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Effect of Methanol Fraction of Ethanol Extract of *Dialium Guineense* Stem Bark on Cardiovascular Disease Risk Factors in Diabetic Rats

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Abstract

As a disease defined by the level of hyperglycemia, diabetes mellitus (DM) causes micro- and macrovascular damage. The present study evaluated the effect of methanol fraction of ethanol extract of Dialium guineense (MEDG) stem bark on cardiovascular disease risk factors in diabetic rats. Male Wistar rats (n = 25, mean weight = 215 ± 15 g) were used. The rats were divided into five groups (5 rats per group): normal control, diabetic control, metformin, MEDG (200 mg/kg body weight, bwt) and MEDG (300 mg/kg bwt) groups. Diabetes mellitus was induced via intraperitoneal injection of streptozotocin (STZ, 50 mg/kg bwt). The diabetic rats were then treated for 21 days with metformin (50 mg/kg bwt) or MEDG (200 and 300 mg/kg bwt, respectively). The results showed that STZ-induced DM significantly increased plasma concentrations of total cholesterol (TC), triacylglycerol (TG), very low-density lipoprotein cholesterol (VLDL-C), low-density lipoprotein cholesterol (LDL-C), atherogenic index of plasma (AIP), atherogenic coefficient (AC) and cardiac risk ratio (CRR), but it significantly reduced high-density lipoprotein cholesterol (HDL-C) ($p < 0.05$). However, treatment of diabetic rats with MEDG stem bark led to significant reductions in circulating levels of lipid profile (except HDL-C, which increased) as well as AIP, AC and CRR ($p < 0.05$). These results suggest that the medicinal plant extract has the capacity to protect against cardiovascular events in diabetic rats induced by STZ.

Keywords: ***Atherogenic coefficient; Cholesterol; Diabetes mellitus; Lipid profile; Streptozotocin.***

1. Introduction

The heart is a muscular organ which pumps blood through the blood vessels of the circulatory system [1]. Blood supplies animal body with oxygen and nutrients, while removing metabolic wastes. In humans, it is located in the middle compartment of the chest between the lungs [2]-[4]. The heart is effectively a syncytium (a meshwork of cardiac muscle cells interconnected by contiguous cytoplasmic bridges) [5]-[7]. Cardiac injury induced by drugs and other chemical

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substances is becoming an increasingly important concern, since it constitutes serious risk to human health [8]. Cardiac dysfunction caused by cardiotoxic agents such as STZ may lead to heart failure, myocardial ischemia, arrhythmias, hypertension, myocarditis, pericarditis, and thromboembolism [9], [10].

Diabetes mellitus (DM) is a major cause of heart disease and stroke. Death rates for heart disease and the risk of stroke are about 2–4 times higher among adults with diabetes than among those without the disease [11]. In DM, macrovascular complications results from damage to large blood vessels and are mainly cardiovascular diseases such as premature atherosclerosis, ischemic heart disease (myocardial infarction) and stroke [12].

It has been asserted that a large population of people in developing countries use herbal medicine for some aspects of their basic health care [13], [14]. Medicinal plants have proven health benefits [15]-[19]. *Dialium guineense* is a medicinal plant used ethno-botanically to treat various ailments [20], [21]. This study investigated the effect of MEDG stem on cardiovascular disease risk factors in diabetic rats.

2. Materials and Methods

2.1 Chemicals

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

2.2 Plant Extraction

Dialium guineense stem barks obtained from Auchi, Edo State, Nigeria, were authenticated at the University of Benin herbarium domiciled in the Department of Plant Biology and Biotechnology, University of Benin, Benin City, Nigeria. The prepared plant specimen was deposited in the herbarium of same department (No. UBHD330).

The plant's stem bark was washed and shade-dried for 4 weeks at room temperature, and thereafter ground into powder using a blender. A portion (500 g) of powdered plant material was steeped in 5,000 mL of absolute ethanol. The resulting extract was filtered through muslin cloth and freeze-dried with a lyophilizer. The ethanol extract was subsequently fractionated with 100% methanol [22]-[27].

2.3 Experimental Animals

Mature male Wistar albino rats (n = 25, mean weight = 215 ± 15 g) were bought from the Department of Anatomy, University of Benin, Nigeria and housed in wooden cages. They were acclimatized for two weeks before commencement of the study, and had free access to feed and water.

2.4 Experimental Design

The rats were divided into five groups (5 rats/group): normal control, diabetic control, metformin, MEDG (200 mg/kg bwt) and MEDG (300 mg/kg bwt) groups. Diabetes mellitus was induced in the rats via intraperitoneal injection of 50

mg/kg bwt STZ. The diabetic rats were then treated with either the standard antidiabetic drug metformin (50 mg/kg bwt) or MEDG (200 and 300 mg/kg bwt, respectively), for 21 days.

2.5 Blood Sample Collection and Preparation

At the end of day 21 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.

2.6 Biochemical Analyses

Lipid profile and cardiovascular disease risk parameters were determined in plasma [28]-[33].

2.7 Data Analysis

Data are presented as mean ± SEM (n = 5). Statistical analysis was performed using SPSS version 21. Statistical differences between means were compared using Duncan multiple range test. Statistical significance was assumed at $p < 0.05$.

3. Results

3.1 Effect of MEDG on Organ Weight

As shown in Fig. 1, induction of DM with STZ significantly reduced the weight of rat heart and the corresponding organ/body weight ratio ($p < 0.05$). However, treatment of the diabetic rats with MEDG markedly increased the heart weight as well as the relative organ weight ($p < 0.05$).

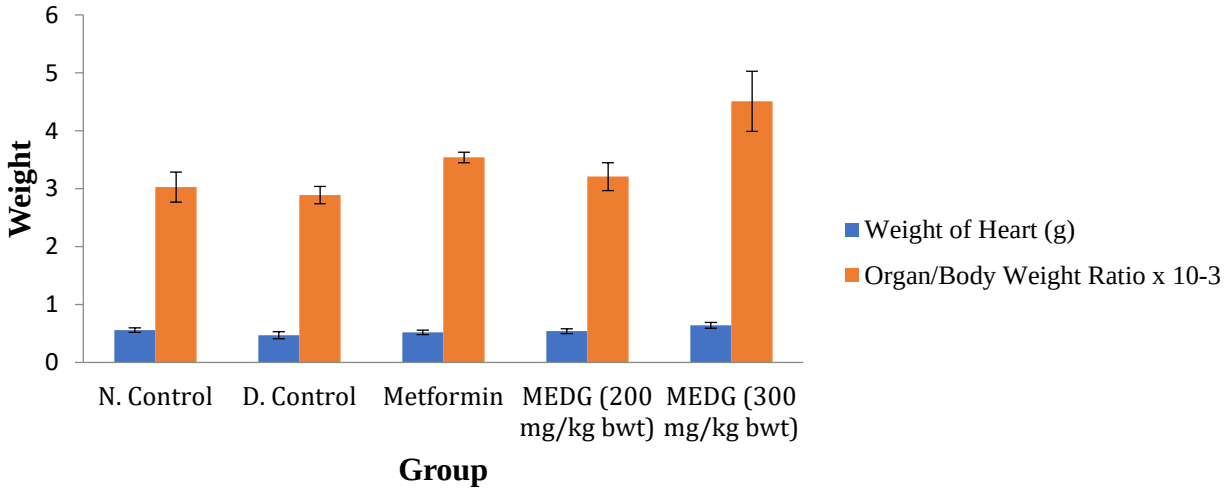

Fig. 1. Comparison of organ and relative organ weights.

3.2 Effect of MEDG Stem Bark on Cardiovascular Disease Risk Factors

Streptozotocin (STZ)-induced DM significantly increased plasma concentrations of TC, TG, VLDL-C, LDL-C, AIP, AC and CRR, but it significantly reduced HDL-C ($p < 0.05$). However, treatment of diabetic rats with the medicinal plant extract led to significant reductions in circulating levels of lipid profile (except HDL-C, which increased) as well as AIP, AC, and CRR ($p < 0.05$). These results are shown in Figs 2 to 5).

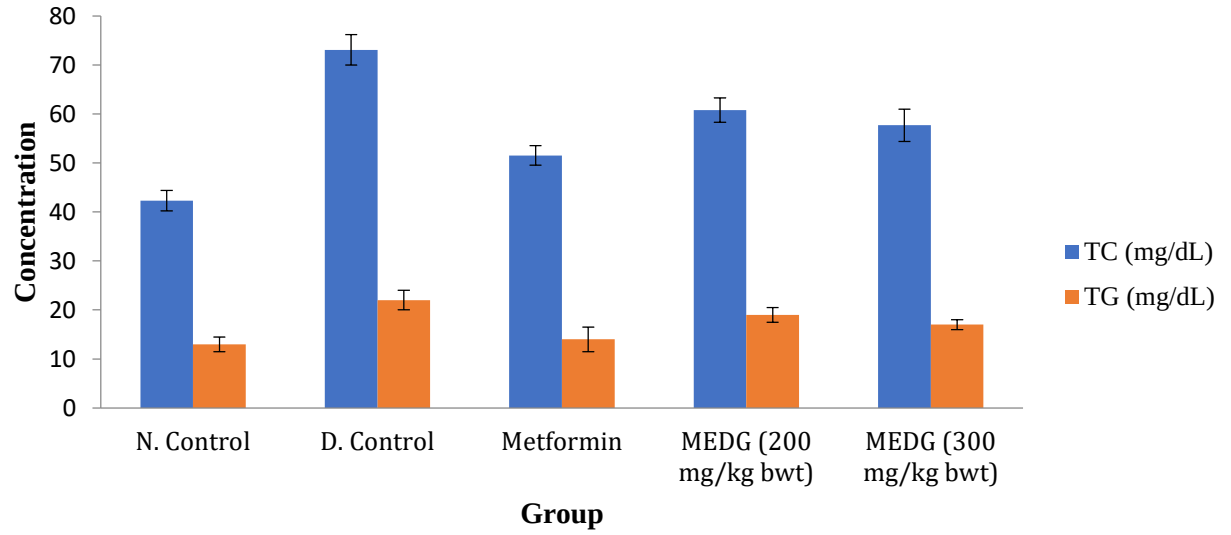

Fig. 2. Concentrations of TC and TG in the rats.

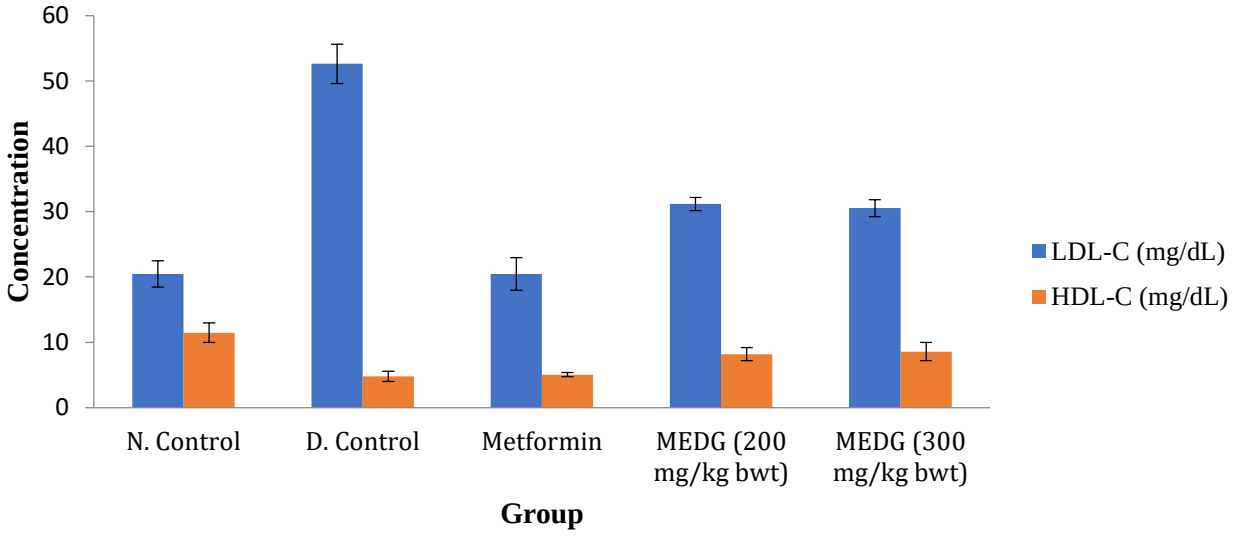

Fig. 3. Concentrations of LDL-C and HDL-C in the rats.

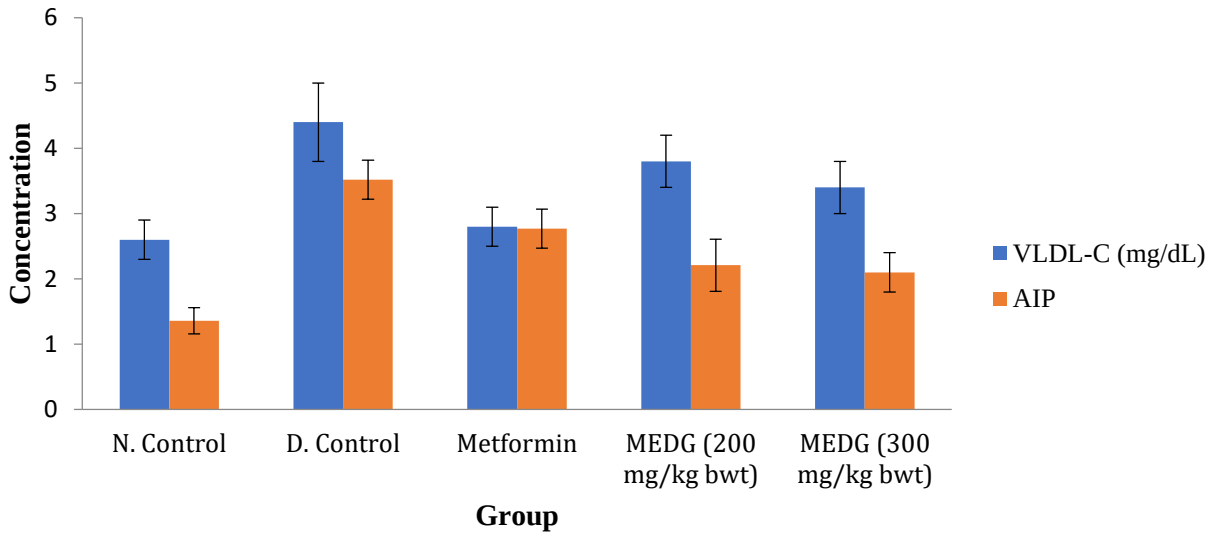

Fig. 4. Concentrations of VLDL-C and AIP in the rats.

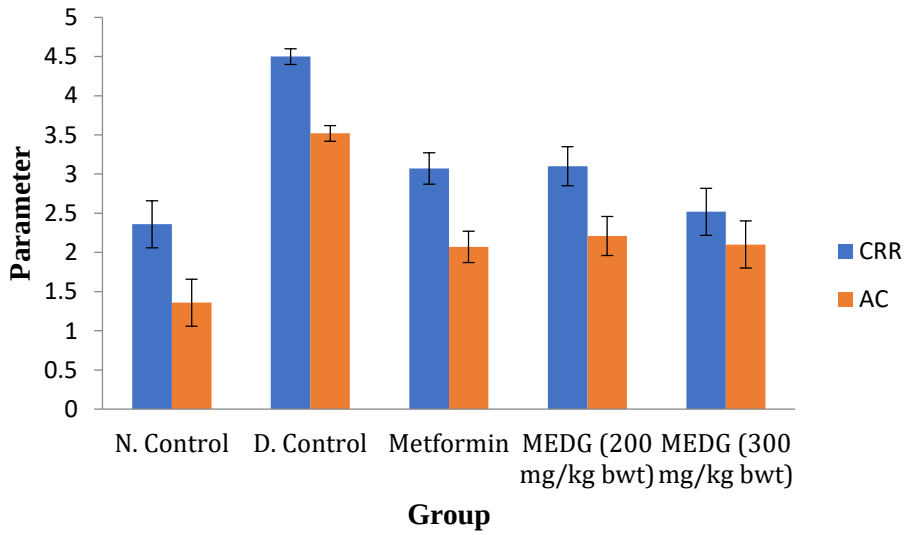

Fig. 5. Comparison of CRR and AC of rats.

4. Discussion

People with Type-2 diabetes mellitus (T2DM) are at risk for both micro- and macrovascular complications [11]. The toxicity produced by STZ impart negatively on organs such as liver, kidneys, heart and lung. The exact molecular mechanism underlying the cytotoxic effect of STZ is not well-understood, however studies suggest that the cytotoxicity could be via production of reactive oxygen species (ROS) thus inducing oxidative stress, causing DNA damage with resultant necrosis due to the DNA methylating activity of the methyl nitroso urea moiety of the drug, release of nitric oxide (NO) which inhibits aconitase activity resulting in mitochondrial dysfunction, or via inhibition of O-linked β -N-acetylglucosaminase (O-GlcNAcase) [9].

Plants are at the center of Traditional Medicine. Their use in disease management is as old as man. Medicinal plants serve as cheap alternative to orthodox medicine since they are readily available [34]-[36]. A variety of indigenous medicinal plants can effectively ameliorates the complications of DM. One of the most significant benefits of medicinal plants is their ready availability and minimal side effects [37]-[39].

Dialium guineense (Velvet Tamarind) is a medicinal plant used in Traditional Medicine for the treatment of infections [40]. It is a tall, tropical, fruit-bearing tree, belonging to the *Leguminosae* family, and has small, typically grape-sized edible fruits with brown hard inedible shells. In Africa, it is found in dense forests along the southern border of the Sahel. The plant grows naturally in West African countries, Central African Republic, and Sudan [41]. In Nigeria, it is known by different local names: *Icheku* (Igbo), *Awin* (Yoruba), *Tsamiyarkurm* (Hausa) and *Amughen* (Bini) [42], [43].

This study investigated the effect of MEDG stem bark on cardiovascular disease risk factors in diabetic rats. The results showed that STZ-induced DM significantly increased plasma concentrations of TC, TG, VLDL-C, LDL-C, AIP, AC and CRR, but it significantly reduced HDL-C. However, treatment of diabetic rats with MEDG stem bark led to significant reductions in circulating levels of lipid profile (except HDL-C, which increased) as well as AIP, AC and CRR. These results have further strengthened the observation that medicinal plants are effective in ameliorating complications of some diseases [44]-[53].

5. Conclusion

The results of this study suggest that the medicinal plant extract has the capacity to protect against cardiovascular events in STZ-induced diabetic rats.

6. Competing Interests

The authors declare that they have no conflict of interest.

7. Acknowledgement

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