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Cardiovascular Disease Risk Factors of Normal Wistar Rats on Prolonged Exposure to Aqueous Stem Bark Extract of Dialium guineense

Abu OD,[1*] Okuo VA,[2] Chukwuma AU,[1] Ohiomah CB,[1] Idehen IO,[1] Etoroma OM,[3] Eze-Nwaobasi OP[1]
[1]Department of Biochemistry, Faculty of Life Sciences, University of Benin, Benin City
[2]Department of Chemistry, College of Arts and Sciences, University of Kentucky
[3]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Benin, Benin City

Correspondence: Abu OD, Faculty of Life Sciences, University of Benin, Benin City, Nigeria; Email osahon.abu@uniben.edu

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Abstract

The use of medicinal plants and their products in health management has gained wide acceptance. However, their usage is limited by the inability to ascertain their potential toxic effect at doses administered and duration. The present study investigated the effect of prolonged exposure of normal Wistar rats to aqueous extract of *Dialium guineense* (AEDG) stem bark on cardiovascular disease risk factors. Male albino rats (Wistar strain, n = 10) weighing between 150 and 180 g (mean weight = 165 ± 15 g) were divided into two groups (5 rats per group): control and observation groups. Rats in the observation group received 1000 mg/kg body weight, bwt, AEDG stem bark orally for twelve weeks, and assays were performed on monthly basis. The results showed that exposure of normal Wistar rats to aqueous extract of *D. guineense* stem bark for a period of twelve weeks (3 months) led to significant and time-dependent increases in their body weight and high-density lipoprotein cholesterol (HDL-C) level ($p < 0.05$), but it did not significantly alter the total protein concentration ($p > 0.05$). In addition, the extract treatment significantly and time-dependently reduced the levels of total cholesterol (TC), triacylglycerol (TG), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), atherogenic index of plasma (AIP), and atherogenic coefficient (AC) ($p < 0.05$). However, the marked reduction in cardiac risk ratio (CRR) was not time-dependent. These results indicate that the medicinal plant stem bark applied over a long period of time can effectively manage disease conditions, which hallmarks are hypercholesterolemia and hypertriglyceridemia.

Keywords: Atherogenic index, Cardiac disease, Lipids, Hypercholesterolemia, Medicinal plant

Introduction

Herbal medicine has gained wide acceptance, globally (Maunder et al., 2020; Negi et al., 2021). The growing interest in the exploitation of plants for medicinal purposes, especially in Africa, has increased tremenduously (Thyagarajan *et al*., 2002). Medicinal plants have proven health benefits (Abu *et al*., 2020, 2021a, 2021b, 2022a and 2022b).

Dialium guineense (Velvet Tamarind) is a tall, tropical, fruit-bearing tree which belongs to the *Leguminosae* family (Abu *et al.,* 2023a). It has small, typically grape-sized edible fruits with brown hard inedible shells. It grows in dense forests in Africa along the southern edge of the Sahel and it can be found in West African countries such as Ghana where it is known as "Yoyi", Sierra Leone, Senegal, Guinea-Bissau and Nigeria where it is known as "*Awin*"or "*Igbaru*" in Yoruba, "*Icheku*" in Igbo, "*Tsamiyarkurm*"in Hausa and "*Amughen"* in Edo (Abu *et al.,* 2023b). The bark and leaves have medicinal properties, and are used against several diseases. Extracts of the plant are reported to be rich in important phytochemicals (Abu *et al.,* 2023c).

As a muscular organ the heart pumps blood through the blood vessels of the circulatory system (Benson *et al*., 2001). Blood provides the animal's body with oxygen/nutrients, and facilitate the removal of metabolic wastes. In humans, it is located in the middle compartment of the chest between the lungs (Guyton and Hall, 2006; Moore *et al*., 2009; Taber and Venes, 2009). The heart is effectively a syncytium, a meshwork of cardiac muscle cells interconnected by contiguous cytoplasmic bridges (Maton *et al*., 1993; DuBose, 1996; MacDonald, 2009). Drug-induced cardiac injury is becoming an increasingly important concern, since it constitutes serious risk to human health (Dessalvi *et al*., 2018). Cardiac dysfunction may lead to heart failure, myocardial ischemia, arrhythmias, hypertension, myocarditis, pericarditis, and thromboembolism (Colombo *et al*., 2013). This study evaluated cardiovascular disease risk factors in normal Wistar rats on prolonged exposure to aqueous stem bark extract of *Dialium guineense.*

Materials and Methods

Chemicals

All chemicals and reagents used in this study were of analytical grade and they were products of Sigma-Aldrich Ltd. (USA).

Collection of Plant Material

The stems of *D. guineense* were collected from Auchi, Edo State, Nigeria, and authenticated at the herbarium of the University of Benin, Nigeria, domiciled in the Department of Plant Biology and Biotechnology (No. UBH_D330).

Extract Preparation

The plant stem bark was washed and shade-dried at room temperature for 30 days and thereafter pulverized. Exactly 500 g of the ground plant material was macerated in distilled water (5 L) with intermittent stirring for 72 h. The resultant extract was filtered with a muslin cloth and consequently freeze-dried via lyophilization (Abu *et al*., 2022a, b, c, d).

Experimental Animals

Male albino rats (Wistar strain, n = 10) weighing between 150 and 180 g (mean weight = 165 ± 15 g) were bought from the Department of Anatomy, University of Benin, Nigeria. The rats were housed in metal cages under standard laboratory conditions (25 ^oC, 60 ± 5 % humidity, and 12-h light/12-h dark cycle). They were acclimatized for fourteen days before commencement of the study, and had free access to feed and water.

Experimental Design

The experimental rats were divided into two groups (5 rats/group): control and observation groups. The observation group rats were administered 1000 mg/kg bwt AEDG stem bark orally for 12 weeks (3 months).

Blood Sample Collection and Preparation

At the end of week-12 of treatment, the rats were euthanized under mild chloroform anaesthesia after an overnight fast. Blood was drawn via cardiac puncture into heparinized sample bottles and centrifuged at 2000 rpm for 10 min to obtain plasma which was used for biochemical analyses.

Biochemical Analyses

Lipid profile and cardiovascular disease risk

were determined in plasma (Friedewald *et al*., 1972; Lopes-Virella *et al*., 1977; Reiser *et al*., 1985; Tietz *et al*., 1990; Frohlich and Dobiášová, 2003; Abu *et al*., 2022c).

Data Analysis

Data are expressed as mean ± standard error of mean (SEM, n = 5). One-Way Analysis of Variance (ANOVA) was performed using SPSS (version 20). Statistical significance was assumed at $p < 0.05$.

Results

Effect of 12-Week Exposure of Normal Rats to Aqueous Extract of *D. guineense* Stem Bark

As shown in Figures 1 – 6, exposure of normal Wistar rats to aqueous extract of *D. guineense* stem bark for a period of twelve weeks (3 months) led to significant and time-dependent increases in their body weight and HDL-C level ($p < 0.05$), but it did not significantly alter the total protein concentration ($p > 0.05$). In addition, the extract treatment significantly and time-dependently reduced the levels of TC, TG, LDL-C, VLDL-C, AIP, and AC ($p < 0.05$). However, the marked reduction in CRR was not time-dependent.

Discussion

Globally, a significant cause of morbidity and mortality are cardiovascular diseases (CVDs). Improper management of risk factors of CVDs can lead to deleterious consequences. Risk factors refer to modifiable biological characteristics (serum lipids, other fractions, blood pressure, blood glucose and insulin, and thrombogenic factors, among others) but can also be applied to behavior, such as smoking or physical inactivity. They are used for two main purposes: detection of individuals and populations at risk of CVD, and determination of the causes of CVD. A risk factor may be useful as a predictor of risk without being casually linked to pathogenic mechanisms. This study evaluated cardiovascular disease risk factors in normal Wistar rats exposed to aqueous stem bark extract of *Dialium guineense* for a prolonged period of 12 weeks (3 months). The results showed that exposure of normal Wistar rats to aqueous extract of *D. guineense* stem bark for a period of twelve weeks led to significant and time-dependent increases in their body weight and HDL-C level, but it did not significantly alter the total protein concentration. In addition, the extract treatment significantly and time-dependently reduced the levels of TC, TG, LDL-C, VLDL-C, AIP, and AC. However, the marked reduction in CRR was not time-dependent. Studies have demonstrated the relationships between lipid profiles and CVD, which include heart attacks and strokes. Elevated levels of conventional lipid indices, such as total cholesterol, low-density lipoprotein cholesterol, and triacylglycerols, are positively correlated with increased risk of CVD incidence, as are decreased levels of high-density lipoprotein cholesterol (Gu *et al*., 2019; Sun *et al.*, 2019). The connections between TC, LDL-C, HDL-C, and the incidence of CVD-related death risk had also been reported (Curb *et al*., 2004; Zhong *et al*., 2020). Because assessment of the correlation between dyslipidemia, CVD events and all-cause mortality using a single lipid score has its drawbacks, some studies proposed that measuring apolipoprotein B (ApoB) should be the first priority in clinical practice, along with lipid ratios and lipoproteins, which contribute additional clinical value (Walldius and Jungner, 2006; Sierra-Johnson *et al.,* 2009). Surprisingly, some studies have revealed that derived lipid indices, such as computed lipid ratio and apolipoproteins, may have a CVD predictive value similar to traditional lipid indices (Yokokawa *et al.,* 2011). The results of this study have further strengthened the observation that extracts of *D. guineense* are effective in ameliorating complications of some diseases (Abu and Onoagbe, 2019; Abu *et al*., 2022e – o; Abu *et al.,* 2023d). The biological/pharmacological effects of plant extracts/plant-derived materials have been linked to the presence of important bioactive compounds (Abu *et al.,* 2015; Abu *et al*., 2017; Ebhohon *et al*., 2019a and 2019b; Okpiabhele *et al*., 2018; Abu *et al*., 2020; Omoregie *et al*., 2020; Abu *et al.,* 2021a and 2021b).

Conclusion

Dialium guineense has been indicated in the treatment of various health ailments in traditional system of medicine. The stem bark extract shows potential for the management of lipid-associated diseases, especially when used for a prolonged duration.

Conflict of Interest

The authors declare no conflicts of interest.

Acknowledgement

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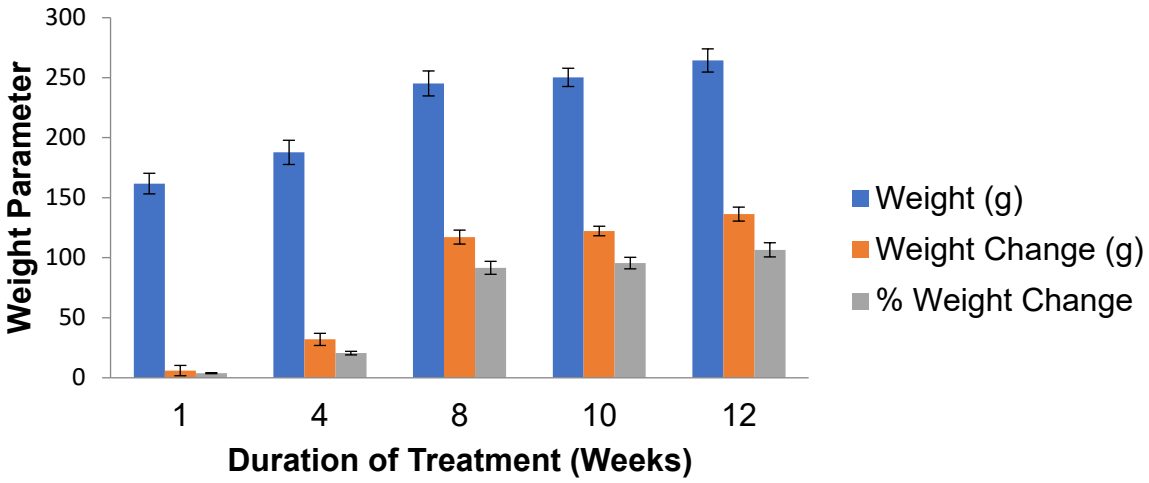

Figure 1: Body Weight of Rat.

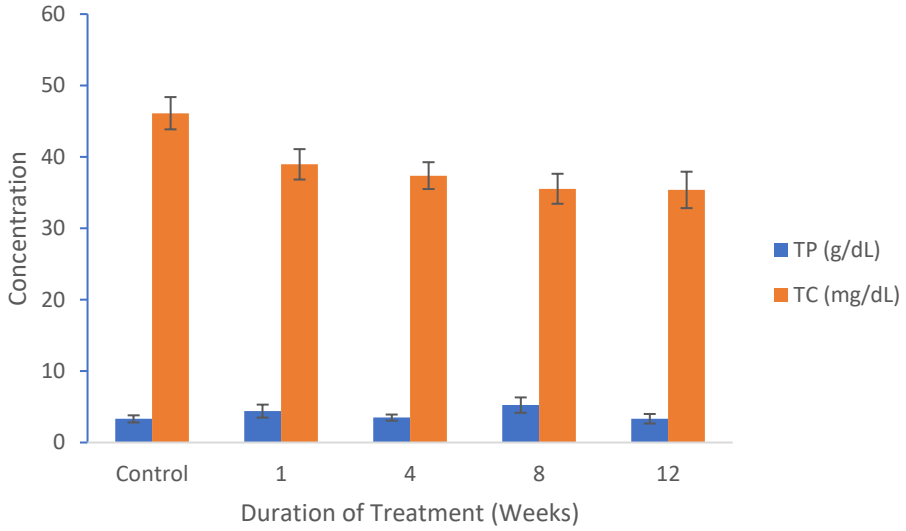

Figure 2: Effect of AEDG Stem Bark on Plasma Total Protein and Cholesterol Concentrations.

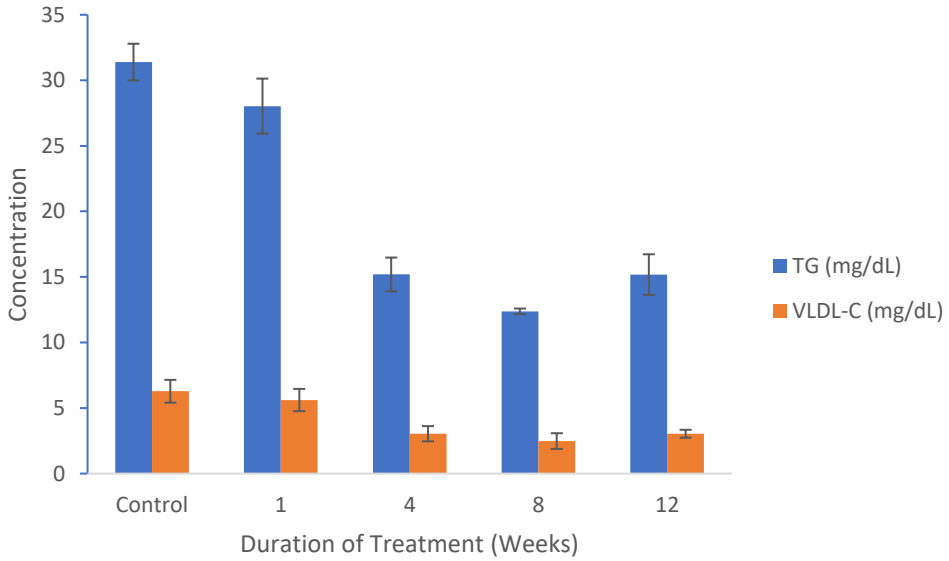

Figure 3: Effect of AEDG Stem Bark on Plasma Triacylglycerol and Very Low-Density Lipoprotein Cholesterol Concentrations.

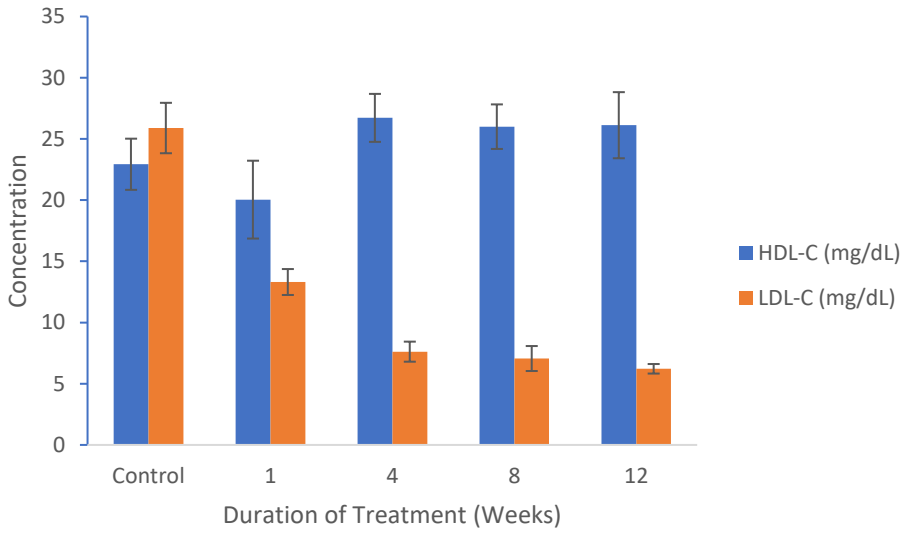

Figure 4: Effect of AEDG Stem Bark on Plasma High-Density Lipoprotein Cholesterol and Low-Density Lipoprotein Cholesterol Concentrations.

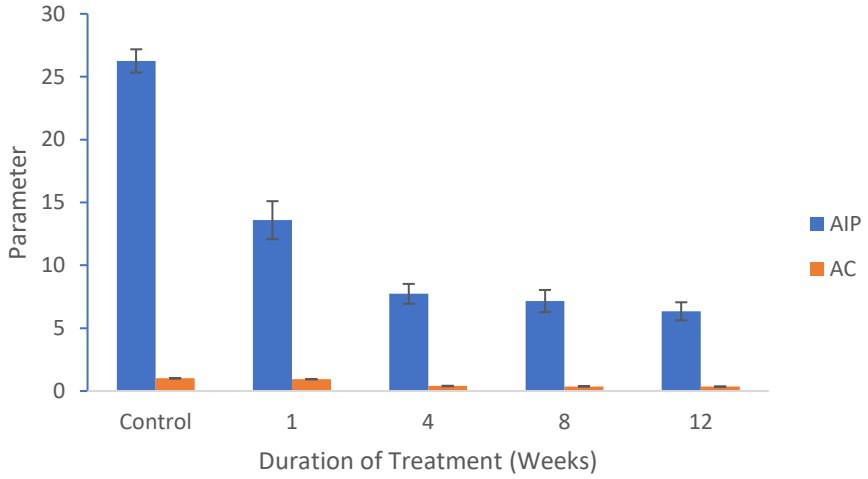

Figure 5: Effect of AEDG Stem Bark on Atherogenic Index of Plasma and Atherogenic Coefficient.

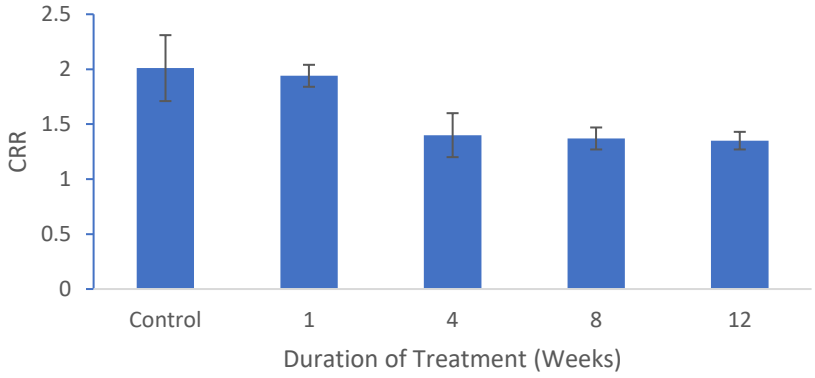

Figure 6: Effect of AEDG Stem Bark on Cardiovascular Disease Risk Ratio in the Rats.

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