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**CF Nyangono Beyegue, RM Chakokam Ngangoum, D Kuate, JL Ngondi, J Enyong Oben**

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# Effect of *Guibourtia tessmannii* extracts on blood lipids and oxidative stress markers in triton WR 1339 and high fat diet induced hyperlipidemic rats

**CF Nyangono Beyegue[1], RM Chakokam Ngangoum[1], D Kuate[1,2], JL Ngondi[1]*, J Enyong Oben[1]**
[1]Department of Biochemistry, P.O. Box 812, University of Yaounde 1, Yaounde, Cameroon.
[2]Department of Biochemistry, P.O. Box 67, University of Dschang, Dschang, Cameroon.

***Corresponding Author:** ngondijudithl@hotmail.com

**Abstract**
The present study evaluated the effect of aqueous and hydroethanolic extracts of *Guibourtia tessmannii* on blood lipids and oxidative stress markers in both triton (WR-1339) and high fat diet induced hyperlipidemic rat models. Results revealed that treatment of tritonized hyperlipidemic rats with *G.tessmannii* extracts at dose of 200 mg/kg BW resulted in a significant reduction in total cholesterol (TC), triglyceride (TG) and lipid peroxide (MDA) levels ($p<0.05$). In high fat diet induced hyperlipidemic rats model, feeding with the atherogenic diet for 30 days significantly increased the plasma levels of TG, TC, LDL-C, LDL/HDL, TC/HDL ratios, as well as a significant elevation of lipid peroxide levels in both plasma and liver. Co-administration of the *G.tessmannii* extracts at dose of 200 mg/kg BW along with a high fat diet reversed these changes. These beneficial effects could be attributed to the antioxidant activities of bioactive ingredients in both extracts.

**Keywords:** Rats; *G.tessmannii*; hyperlipidemia; oxidative stress; blood lipids.

## Introduction

Coronary heart disease resulting from progressive atherosclerosis, remains the most common cause of morbidity and mortality all over the world (Yusuf *et al*., 2001). Hyperlipidemia has been ranked as one of the greatest risk factors contributing to the prevalence and severity of coronary heart diseases (Gopichandchinta *et al*., 2009). Hyperlipidemia is characterized by elevated serum total cholesterol and low density and very low-density lipoprotein cholesterol and decreased high-density lipoprotein levels. Hyperlipidemia associated lipid disorders are considered to cause atherosclerotic cardiovascular disease (Edijala *et al*., 2005).Several studies demonstrated that hyperlipidemia is associated with oxidative stress due to the overproduction of oxygen free radicals (Rehman *et al*., 2003; Giao *et al.,* 2008). However, the innate antioxidant defense system cannot significantly reduce oxidative stress and this can be an important mediator of progressive damage to cell structures. Consequently, to prevent or treat atherosclerosis and reduce the incidence of cardiovascular disease is to target the hyperlipidemia by diet restriction and or lipid lowering drugs such as statins. Statins, a class of cholesterol lowering drugs which act by inhibiting cholesterol synthesis have been widely prescribed for treating hypercholesterolemia and reducing cardiovascular diseases (Sweetman, 2009). However, statins therapy is associated with adverse effects such as liver damages (Parra and Reddy, 2003), myopathy (Kiortsis *et al*., 2007) and potential drug-drug interaction (Trifiro, 2006). Therefore, there is an urgent need to have a drug with a dual property of lowering lipid level and increasing antioxidant activities. Bioactive components with hypolipidemic and free radical-scavenging activities have received much attention as potential, nontoxic alternative.

The present study was undertaken to evaluate the hypolipidemic and antioxidant activities of aqueous and hydroethanolic extracts of *Guibourtia tessmannii* stem bark (Caesalpinoidae) commonly used in traditional medicine of Central Africa for many purposes in Triton WR 1339 and high fat diet induced hyperlipidemic rat models.

## Materials and Methods

*(a) Collection and identification of plant material*

Leaves and barks were collected in Mbalmayo and identified at National Herbarium under the reference number N° 1037/HNC. The barks were dried in drying room and ground into uniform powder.

*(i) Preparation of aqueous extract*

The stem barks powder was boiled in distilled water (1:8) for 15min. After boiling, mixture was cooled and filtered through Whatman #2

filter paper (Whatman International Limited, Kent, England) using a funnel and concentrated to about 10% of the original volume by a rotary evaporator before drying in the oven at 50°C for 72h. The extracts obtained were stored at room temperature.

*(ii) Preparation of hydroethanolic extract*
The stem barks powder was dissolved in distilled alcohol/water solution (1:1) reagent. After homogenization, mixture was macerated during 48h at room temperature and filtered using Whatman #2 filter paper using a funnel and concentrated to about 10% of the original volume by a rotary evaporator before drying in the oven at 50°C before evaporation to oven (50°C) for 72h.

*(b) In vitro experiments*

*(i) Phytochemical analysis*
The presence of saponins, tannins, alkaloids, flavonoids, anthraquinones, glycosides and reducing sugars in the extract was tested for using simple and standard qualitative methods earlier described by Trease and Evans (1989).

*(ii) Determination of polyphenol concentrations*
The amount of total phenolic content of both extracts was determined according to the procedure of Singleton and Rossi, (1965) with some modification, using 1 mL of Folin-Ciocalteu's phenol reagent 0.2 N and 30 µL to develop a pigment whose absorbance was determined at 750 nm. The results were expressed as catechin equivalent.

*iii) Ferric Reducing Antioxidant Power (FRAP)*
The ferric reducing activity of the plant extracts was estimated based on the Ferric Reducing Ability of Plasma (FRAP) assay developed by (Benzie and Strain, 1996). The assay was performed as followed: 2000 µL of freshly prepared FRAP reagent was mixed with 75 µL of sample, water or hydroalcoholic solvent as appropriate for reagent blank. The absorbance was read at 593 nm using Spectronic Genesys 20 (Thermo Electron Corporation) after 30 min of incubation. The results were expressed as catechin and ascorbic acid equivalent respectively.

*iv) Free radical scavenging activity on α,α-diphenyl-β-picrylhydrazyl (DPPH)*
The antioxidant activity of *Guibourtia tessmanni* extracts was measured in terms of hydrogen donating or radical scavenging ability, using the stable radical, DPPH method (Katalinie *et al*., 2003). A solution (20µL) of the sample extracts was added to 1000 µL of DPPH solution. The decrease in absorbance at 517 nm was determined continuously every minute with a Spectronic Genesys 20 (Thermo Electron Corporation). The percentage of DPPH inhibition was calculated as follows. DPPH Scavenging Effect (%) = $((A_0 - A_1)/(A_0)100)$, where $A_0$ was the absorbance of the DPPH solution control and $A_1$ was the absorbance in the presence of the sample DPPH assay.

*(c) In vivo experiments*

*(i) Preparation of diet*
The following two types of diets were prepared.
*Normal diet:* The standard diet consists of flour (5 kg), chokar (5 kg), salt (75 g), nutrivet L (33 g), molasses (150 g), potassium meta bisulphate (15 g), fish meal (2.25 kg), powdered milk (2 kg) and oil (500 g) for a total of about 15 kg of the food material.
*Atherogenic diet:* Cholesterol (2% w/w), cholic acid (0.5% w/w) and butter fat (5% w/w) were added to normal diet, as described by (Dhandapani, 2007) with slight modification.

*(ii) Experimental design*
Two main experiments were conducted as follows: *Triton WR 1339-induced model of hyperlipidemia*: The tyloxapol-induced hyperlipidemic model earlier described by (Yu *et al*., 2002) with slight modifications. Male Wistar rats weighing 200-220 g were caged in uniform hygienic conditions with standard pellet diet and water provided *ad libitum*. After 5 days of acclimatization, twelve-hour fasted animals were randomly divided into 4 groups of 5 rats: group 1 (negative control); group 2, the tritonized group (positive control); and groups 3 and 4 (receiving 200 mg/kg BW of aqueous extract or hydroethanolic extracts respectively). Rats in groups 2 to 4 received a single intravenous injection of triton WR 1339 (tyloxapol) (850 mg/kg; .iv.) while rats in negative control group received an injection of saline solution 9‰ through the same route. Rats were given food and water one hour after injection of triton WR 1339. On the next day, the animals in groups 3 and 4 were treated with *Guibourtia tessmannii* extracts 3 times per day during a one-day experimental period. At the end of treatment, rats were sacrificed by decapitation under anesthesia with diethyl ether, after an overnight fasting. Blood and liver were collected; plasma, erythrocyte hemolysate and liver homogenate were prepared.

*Atherogenic diet-induced model*: The atherogenic diet-induced hyperlipemia model was used as earlier described (Dhandapani, 2007) with slight modifications. The adult Wistar rats (200-250g) were randomly divided into four groups of 5 rats. To the control group was given normal diet (served as normal control), whereas positive control and experimental groups received respectively atherogenic diet and atherogenic diet with oral administration of 200 mg/kg BW of either aqueous or hydroethanolic extracts of *Guibourtia tessmannii*. All groups had free access to water and diet. The diet consumption was monitored daily and the gain in body weight was monitored weekly. At the end of the treatment, 12 hours fasted rats were sacrificed by decapitation under anesthesia. Blood was collected for plasma and erythrocytes hemolysate preparation and stored at –20°C until assay. The heart, liver and kidney were collected, carefully washed and rinsed with ice-cold saline (0.9% NaCl) for the preparation of homogenate as described above.

*d) Biochemical analysis*

*i) Measurement of lipid profile parameters*

Total cholesterol, total triglycerides and total HDL were estimated using standard kits of Chronolab. Low Density Lipoprotein Cholesterol (LDL-C) concentration was calculated by using formula of (Friedwald *et al*., 1972) using the following equation: LDL-Cholesterol = Total cholesterol - (HDL-c + TG/5). The Atherogenic Index was calculated using the formula of Abbot *et al*. (1988), and Coronary Risk Index (CRI) was obtained by the method of Alladi*et al*. (1989).

*Atherogenic Index* (AI) was calculated using the LDL-c/HDL-c ratio.

*Coronary Risk Index* (CRI) was calculated using the total cholesterol/HDL-c ratio.

*ii) Evaluation of oxidative stress markers*

*Lipid peroxidation:* Lipid peroxidation was estimated as lipid hydroperoxides according to the method of Jiang *et al*. (1992) and thiobarbituric reactive substance (TBARS) by measuring the pink colored chromophore formed by the reaction of thiobarbituric acid with malondialdehyde (MDA) according to the method of Yagi (1976).

*Proteins thiols:* the proteins thiols content was estimated (Ellmann, 1959). This method was based on the development of a yellow color when DTNB was added to compounds containing sulfhydryl groups.

*Total protein:*Total protein was performed by Lowry's method (Lowry *et al*., 1954)

*Catalase (CAT)*: Activity of catalase was assayed (Sinha, 1972) using hydrogen peroxide as substrate. The activity is expressed in U/g protein. The CAT unit (UCAT) is defined as the enzyme concentration required decomposing 1 mmol of hydrogen peroxide in min.

*iii) Liver and kidney functions*

Plasma aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT) activities were estimated using colorimetric methods (Reitmann and Frankel, 1957) in order to evaluate the liver function. The creatinine level in plasma was also estimated (Bartels *et al*., 1972) in order to evaluate the kidney function.

*e) Statistical analysis*

Results were expressed as mean ± standard error mean. Statistical analysis was carried out using SPSS 10.1 for Windows. 1–factor ANOVA followed by LSD and Tamhane post hoc were used to evaluate antioxidant activity. On the other hand, Kolmogorov test was used to evaluate hypolipidemic activity comparing two groups.

## Results

*Total polyphenolic content and in-vitro antioxidant activity*

The hydroethanolic extract of *Guibourtia tessmannii* showed a higher polyphenolic content (70.45±12.62 vs 56.98±9.35 (mg Eq catechin/g of dry extract) as well as the DPPH radical scavenging activity (94.58± vs 77.73±) compare to the aqueous extract (Table 1).

**Table 1: Antioxidant activity of *Guibourtia tessmannii*.**

| Different extracts | Antioxidant capacity (mg Eqcatechin/g of dry extract) | Phenol contents (mg Eqcatechin/g of dry extract) | DPPH• radicals scavenging activity (%) |
|---|---|---|---|
| Aqueous | 2.21±0.005[a] | 56.98±9.35[a] | 77.73±2.027[a] |
| Hydroalcoholic | 2.28±0.001[b] | 70.45±12.62[b] | 94.58±0.564[b] |

Different letters mean p<0.05

*Effect of Guibourtia tessmannii extracts on blood lipids and oxidative stress markers in triton WR-1339 induced hyperlipidemic rats*

Administration of tyloxapol (triton WR-1339) caused a significant increase ($p<0.05$) in plasma total cholesterol and triglyceride of tritonized group as compared to animals in the control group. Subsequent treatment with *Guibourtia tessmannii* extracts at dose of 200 mg/kg BW to the rats caused a significant reduction in cholesterol and triglyceride levels (Table 2). The intravenous injection of triton WR1339 significantly increased plasma level of malondialdehyde and decreases the level of protein thiols in untreated tritonized rats compared to negative control. In general, treatment has improved the level of these markers (Table 2). Intravenous injection of triton WR 1339 also significantly decreased the erythrocytic catalase activity in control compared to normal. The treatment with 200 mg/kg BW of aqueous extract of *Guibourtia tessmannii* significantly increased catalase activity (Table 2).

**Table 2: Effect of *G. tessmannii* extracts on blood lipids and oxidative stress in triton WR 1339 induced hyperlipidemic rats.**

| Parameters | | Control | Untreated tritonized rats | Tritonized rats treated with 200 mg/kg of AE | Tritonized rats treated with 200 mg/kg of HEE |
|---|---|---|---|---|---|
| Total cholesterol (mg/dl) | | 67.00±12.72 | 222.00±31.35*[a] | 312.00±96.22[a] | 179.25±39.51[a] |
| Triglycerides (mg/dl) | | 46.25±20.74 | 2221.75±282.95*[a] | 2020.25±1168.43[a] | 1915.25±330.32[ab] |
| TBARS (µmol/l) | Plasma | 6.93±0.75 | 12.53±0.52 *[a] | 9.80±1.50[b] | 6.83±0.23[bc] |
| | Liver | 3.94±0,6 | 8.94±1.10 *[a] | 2.12±0.05[b] | 6.40±0.40[a] |
| | Heart | 2.53±0.18 | 5.59±0.66*[a] | 6.32±1.01[a] | 2.72±0.07[b] |
| | Kidney | 3.21±0.11 | 7.29±0.33 *[a] | 4.08±0.34[bc] | 6.10±0.24[b] |
| | Liver | 2.28±0.19 | 1.16±0.21*[a] | 1.31±0.26[a] | 0.79±0.06[a] |
| Plasma proteins thiols (µmol/g proteins) | | 1.86±0.15 | 0.80±0.04*[a] | 1.32±0.44[a] | 1.88±0.17[b] |
| Liver proteins thiols (µmol/g proteins) | | 2.28±0.19 | 1.16±0.21*[a] | 1.31±0.26[a] | 0.79±0.06[a] |
| Erythrocyte catalase activity (U/g protein) | | 130.00±9.00 | 32.00±6.00*[a] | 248.00±15.20[b] | 16.00±5.00[c] |

*= $p<0.05$ significant between control and untreated tritonized rats.
Different letters ($p<0.05$).

*Effect of Guibourtia tessmannii extracts on blood lipids and oxidative stress markers in rats fed atherogenic diet*

Oral administration of *Guibourtia tessmannii* extracts at dose of 200 mg/kg with an atherogenic diet for 30 days prevented the elevation of plasma total cholesterol, triglycerides LDL-C, TC/HDL and LDL/HDL ratio. The two extracts prevented the rise in total cholesterol level by 14.59 – 19.41%. We also noticed a decrease in LDL cholesterol level upon treatment with both extracts (Table 3). As shown in Tables 3, the biochemical index of tissue lipid peroxidation was assessed in terms of MDA formation. As compared with negative control group, the hyperlipidemic rats showed a significant elevation in the level of MDA and significantly depletion in the non-enzymatic antioxidant system (proteins thiols). The data in Table 3 reveals that co-administration of *Guibourtia tessmannii* extracts with atherogenic diet for 30 days significantly protect the liver and heart tissues from oxidative stress as evidence from the maintenance of lipid peroxidation marker (MDA) near normal levels, and significant increase in thiol protein levels in plasma.

**Table 3: Preventive effect of *G. tessmannii* on blood lipids and oxidative stress markers in atherogenic diet fed rats.**

| Groups | | Control | Rats fed atherogenic diet | Rats fed atherogenic diet treated with 200 mg/kg of AE | Rats fed atherogenic diet treated with 200 mg/kg of HEE |
|---|---|---|---|---|---|
| % of change in body weight | | 2,42 | 6,39 | 5,80 | -3,71 |
| Total cholesterol (mg/dl) | | 147,63±3,61 | 201,71±10,16$^{*a}$ | 162,54±5,34$^{b}$ | 161,32±6,88$^{abc}$ |
| Triglycerides (mg/dl) | | 39,350±2,71 | 63,15±5,90$^{*a}$ | 80,39±2,20$^{b}$ | 71,17±2,08$^{a}$ |
| HDL-C (mg/dl) | | 109,38±0,59 | 131,44±3,50$^{*a}$ | 130,52±1,770$^{a}$ | 138,09±4,011$^{a}$ |
| LDL-C (mg/dl) | | 30,38±3,48 | 57,64±13,25$^{a}$ | 26,21±1,94$^{a}$ | 30,00±2,38$^{a}$ |
| AI | | 0,276±0,031 | 0,46±0,112$^{a}$ | 0,202±0,016$^{a}$ | 0,222±0,021$^{a}$ |
| CRI | | 1,348±0,029 | 1,563±0,105$^{a}$ | 1,250±0,046$^{a}$ | 1,173±0,050$^{bc}$ |
| TBARS (µmol/l) | Plasma | 3,69±0,132 | 6,82±0,228$^{*a}$ | 3,532±0,296$^{b}$ | 3,426±0,375$^{b}$ |
| | Liver | 8,55±0,553 | 12,92±0,599$^{*a}$ | 12,321±0,325$^{a}$ | 3,09±0,031$^{b}$ |
| | Heart | 7,63±0,286 | 8,99±0,353$^{*a}$ | 5,968±0,118$^{b}$ | 6,459±0,916$^{b}$ |
| | Kidney | 7,16±0,316 | 5,38±0,142$^{*a}$ | 4,078±0,343$^{bc}$ | 6,104±0,243$^{b}$ |
| Plasma proteins thiols (µmol/g proteins) | | 0,098±0,006 | 0,058±0,008$^{*a}$ | 0,195±0,033$^{b}$ | 0,122±0,0008$^{bc}$ |
| Liver proteins thiols (µmol/g proteins) | | 2,28±0,190 | 1,160±0,217$^{a}$ | 1,313±0,268$^{a}$ | 0,788±0,067$^{a}$ |
| Erythrocytes catalase activity (U/g protein) | | 0,06±0,01 | 0,05±0,01*$^{a}$ | 0,46±0,20$^{b}$ | 0,05±0,01$^{a}$ |

Values shown are mean ± SEM (n=5)
*= p<0.05 significant between control and untreated rats fed atherogenic diet
Different letters (p<0.05)

*Effect of Guibourtia tessmannii extracts on liver and kidney functions*

As shown in Table 4, the intravenous injection of triton has significantly increased (p<0.05) transaminases activity and creatinine level in control compared to normal. However, treatment improved transaminase activities but has no effect on creatinine and protein levels (Table 4).

Results in Table 4 also revealed that untreated rats fed with atherogenic diet (positive control group) had significant increases in plasma levels of ASAT, ALAT and creatinine as compared to the normal control. Treatment with *Guibourtia tessmannii* extracts lead to a significant reduction in transaminases activity as well as creatinine level.

**Table 4: Effect of treatment on plasma ASAT, ALAT and creatinine level in triton WR 1339 induced hyperlipidemic rats and those fed with atherogenic diet.**

| | Liver function | | | Kidney function |
|---|---|---|---|---|
| | **Groups** | **ASAT (Ue/ml)** | **ALAT(Ue/ml)** | **Creatinine (mg/dl)** |
| Normal rats | Control | 25.42±3.53$^{+}$ | 20.34±1.87$^{+}$ | 3,06±0,50$^{+}$ |
| Triton WR 1339 induced hyperlipidemic rats | Untreated | 280.41±81.96$^{a}$ | 224.43±70.05$^{a}$ | 17,08±1,25$^{a}$ |
| | 200 mg/kg of EA | 60.90±12.95$^{b}$ | 39.94±7.54$^{b}$ | 21,97±5,26$^{a}$ |
| | 200 mg/kg of HEE | 174.93±46.82$^{a}$ | 210.51±5.81$^{a}$ | 89,38±11,75$^{b}$ |
| | | | | |
| Normal rats | Control | 46,041±0,918* | 63,92±0,20* | 1,023±0,004* |
| Rats fed atherogenic diet | Untreated | 126,94±0,974$^{a}$ | 70,11±1,56$^{a}$ | 2,99±0,323$^{a}$ |
| | 200 mg/kg of EA | 41,041±5,115$^{bc}$ | 37,95±5,21$^{b}$ | 0,771±0,052$^{b}$ |
| | 200 mg/kg of HEE | 40,48±0,149$^{bc}$ | 36,59±0,05$^{b}$ | 0,94±0,014$^{b}$ |

Values shown are mean ± SEM of five separate observations (n=5)
*= p<0.05 significant between control and untreated rats fed atherogenic diet
$^{+}$P<0.05 significant between control and untreated tritonized rats

## Discussion

Several epidemiological studies concluded that a high intake of food rich in natural antioxidants increases the antioxidant capacity of the body and reduces the risk of several diseases. Herbal remedies or food supplements have increasingly become attractive alternatives to prevent or treat

hypercholesterolemia, especially for those with cholesterol at the borderline levels (Deng, 2009). *Guibourtia tessmannii* has been considered useful in neurodegenerative diseases such as hypertension, atherosclerosis and malaria. In this study we screened the in vitro antioxidant potential and evaluate the effect of *Guibourtia tessmannii* on oxidative stress and blood lipid makers using two animal models of hyperlipidemia. Results obtained showed that *Guibourtia tessmannii extracts* have considerable amounts of polyphenolic compounds which are groups of secondary metabolites with broad range of biological properties such as: antioxidant, anti-inflammation, anti-artherosclerosis, cardiovascular protection, improvement of the endothelial function, as well as inhibition of angiogenesis and cell proliferation activity (Han *et al.,* 2007;Rice-Evans, 1996) it has been reported that antioxidant activity of the phenolic compounds is mainly due to their redox properties which allow them to act as reducing agents, hydrogen donors play an important role by adsorbing and neutralizing reactive free radicals, and chelating ferric ions which catalyses lipid peroxidation, and regarded as promising therapeutic agent for free radical-linked pathologies (Said and Zeinab, 2009).

In vivo experiments were conducted in two rat's models of hyperlipidemia. In the first model, we used Tyloxapol which is a non-anionic detergent of polymeric structure that has been successfully used in several studies to induce hypercholesterolemia (Kourounakis*et al*., 2002; Perez *et al*., 1999). The experimental protocol was designed according to conclusion of the study of Bertges*et al*. (2010) which showed that induction of hypercholesterolemia by Tyloxapol has shown to be effective in Wistar rats within 72 hours of application of the drug, after that period the results may not reflect the action of cholesterol-lowering agents using this model. Based on the suggestions, injection of Tyloxapol to Wistar rats causes a drastic increase in plasma triglycerides levels and a moderate hypercholesterolemia probably due to elevated hepatic cholesterol synthesis particularly by the increase in HMG Co-A (3-hydroxy-3-methyl-glutaryl Co-A) activity and by the inhibition of lipoprotein lipase responsible for hydrolysis of plasma lipids (Schotz and Scanu, 1957). The administration of *Guibourtia tessmannii* extracts one day after induction of hyperlipidemia significantly inhibited the rise in cholesterol level in this model. Knowing that in fasting condition the only source of serum lipid levels is the endogenous production, *Guibourtia tessmannii* extracts may act by inhibiting of cholesterol biosynthesis through inhibition of HMG Co-A, an enzyme which plays a key role in controlling lipid levels in plasma and other tissue. The observed effect may be associated to the presence of bioactive components such as polyphenols, triterpenoids, flavonoids, tannins and saponins, glycosides and cardiac glycosides found in *Guibourtia tessmannii* extract (Nyangono *et al*., 2008;Kaamanen*et al*., 2003; Del Bas *et al*., 2005) which suggest that flavonoids, anthocyanins and antioxidant vitamins present a large variety of pharmacological activities including antioxidant and anti-atherogen activities, thus they would inhibit oxidation of cholesterol. Some of these bioactive compounds like flavonoids have been reported to inhibit lipid biosynthesis (Glasser *et al*., 2002).

In the second model,atherogenic diet induces endothelial dysfunction, atherosclerosis (Hayashi *et al*., 1999) and increases oxidative stress by increasing the levels of oxidative stress markers in plasma and tissues in both models. Feeding rats with the experimental diet for 30 days resulted in the elevation of total cholesterol, LDL-C, atherogenic index and decrease in HDL-C probably by enhancing intestinal absorption and secretion and decreasing catabolism of cholesterol (Heuman *et al*., 1988).

Treatment with *Guibourtia tessmannii* extracts caused a significant decrease in mean serum TC and LDL-C while increasing HDL-C. The plant extracts also caused significant reduction in the atherogenic index, which is considered a better indicator of coronary heart disease risk than individual lipoprotein concentration (Vijayakumar*et al*., 2004). The increase in HDL cholesterol in all treated groups suggests that *Guibourtia tessmannii* mobilizes cholesterol from extra-hepatic tissues where it is catabolized (Soudamini *et al*., 1992) and stimulate cholesterol 7α-hydroxylase which converts cholesterol to bile acids, an important pathway of degradation of cholesterol. Moreover, this increasing of HDL cholesterol is inversely correlated with cardiovascular risk in humans and experimental animals and reduces arteriosclerosis (Oh *et al.*, 2006). The treatment with both extracts reduced the atherogenic index and increased percentage of protection by 55-59%. The atherogenic diet also causes oxidative stress (enzymatic and non-enzymatic) in rats. Jadhav *et al.*(1996) showed that cholesterol oxidation could contribute to the development of a progressive thickening of the artery wall, due to the

accumulation of cholesterol oxidation products in low-density lipoprotein (LDL) particles after they are oxidized. Vijayabaskar *et al.*(2008) proved that the significantly elevated levels of plasma cholesterol in rats fed with atherogenic diet might damage the endothelial cell membrane lining the large arteries such as aorta and might be the initial events in the etiology of atherosclerosis. The high levels of MDA in the group of rats fed atherogenic diet alone is a clear manifestation of the excessive formation of free radicals and progression of the lipid peroxidation. Also the depleted level of proteins thiols may be due to increased utilization to counteract the overproduction of the free radicals. Previous studies reported that hypercholesterolaemia increases cholesterol content of platelets, polymorphonuclear leukocytes and endothelial cells so that endothelial and smooth muscle cells, neutrophils, monocytes and platelets may be the source of oxygen free radicals in hypercholesterolaemia (Kumar *et al.,* 2008; Esterbaeuer *et al.,* 1998). It has been suggested that the resistance of erythrocytes against oxidative stress is reduced during hyperlipidemia (Simon *et al*., 1998). Antioxidants are known to effectively prevent this kind of damage (Kinosian *et al*., 1995). The presence of strong antioxidant activities in *Guibourtia tessmannii* extracts may offer additional benefit in combating the oxidative stress caused by high cholesterol. Based on the evidences of the current results, our study suggested that the health promoting capabilities effects of *Guibourtia tessmannii* extracts in these animal models of hyperlipidemia could be attributed to the high polyphenolic content along with the enhancement of the total antioxidant defense system of body. As preventive antioxidants, *Guibourtia tessmannii* extracts can directly intercept free radical before any significant oxidation can occur. As chain-breaking antioxidant, *Guibourtia tessmannii* extracts can retard or slow the oxidative processes leading to decrease MDA (the lipid peroxidation near normal level and thus inhibit the oxidative stress. Treatment with aqueous extracts of *Guibourtia tessmannii* induced an elevation of antioxidant enzyme activity such as catalase; these extracts could increase hydrolysis of hydrogen peroxide to water by boosting catalyse enzyme.

Results also show that administration of atherogenic diet alone induced a reduction in plasma and liver protein thiols level which is prevented by co-administration of *Guibourtia tessmannii* extracts. Sulfuryl groups of proteins like albumin serve as antioxidants in extravascular spaces. Thiols intervene to reinforce the principal antioxidant system of the body which is glutathione when this antioxidant system is overflowed by oxidative agents. The decrease in thiols in rats fed with atherogenic diet alone reflects their massive utilisation to fight against oxidative agents (Halliwel, 2000).

The significant increase of transaminases activity in positive control animals could reflect hepatic damages. The liver is an organ with diverse functions; hepatoprotective activity of drug would be based on his ability to reduce hepatic damages or preserve architecture and physiological functions of liver after exposure to hepatotoxin. Hepatocytes participate in different metabolic activities via their enzymes. Assy *et al*. (2000) showed that fatty acids infiltration on liver is a condition responsible for cirrhosis and hepatic damages. The improvement of transaminase activities after treatment with both extracts could be due to bioactive substances like flavonoids and glycosides. Hyuncheol *et al.* (2004) and Oshima *et al.* (1995) showed that flavonoids and glycosides of medicinal plants could have hepatoprotective effect. These results showed the ability of extracts of *Guibourtia tessmannii* to restore functional status of liver.

## Conclusion

The results from this study rationalize the medicinal use of *Guibourtia tessmannii* in the management of cardiovascular diseases. Thus it could be used as potential medicine to prevent or slow the progression of atherosclerosis through a reduction in oxidative stress. However, further studies are required to assess the safety and the mechanisms of anti-hyperlipidemic activities.

## Ethical Approval

The study was approved by the Animal Ethics Committee of the Faculty of Sciences, University of Yaounde I, Cameroon.

## Conflict of Interests

Authors have no conflicting interests.

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