ed.), ISBN: 978-953-307-904-2.
- Trinder P. (1969). Cholesterol enzymatic end point manual. *Ann. Clin. Biochem.* 6:23-28.
- Vesselinitch, D., Wisseler, R.W., Schiffner, T.T. and Borenaztajn, I. (1980). The effect of various diet on atherogenesis in rhesus monkey. *Atherosclerosis*. 35:187-207.
- Yokozawa, T., Cho, E.J. and Sasaki, S. (2006). The protective role of Chinese prescription kangen-karyu extract on diet induced hypercholesterolemia in rats. *Biol. Pharm. Bull.* 29:760-765.
- Zhang, X., Patel, A., Horibe, H., Wu, Z., Barzi, F. and Rodgers, A. (2003). Cholesterol, coronary heart disease and stroke in the Asia Pacific region. *International Journal Epidemiology*. 32:563-72.
- Zimmermann, M. (1983). Ethical guidelines for investigation of experimental pain in conscious animals. *Pain*. 19:109-110.