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ORIGINAL ARTICLE

The Effect of Ivory Coast *Garcinia Kola* Heckel (Guttiferae) Seeds on Hyperlipidemia, Hyperglycemia and Obesity in Wistar Rats

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ABSTRACT

Background: Many studies have reported the beneficial health properties of *Garcinia kola* (*G. kola*) seed from Ivory Coast. This study aimed to investigate the toxicity, anti-hyperlipidemic, and anti-hyperglycemic effect of aqueous extract of *G. kola* (AE*Gk*) seed in rats subjected to the High Fat and Sucrose Diet (HFSD).

Methods: Acute toxicity study was performed according to Organisation for Economic Co-operation and Development (OECD) Guidelines 423. In this study, AE*Gk* was administered starting at 2000 mg/kg and followed by 4000 mg/kg. Rats were observed for toxic signs at 24 h and the next 14 days. For the AE*Gk* effect on hyperlipidemia, hyperglycemia and liver and kidney biochemical markers, animals were divided into five groups. Group I (Control) was fed with a normal diet; Group II, III, IV and V were fed with HFDS and received respectively, 0,9% NaCl, 10 mg/kg statin, and 600 or 1000 mg/kg AE*Gk* daily for four weeks. Finally, histological assessment of liver, kidney and adipose tissue was undertaken.

Results: AE*Gk* at single dose of 4000 mg/kg revealed no lethal effects. Treatment with AE*Gk* significantly decreased hyperlipidemia ($p<0.05$), hyperglycemia and the relative weight of adipose tissue ($p<0.001$ for 1000 mg/kg). Histologically, fat deposits in the liver and kidney damage decreased.

Conclusion: Overall, AE*Gk* was relatively safe in rats at a single dose except for some transient disturbances (4000 mg/kg) and showed some potential in the management of cardiometabolic diseases.

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Introduction

The main goal of food intake is to cover the quantitative and qualitative needs of nutrients to ensure a nutritional balance and a harmonious development of the human (1). Insufficient or excessive intake of macronutrients and micronutrients in the body is believed to be the cause of nutritional pathologies (2). Indeed, in recent decades, the eating habits of the populations of Sub-Saharan Africa, including those in Côte

d'Ivoire, are undergoing considerable changes due to the nutritional transition (3-6). This transition is caused by significant socio-economic development and especially by the intense industrialization of food industries. Modifying these eating habits is characterized by the substantial consumption of foods rich in refined sugar (sodas, cake, candy, etc.), fats, and salt, associated with a strong sedentarization (5). This leads to increased non-communicable diseases (NCDs), in particular diabetes, atherosclerosis, heart disease, liver disease, and dyslipidemia (7).

Many drugs are used to manage diabetes and dyslipidemia, but most have serious adverse effects and are expensive. The populations, therefore, opt for therapeutic alternatives such as *Garcinia kola* Heckel (Guttiferae) seed. *G. kola* phytochemical analysis revealed several chemical compounds, including 9-octadecenoic acid, linoleic acid, 14-methylpentadecanoic acid, 1-butanol, hexadecanamide, glutinol, Garcinia biflavonoid (GB-2a-II-4′-OMe), tirucallol, lupeol, β–amyrin, obtusifoliol and Kolaviron and many micronutrients such as vitamin C, calcium, magnesium, zinc and copper (8-10). A large number of pharmacological studies on several experimental models have confirmed the traditional use of *G. kola* seeds in treating diabetes, dyslipidemia, and liver diseases (11-13). However, few studies have used a nutritional hyperglycemia model induced with High Fat and Sucrose Diet (HFSD). This model is closer to predominant hyperglycemia and obesity in the Ivorian population. The present study was carried out to study the effects of aqueous extract of *G. kola* (AE*Gk*) on hyperlipidemia, glycemia, liver and kidney biomarkers and histological changements in Wistar rats fed HFSD adapted to Ivorian new eating habits.

Materials and Methods

The seeds of *G. kola* (Guttiferae) was collected at Sikensi (Côte d'Ivoire). This plant was authenticated in July 10, 1980, from south of Côte d'Ivoire, by an expert in Botany (Professor Ake-Assi Laurent). A voucher specimen was recorded under No. 10857 and 15189 in the Centre National de Floristique (UFR Biosciences, Félix Houphouët-Boigny University, Abidjan, Côte d'Ivoire). The fresh seeds of *G. kola* Heckel (Guttiferae) were cut into small pieces, dried in ambient air, away from the sun. They were then milled in a micro mill (Culatti® MFC, Allemagne). One hundred grams (100 g) of ground matter were mixed with slow magnetic stirring for 24 hours in one liter of distilled water. The obtained solution was carefully filtered with hydrophilic cotton and «Wattman» filter paper. The filtrate was collected in a flask and then evaporated at 60°C, using a rotary evaporator (Büchi) and oven-dried at 50±5°C. A fine water-soluble powder was provided which represents AE*Gk*.

All animal experiments have been carried out in accordance with EU guidelines (2007/526/CE). They were reproduced in plexiglas cages, at Laboratory of Biology and Health, UPR of Nutrition and Pharmacology, UFR Biosciences, Félix Houphouët-Boigny University. The resulting litters were fed and watered ad libitum to reach a weight between 110 and 120 g under standard environmental conditions, temperature 25°C, with a light-dark cycle of 12 hours. The acute toxicity study was carried out according to OECD Guidelines 423 for testing chemicals (14). Nine healthy female Wistar rats weighing between 130 and 150 grams were enrolled for the study. They were randomly divided into three groups with three female rats per group. The control group received 0.9% NaCl (vehicle), while the experimental groups were treated by gavage with a single dose of AE*Gk* (2000 or 4000 mg/kg) and were observed for 14 days. During the testing period, the body weights of all groups were measured three times per week. Rats were also continuously monitored to detect changes in behavioral patterns such as Changement in physical appearance, symptoms of illness, or mortality.

Twenty-four rats were fed for 16 weeks with HFSD and tap water was added with sucrose. HFSD content was 18% proteins, 36% lipids and 40% carbohydrates per 100 g of dry matter (DM). Six other rats were subjected during the same period to the standard diet (18% proteins; 5% lipids and 65% carbohydrates per 100 g of DM) with tap water and was considered as control (Table 1). During this period, the animals received no pharmacological treatment.

After 16 weeks, rats were randomized to assess the effect of aqueous extract of *G. kola* Heckel (Guttiferea) seeds on HFSD induced dyslipidemia and hyperglycemia in rats (15). Briefly, experiments were carried out with 30 rats, weighing between 250-300 grams, and were randomly divided into 5 groups of 6 rats as follows: Group I (Control) was subjected to standard diet, received only 0.9% NaCl at 2 mL/100g; Group II (HFSD) was exposed to HFSD and received 0.9% NaCl (2 mL/100g; Group III (HFSD+statin 10 mg/kg) was treated with HFSD and received statin (STORVAS®, Inde) at a dose of 10 mg/kg; Groups IV (HFSD+AE*Gk* 600 mg/kg) was subjected to HFSD and received AE*Gk* at a dose of 600 mg/kg; Groups V (HFSD+AE*Gk* 600 mg/kg) was exposed to HFSD and received AE*Gk* at

Table 1: Diet composition.

Components	Control diet+Normal drinking water	HFSD+Sweetened drinking water (300 g of sucrose per 1000 mL of water)
Crude protein (%/100g of DM)	18	18
Crude fat (%/100g of DM)	5	36
Crude carbohydrate (%/100g of DM)	65	40
Corn flour	634	287
Milk powder	100	200
Beef meat powder	100	150
Beef fat	_	200
Sunflower oil	30	50
Sucrose	60	56,90
Agar agar	5	5
Vitaminic mix	0,1	0,1
Mineral mix	1	1
Total (g)	1000	1000
Energy (Kcal/kg of DM)	3032	4048

Cow's milk powder: whole cow's milk containing 28% fat; Kcal/kg of DM: kilocalorie per kilogram of dry matter; Vitamin and mineral mixture (AMIN'TOTAL®), 150 g (LAPROVET, France): Vit A (10 M IU), Vit D3 (3 M IU), Vit E (2500 mg), Vit K3 (4000 mg), Vit B1 (5000 mg), Vit B2 (500 mg), Vit B6 (2500 mg), Vit B12 (5 mg), Vit B9 (250 mg),Vit C (2500 mg), Vit PP (2000 mg), Calcium pantothenate (5000 mg), Potassium chloride (15000 mg), Chloride sodium (70,000 mg), Choline chloride (17,500 mg).

a dose of 1000 mg/kg. Treatment was administered orally once a day for 28 days. Body weight of animals was determined every 3 days.

For biochemical analysis, after fasting for 12 h under anesthesia (Ethyl ether, Gifrer®; France), blood samples were collected by retro-orbital puncture in dry Vacutainer® tubes to determine blood glucose levels (weekly) in all groups. Moreover, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), urea and creatinemia were evaluated at the end of observation. The blood was collected, and serum was separated using a centrifuge and analyzed using commercially available biochemical kits, using the spectrophotometer (visible UV, HITACHI® 704R analyzer, Japan). Animals were sacrificed by cervical dislocation for liver, kidney, and adipose tissue collection. Serum lipids, including cholesterol, triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL), were assayed according to the methods of Friedewald *et al.* (16). Creatinine and blood urea nitrogen were analyzed using standard methods. Serum enzymes, ALT and AST were determined following the methods of Karmen (1955) (17) and Knight et Hunter (1968) (18). Blood glucose was measured according to the method of Trinder (1969) and Dingeon *et al.* (1975) (19, 20). The area under the curve is used as a cumulative measure of the drug and is measured in this study with Graph pad Prism software. Areas are calculated using the trapezoid rule. Finally, hepatic lipids were assessed according to the method described by Folch *et al.* (21).

For histological examination, the liver, kidney and adipose tissue (Inguinal and visceral) were collected, fixed in 10% formalin, and embedded in paraffin. Standard sections of 5 μm thickness were cut and stained with hematoxylin and eosin (H&E). The slides were examined by light microscopy.
Data were presented as mean±standard error of the mean of six experiments (mean±SEM). GraphPad Prism 7 software (Microsoft, San Diego, California, USA) was used for statistical data analysis and graphical representations. The significance of differences between treatments was determined using the variance analysis (ANOVA) of the Tukey-Kramer multiple comparison test. The difference was considered statistically significant when $p<0.05$.

Results

AE*Gk* at a dose of 2000 mg/kg did not induce any toxic effects on behavioral responses in rats. However, at a dose of 4000 mg/kg, AE*Gk* caused the stretching and isolation of the treated rats after 30 minutes and a reduction in food after one hour (Table 2). There was no change in body weight after 14 days. Body weight increased gradually in control group fed by the standard diet and decreased in HFSD rats. Treatments with AE*Gk* at the dose of 600 mg/kg reduced significantly the observed weight loss compared to thoses of dyslipidemic (HFSD) untreated rats. ($p<0.05$; Figure 1). Treatments with statin (10 mg/kg) and AE*Gk* (1000 mg/kg) failed to increase body weight when compared with dyslipidemic (HFSD) untreated rats

Table 2: Acute toxicity of AE*Gk* administered per os to female Wistar rats.

Observation Period	30 to 60 minutes			24 hours			14 Days		
				Distilled water or *AEGk* doses (mg/kg of B. W.)					
Toxic symptoms mortality	**Control**	**2000**	**4000**	**Control**	**2000**	**4000**	**Control**	**2000**	**4000**
Cotortion/Isolation	No	No	**Yes**	No	No	No	No	No	No
Salivation/Diarrhea	No	No	No	No	No	No	No	No	No
Bleeding	No	No	No	No	No	No	No	No	No
Feeding perturbation	No	No	**Yes**	No	No	No	No	No	No
Body weight variation	No	No	No	No	No	No	No	No	No
Mortality	No	No	No	No	No	No	No	No	No

No: Absence of toxic symptoms or mortality; Yes: Presence of toxic symptoms or mortality.

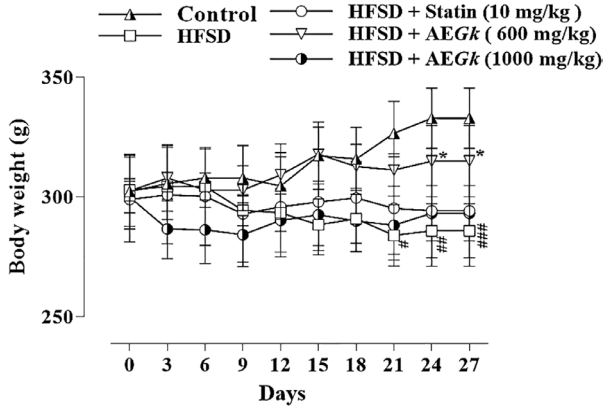

Figure 1: Effect of AE*Gk* on body weight in wistar rat fed with HFSD. Data were shown as mean±standard error of the mean (SEM) of 6 rats per group; #p<0.05, ##p<0.01, or ###p<0.001 versus control group; *p<0.05 versus HFSD group. Abbreviations: AE*Gk*: Aqueous extract of Garcinia kola; HFSD: High fat and sucrose diet.

(p>0.05, Figure 1).

At the end of the observations, the abnormalities in the relative weights of the liver, kidney and adipose tissue improved in different groups of treated rats. Treatment with AE*Gk* at a dose of 1000 mg/kg appeared to be more effective in improving this parameters with an increase (2.30±0.09 *versus* 3.52±0.37%) in relative liver weight in treated HFSD rats (p<0.01, Table 3). As for the relative weight of the kidney, treatment with AE*Gk* at a dose of 1000 mg/kg has increased significantly (0.46±0.01 *versus* 0.72±0.01%) in HFSD rats (p<0.01, Table 3). Treatment with statins (10 mg/kg) did not affect the relative weight of adipose tissue in HFSD rats (p>0.05; Table 3). In rats treated with AE*Gk* at a dose of 600 or 1000 mg/kg, the relative weight of adipose decreased as 4.03±0.15 at 3.10±0.10 and 2.23±0.11, respectively (p<0.01, p<0.0001, Table 3).

HFSD has induced a significant increasing effect on serum triglyceride level (0.59±0.04 to 0.95±0.03 g/L, p<0.05), total cholesterol (0.57±0.03 to 1.01±0.06 g/L, p<0.05), LDL cholesterol (0.12±0.03 to 0.57±0.06 g/L, p<0.0001) and a significant decreasing impact on HDL cholesterol level (0.38±0.08 to 0.27±0.04 g/L) when compared to control rats fed with normal diet (p<0.05). At day 28th of treatment measures, the most effective effects were obtained with the dose of AE*Gk* of 1000 mg/kg. It significantly lowered the serum triglyceridemia level (0.95±0.03 to 0.69±0.09 g/L), total cholesterolemia (1.01±0.06 to 0.66±0.05 g/L) and LDL cholesterol (0.57±0.06 to 0.18±0.04 g/L) in dyslipidemic rats (p<0.0001). However, a significant increase was noticed in serum HDL-C of 0.27±0.04 at 0.32±0.09 g/L (p<0.05; Table 4).

In HFSD rats, serum glucose concentration significantly increased (0.75±0.02 *versus* 1.28±0.05 g/L) when compared to control group rats (p<0.001, Figure 2 A). In addition, the AUC significantly increased in HFSD rats in comparison to that of the rats of the control group (22.53±1.32 *versus* 34.76±1.41 g/L. 28 d, p<0.001, Figure 2 B). Treatment of AE*Gk* (600 or 1000 mg/kg) were significantly enhanced with antihyperglycemic effects after 14 days of observation when treated with HFSD (0.92±0.01 *versus* 1.28±0.05 g/L and 0.90±0.02 *versus* 1.28±0.05 g/L, p<0.01; Figure 2 A).

At the end of the treatments (28 days), AE*Gk* (600 or 1000 mg/kg) induced a decrease in hyperglycemia in HFSD rats at 0.81±0.07 and 0.57±0.03 g/L, respectivly for rats treated with AE*Gk* of 600 or 1000 mg/kg (p<0.001). AE*Gk* (600 or 1000 mg/kg) had antihyperglycemic activity, greater than that of the statin (10 mg/kg). The analysis of the AUC relative to blood sugar confirmed the efficacy of AE*Gk* in hyperglycemia of HFSD rats (Figure 2B). Treatment with AE*Gk* (600 and 1000 mg/kg) resulted in a reduction of this parameter of treated HFSD rats (26.34±1.98 *versus* 34.76±1.41 g/L.28d and 26.42±1.98 *versus* 34.76±1.41 g/L.28d) (p<0.05, Figure 2B). As for the statin (10 mg/kg), it induced a decrease in AUC in HFSD rats, however this variation remained insignificant (p>0.05, Figure 2B).

Rats subjected to HFSD showed a 19%, 41%, and 80% increase in their initial serum AST, creatinine and urea, respectively when compared to those of control group rats (P<0.05; Figure 3A, 3C, 3D). Treatment with AE*Gk* (1000 mg/kg) reduced

Table 3: Effect of AE*Gk* on the relative weight of organs in Wistar rats fed with HFSD.

Group	Adipose tissue (%)	Kidney (%)	Liver (%)
Control	3.06±0.13	0.63±0.02	3.19±0.05
HFSD	4.03±0.1^{5}#	0.46±0.0^{1}#	2.30±0.0^{9}#
HFSD+Statin (10 mg/kg)	4.00±0.42	0.49±0.09	2.99±0.09
HFSD+AE*Gk* (600 mg/kg)	3.10±0.1^{0}**	0.57±0.02	2.54±0.10
HFSD+AE*Gk* (1000 mg/kg)	2.23±0.1^{1}****	0.72±0.0^{1}**	3.52±0.3^{7}**

Data were shown as mean±standard error of the mean (SEM) of 6 rats per group; #p<0.05 versus control group; **p<0.01; ***p<0.001 or ****p<0.0001 versus HFSD group. Abbreviations: AEGk: Aqueous extract of Garcinia kola; HFSD: High fat and sucrose diet.

Table 4: Effect of AE*Gk* on lipid profiles in Wistar rats feed with HFSD

Group	TG (g/L)	TC (g/L)	HDL-C (g/L)	LDL-C (g/L)
Control	0.59±0.04	0.57±0.03	0.38±0.08	0.12±0.03
HFSD	0.95±0.03$^{\#}$	1.01±0.06$^{\#}$	0.27±0.04$^{\#}$	0.57±0.06$^{\#\#\#\#}$
HFSD+Statin (10 mg/kg)	0.81±0.12	0.65±0.02*	0.32±0.09*	0.32±0.02**
HFSD+AE*Gk* (600 mg/kg)	0.86±0.08	0.86±0.05	0.30±0.02	0.38±0.02*
HFSD+AE*Gk* (1000 mg/kg)	0.69±0.09*	0.66±0.05*	0.32±0.09*	0.18±0.04****

Data were shown as mean±standard error of the mean (SEM) of 6 rats per group; #p<0.05 or ####p<0.0001 *versus* control group; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 *versus* HFSD group. Abbreviations: AEGk: Aqueous extract of *Garcinia kola*; HFSD: High fat and sucrose diet. TG: Triglyceride, TC: Total cholesterol, HDL-C: HDL cholesterol, LDL-C: LDL cholesterol.

significantly the serum AST level to approximately 19% in treated HFSD rats when compared to those of untreated HFDS rats. AST level was respectively 172.5±1.33 UI/L, 205.8±1.28 UI/L and 166.1±6.43 UI/L in control group rats, untreated HFDS rats and AE*Gk* 1000 mg/kg treated rats, respectively (p<0.05). But, treatment with statin (10 mg/kg) or AE*Gk* (600 mg/kg) failed to decrease this variable when compared to HFSD untreated rats (p>0.05, Figure 3A). The untreated HFSD rats showed unchanged serum ALT concentration and treatments with AE*Gk* (600 or 1000 mg/kg) and statin (10 mg/kg) did not affect this parameter (p>0.05, Figure 3B).

The HFSD diet caused a significant increase in serum creatinine (41%) and urea (80%) of rats compared to those of control group (p<0.05; Figure 3C, 3D). Administration of AE*Gk* (1000 mg/kg) demonstrated a significant reduction in serum creatinine and urea levels (p<0.05, Figure 3C). For instance, serum creatinine level was respectively, 4.5±0.22 mg/L, 6.33±0.21 mg/L and 4.67±0.21 mg/L in control rats, untreated HFDS animals and AE*Gk* (1000 mg/kg) treated ones (p<0.05).

After the induction, the HFSD diet caused a significant increase in the rate of hepatic lipids in rats (p<0.05). Thus, this parameter was modified from 2.5±0.22% for rats in the control group to 3.5±0.15% in untreated HFSD rats and an increase about 40% of the hepatic lipid level wwas noted (p<0.05). Treatment with statin (10 mg/kg) or with AE*Gk* (600 or1000 mg/kg) induced a significant reduction in the level of hepatic lipids in the HFSD rats (p<0.001, p<0.05). Hepatic lipid went from 3.5±0.15% to 2.0±0.36% and to 2.5±0.11%, respectively, after

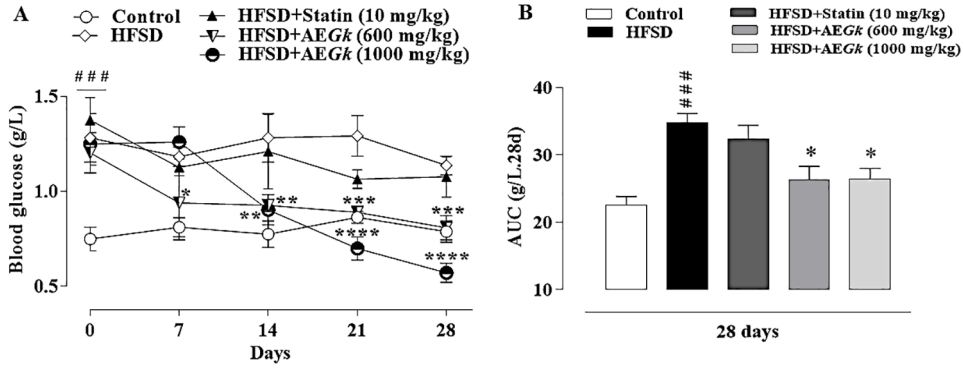

Figure 2: Effect of AE*Gk* on Blood glucose (A) and AUC (B) in Wistar rats subjected to high fat and sucrose diet. Data were shown as mean±standard error of the mean (SEM) of 6 rats per group; ###p<0.001, *versus* control group; *p<0.05 or **p<0.01 *versus* HFSD group. Abbreviations: AE*Gk*: Aqueous extract of *Garcinia kola*; HFSD: High fat and sucrose diet; 28d: 28 days.

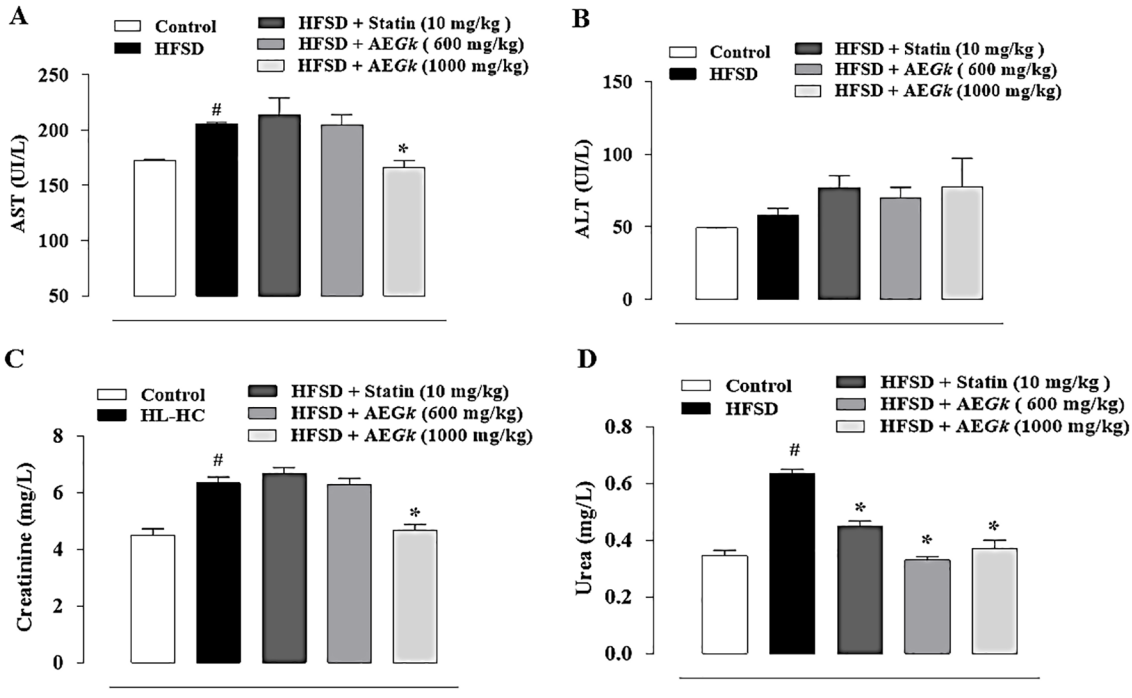

Figure 3: Effect of AE*Gk* serum AST (A), ALT (B), creatinine (C) and urea (D) in wistar rats fed with high fat and sucrose diet. Data were shown as mean±standard error of the mean (SEM) of 6 rats per group; #p<0.05 *versus* control group; *p<0.05 *versus* HFSD group. Abbreviations: AE*Gk*: Aqueous extract of *Garcinia kola*; HFSD: High fat and sucrose diet.

administration of the statin (10 mg/kg) or AE*Gk* (1000 mg/kg).

The histopathological examination of liver and adipose tissue of the control fed with standard diet displayed a normal cell architecture. While HFSD rat group illustrated a significant morphological change in numerous prominent fat deposits in hepatocytes and adipocytes together with renal tissue disorganization when compared to control rats. On the other hand, treatment with statin (10 mg/kg) or AE*Gk* (600 and 1000 mg/kg) reduced the fat accumulation in liver and adipose tissue significantly in HFSD rats after a period of 28 days (Figure 4).

Discussion

This study was designed to investigate the effect of different doses of aqueous extract of AE*Gk* on metabolic dysfunctions such as dyslipidemia and hyperglycemia induced by HFSD in Wistar rats. The acute oral toxicity study of AE*Gk* at the single dose of 2000 mg/kg in female rats did not cause a change in behavior or mortality. However, AE*Gk* at 4000 mg/kg resulted in a temporary stretching and isolation of the treated rats and a reduction in food after one hour without any leading mortality. Therefore, AE*Gk* would not be toxic according to the OECD Global Harmonized Classification System and is classified in category 5 with an LD50 greater than 5000 mg/kg (14, 22).

Kim *et al.* (23) and Malafaia *et al.* (24) highlighted significant gains in weight of rats on HFSD diet compared to those fed on the standard diet. Thus, the increase in body mass associated with the consumption of this diet was the result of these components. However, a significant increase in adipose tissue and fat deposits was reported and remained a standard indicator of adverse effects associated with this diet (23, 25, 26). Also, Ji *et al.* (27) showed that HFSD caused non-alcoholic fatty liver disease (NASH) after 12 weeks of experiments in dyslipidemic rats. The weight loss could be explained by a probable NASH, given the fatty infiltrations observed in the liver. Hepatobiliary pathologies caused an increase in muscle myostatin which would stimulate the activity of the autophagic protein 1A/1B microtubule-associated light chain 3 (LC3). On the other hand, it would modulate the Akt and mTOR proteins involved in the regulation of protein synthesis. These different mechanisms would lead to skeletal muscle atrophy leading to weight loss (28).

AE*Gk* (600 and 1000 mg/kg) and statin (10 mg/kg) reduced liver lipid levels in HFDS rats. Indeed, in rats subjected to HFSD diet, respectively, with quercetin (50 mg/kg)), berberine (50 mg/kg), or o-coumaric acid (75 mg/kg) for six weeks, a significant reduction in hepatic lipids notably triglycerides and total cholesterol was observed (29). Likewise, the administration of *Camellia sinensis* tea extract, at a rate of 0.6 mg/kg, promoted lowering of cholesterol and hepatic triglycerides without any change in total hepatic lipids in the rats subjected

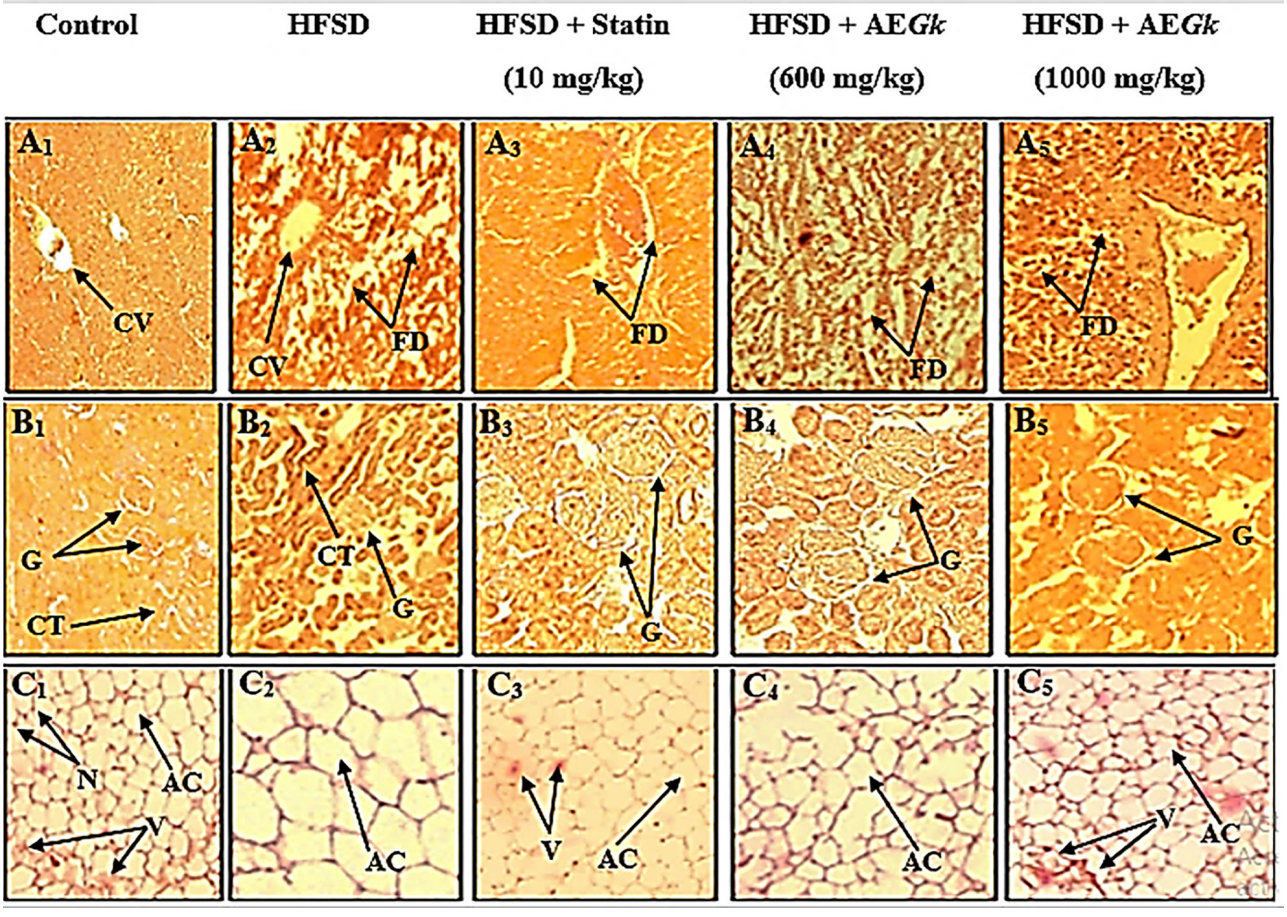

Figure 4: Histopathology examinations of the liver (A) kidney (B) and adipose tissue (C). Section of Wistar rats subjected to high fat and sucrose diet, treated with statin or AE*Gk* for 28 days. Sections stained with H&E; Magnification: 40×; AE*Gk*: Aqueous extract of *Garcinia kola*; HFSD: High fat and sucrose diet. Normal control (A_1; B_1; C_1); HFSD (A_2; B_2; C_2); statin (10 mg/kg) (A_3; B_3; C_3); AE*Gk* (600 mg/kg) (A_4; B_4; C_4) ; AE*Gk* (1000 mg/kg) (A_5; B_5; C_5). Abbreviations: CV: Central vein; CT: Convoluted tube; FD: Fat deposition ; N: Nucleus; AC: Adipose cell; G: Glomerulus; V: Blood vessels.

to the same diet (30). The strong expression of Cyp7a1 (Cholesterol 7α hydroxylase) and Abcg5 (ATP binding cassette g5), two genes involved in excretion of cholesterol in the form of bile, were believed to be responsible for the reduction of hepatic lipid levels (31). Thus, the results of this study indicated a possible modulation of hepatic lipogenesis by AE*Gk* via the stimulation excretion of cholesterol in the form of bile through these genes. In addition, the stimulation of lecithin cholesterol acyltransferase (LCAT) had an important role in the reverse transport of cholesterol from peripheral tissues to the liver for excretion via bile (32). Besides, treatment of HFSD rats with AE*Gk* (600 or 1000 mg/kg) for 28 days resulted in a decrease in blood sugar. These data clearly indicated that AE*Gk* would have antihyperglycemic properties. Similar effects were reported by Chen *et al.* (10), Idris *et al.* (33) and Seke *et al.* Too (34). Indeed, several secondary metabolites such as polyphenols and saponosides mimicked the effects of oral anti-diabetics by closing K^+/ATP channels, membrane depolarization, and stimulation of Ca^{2+} influx, that is the first key step for insulin secretion (35).

The significant increase in creatinine and urea levels in hyperglycemic rats could cause renal damage (36). The improvement of these markers' activities after treatment with AE*Gk* could be due to antioxidant bioactive substances like polyphenols in this medicinal plant (11). Li *et al.* (35) and Morand and Milenkovic (37) showed that antioxidants could have hepatoprotective and nephroprotective effects and could restore the functional status of the liver and kidney.

AE*Gk* (600 or 1000 mg/kg) reduced adipocyte hypertrophy in Wistar rats fed on diet rich in fats. The anti-obesity properties of the genus Garcinia have already been reported. The natural compound in fruits, such as 1,2 dihydroxypropane -1,2,3-acid tricarboxylic, is known for its anti-obesity properties (38, 39). Histopathologically, this study has shown that treatments with AE*Gk* (600 or 1000 mg/kg) had protective effects on the liver, associated with possible anti-adipogenic activity (40). Indeed, for all these organs, tissue remodeling is observed and reduced lipid infiltration. Likewise,

inhibition of proliferation and adipocyte hypertrophy were observed. Treatments improved structural abnormalities induced by the HFSD after 28 days of AE*Gk* treatment. Many authors reported similar effects (9, 11, 12). These pharmacological effects seem to be correlated with the presence of many natural compounds in the *G. kola* extract, such as polyphenols (9, 12). This work showed that *G. kola* could be a potential candidate for preventing dyslipidemia and hyperglycemia induced by HFSD adapted to new Ivorian eating habits due to the nutritional transition. This diet must be improved to better pathological approach models to be more specific to this phenomenon.

Conclusion

This study indicated that AE*Gk* was not toxic in acute oral administration. It induced an antihyperglycemic and possible hypoglycemic effects after 28 days in HFSD rats with an important adipose tissue weight reduction. These properties would help a reduction in cardiovascular risks and in the treatment of obesity.

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Conflict of Interest

None declared.

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