Effect of *Telfairia occidentalis* leaves on cardiac enzymes of diet-induced hypercholesterolemia in rats

[1]Sule, M.S., *[2]Balogun, A. and [3]Adisa, K.O.

1. Department of Biochemistry, Bayero University, Kano, Nigeria
2. Department of Biological Sciences, Al-Hikmah University, Ilorin, Nigeria
3. Department of Biochemistry, Federal University of Health Sciences, Ila-Orangun, Nigeria

Abstract

This study assessed the cardioprotective effect of *Telfairia occidentalis* leaves in rats fed cholesterol-rich diet. Thirty-five (35) Wistar rats were fed with a basal diet containing cholesterol (2%) along with or without T. occidentalis leaves supplements at 3%, 6% and 9% levels for 42 days. The result of this study revealed that there was a significant increase ($p < 0.05$) in serum activities of lactate dehydrogenase (LDH), creatine kinase (CK) and aspartate aminotransferase (AST) of the rats fed with diet containing 2% cholesterol supplement when compared with the rats fed on control diet. However, there was a significant decrease ($p < 0.05$) in serum LDH, CK and AST activities of the rats fed on diets containing 2% cholesterol along with *T. occidentalis* supplements when compared with those rats fed on diet containing 2% cholesterol supplement only. *T. occidentalis* supplements had a regime-dependent reduction in the activities of the myocardial infarction indicators (AST, CK and LDH). Results indicated that *T. occidentalis* produced potent cardioprotective effect in hypercholesterolemic rats. This study recommends that *T. occidentalis* supplements may be beneficial for management of hypercholesterolemia or arteriosclerosis.

Keywords: Arteriosclerosis, Aspartate aminotransferase, Cardioprotective, Creatine kinase, Lactate dehydrogenase.

1. Introduction

Hypercholesterolemia is a condition characterized by the presence of high level of cholesterol in the blood, which is clinically manifested by an increase in low density lipoprotein (LDL) or a decrease in high density lipoprotein (HDL) cholesterol in plasma [1]. Hypercholesterolemia is a well-known risk factor for cardiovascular diseases (CVD) [2]. Emerging evidence identifies CVD as the major cause of morbidity and mortality globally including sub-Saharan Africa [3,4]. The World Health Organization report [5] revealed that 80% of deaths from CVD and 87% of related disabilities currently occur in low and middle income countries. In the report, it was further emphasized that CVD have become the leading cause of death in many developing countries and will soon attain that status in several others. CVD are currently responsible for at least 20% of all deaths in Nigeria and constitute up to 60% of the patients admitted into the medical wards of most tertiary hospitals in Nigeria [6-8]. It is estimated that by the year 2030 the death rates from CVD will increase and will remain as leading cause of death in the world [5].

Numerous clinical trials of lipid-lowering interventions through diet, drugs and surgery have been well established. In addition to this, diet treatment or drug therapy to regulate HDL and LDL-cholesterol (LDL-c) levels promises to reduce subsequent pathological conditions associated with coronary heart diseases. Based on the evidence, great strides have been made to reduce the risk of coronary heart disease worldwide by monitoring cholesterol levels through diet and drug therapy. Because of an increased resistance of LDL-c to oxidation after treatment with various synthetic pharmaceutical drugs, there is a great need to identify natural food products that can offer antioxidant protection against LDL-c oxidation [9,10].

Telfairia occidentalis is a darkish-green leafy vegetable. It belongs to the family *Cucurbitaceae* and is one of the commonly consumed leafy vegetables [11]. Commonly called fluted pumpkin, it is an important leaf and seed vegetable indigenous to Southern Nigeria and grown in the forest zone of west and central Africa including Ghana and Sierra Leone. It probably originated in southeast Nigeria and distributed by Igbos who have been cultivated this crop since time immemorial [12,13]. *Telfairia occidentalis* is popularly known as *Ugu* in Igbo, *Aworoko*/*Eweroko* in Yoruba, *Ubong* in Efik, *Umee* in Urhobo and *Umeke* in Edo [14,15].

*Corresponding Author E-mail address: abalogun@alhikmah.edu.ng
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The leaves contain essential oils, and vitamins, while the root contains cucurbitacin, sesquiterpene, and lactones. The leaves are also noted for lactating properties and are in high demand for nursing mothers. The leaves are used mainly for soups, and salads to accompany the main course while the roots are used as rodenticide and ordeal poison [16,17]. It is used in herbal preparations for the management of many diseases such as anaemia, convulsion, diabetes, heart diseases and hypertension [11,18]. Pharmacological activities reported for this plant include antioxidant, hepatoprotective, hematological, anti-plasmodial, antimicrobial, testiculoprotective, anticancer, anti-inflammatory, anxiolytic and sedative properties [19]. The antidiabetic activity of the leaf extract and its beneficial effect in oxidative stress related diseases have also been reported [18, 20-25]. The presence of tannins, flavonoids, alkaloids, saponins, steroids, anthraquinones, reducing sugars (glycosides) and long chain n-3-unsaturated fatty acids in the leaves have also been reported [25-27]. Despite the widespread consumption of *Telfairia occidentalis*, there is a paucity of information on its protective role against cardiovascular enzymes. The present study investigates the protective effects of *Telfairia occidentalis* leaves on diet-induced hypercholesterolemia.

2. Materials and Methods

2.1 Assay kits, chemicals and reagents

Diagnostic kits for total cholesterol, triglyceride, HDL-cholesterol, lactate dehydrogenase, creatine kinase and aspartate aminotransferase were products of Randox Laboratories Ltd., Co. Antrim, United Kingdom. All other chemicals and reagents were products of Sigma-Aldrich Inc., St Louis, USA.

2.2 Plant materials, authentication and preparation

Telfairia occidentalis was obtained from Yankura Market in Kano, Nigeria. The plant was authenticated in Botany Unit, Department of Biological Sciences, Bayero University, Kano, Nigeria. The leaves were rinsed with distilled water, air-dried for 4 days, pulverized into fine powder and subsequently used in diet formulation.

2.3 Experimental animals

Male Wistar rats with mean weight of 150 ± 7.5 g were obtained from the Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria, Nigeria. The animals were kept in cages and maintained at room temperature with a 12 h light-dark cycle for 2 weeks to acclimatize. The animals were allowed free access to feed (Vital Feed Ltd., Ibadan, Nigeria) and water *ad libitum*.

2.4 Formulation of cholesterol-rich diet

The cholesterol-rich diet used in this study was formulated according to the method described by Vesselinvitch et al. [28]. The composition of the diet is presented in Table 1.

Table 1: Composition of diet (g/kg)

Component	Feed A	Feed B	Feed C	Feed D	Feed E
Basal diet	1000	780	750	720	690
Cholesterol	0	20	20	20	20
Red oil	0	200	200	200	200
T. occidentalis	0	0	30	60	90

Feed A: Control diet (g/kg); Feed B: Cholesterol-rich diet (g/kg); Feed C: Cholesterol-rich diet + 3% *T. occidentalis* leaves; Feed D: Cholesterol rich diet + 6% *T. occidentalis* leaves; Feed E: Cholesterol-rich diet + 9% *T. occidentalis* leaves.

2.5 Animal grouping and treatment

Twenty-five (25) male Wistar rats were randomly distributed into five treatment groups of five animals each. Rats in Group 1 (control) were fed normal basal diet. The animals in Group 2 were fed a cholesterol-rich diet (hypercholesterolemic rats), while those in groups 3, 4 and 5 were fed cholesterol-rich diets supplemented with *T. occidentalis* leaf powders at 3%, 6% and 9% respectively (as presented in Table 1) for 42 days. The animals had free access to feed and water throughout the period of the experiment.

2.6 Collection of blood and preparation of serum

At the end of the 42-day feeding period, the rats were fasted overnight and humanely sacrificed by cervical dislocation. Blood was collected by heart puncture into centrifuge tubes and allowed to clot for 15 min before spinning at 3,000 *g* for 15 minutes using a bench top centrifuge (Beckman and Hirsch, Burlington, IO, USA). The serum was carefully collected and used for cardiac function test and lipid profile.

2.7 Biochemical assay

Serum total cholesterol (TC) and triglycerides were determined as described by Aliain et al. [29] and Burstein et al. [30] respectively. The high-density lipoprotein cholesterol (HDLc) was determined using the procedure described by Burstein et al. [30]. Low-density lipoprotein cholesterol (LDLc) was calculated using the method of Friedewald et al. [31]. Activities of aspartate aminotransferase (AST), creatine kinase (CK) and lactate dehydrogenase in the serum were determined using standard methods [32-34].

2.8 Statistical analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) for Windows, version 18 (SPSS Inc., Chicago, IL, USA). Results were expressed as mean ± standard deviation (SD) of five determinations. Individual differences among groups were analyzed by Dunnett's test and those at $p < 0.05$ were accepted as significant.

3. Results

Figure 1 shows the effect of *T. occidentalis* leaves supplement on serum cholesterol in rats fed with cholesterol-rich diets. There was 14.63% increase in total cholesterol in rats fed with cholesterol-rich diet when compared to rats fed with basal diet (Figure 1). Supplementation of cholesterol-rich diet with *T. occidentalis* leaves at the tested regimes 30, 60 and 90 g/kg significantly ($p<0.05$) decreased serum total cholesterol by 19.14%, 26.81% and 34.47% respectively when compared to rats fed cholesterol-rich diets (Figure 1).

Cholesterol-rich diet produced a significant ($p<0.05$) increase in triglycerides by 48.78% when compared to rats fed basal diet (Figure 2). The increase was significantly lowered ($p<0.05$) by cholesterol-rich diet supplemented with *T. occidentalis* leaves (Figure 2). LDL-c of cholesterol-rich diet-fed rats increased significantly ($p<0.05$) after 42-days of treatment by 56% when compared to basal diet-fed rats (Figure 3). *T. occidentalis* leaves supplement at the tested regimes 30, 60 and 90 g/kg to rats fed cholesterol-rich diets, significantly ($p<0.05$) decreased serum levels of LDL-c by 25.64, 35.90 and 51.28% when compared to rats fed cholesterol-rich diets as shown in Figure 3. Conversely, *T. occidentalis* leaf supplement at 30, 60 and 90 g/kg significantly ($p<0.05$) increased serum HDL-c concentration by 38.52, 49.18 and 74.59% respectively when compared to rats fed cholesterol-rich diets (Figure 4).

It is clearly shown in Figure 5 that rats fed cholesterol-rich diets had a significant ($p<0.05$) increase in serum AST activity by 26.67% when compared to rats fed normal basal diets. *T. occidentalis* leaves supplement at the tested regimes 30, 60 and 90 g/kg to rats fed cholesterol-rich diet significantly ($p<0.05$) decreased serum AST activity by 14.98, 19.27 and 22.31% when compared to rats fed with cholesterol-rich diet (Figure 5).

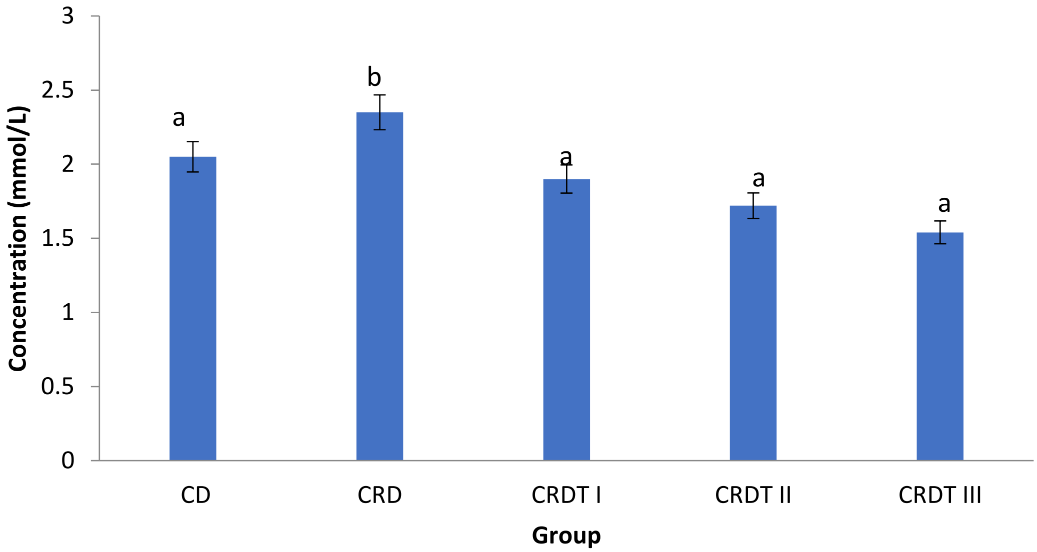

Figure 1: Effect of *T. occidentalis* leaf supplement on serum total cholesterol of rats fed with cholesterol-rich diet. Bars with different letters indicate significant differences at $p < 0.05$. CD: Control diet, CRD: Cholesterol rich diet, CRDT I: Cholesterol rich diet + 3% of *T. occidentalis* leaves, CRDT II: Cholesterol rich diet + 6% of *T. occidentalis* leaves, CRDT III: Cholesterol rich diet + 9% of *T. occidentalis* leaves.

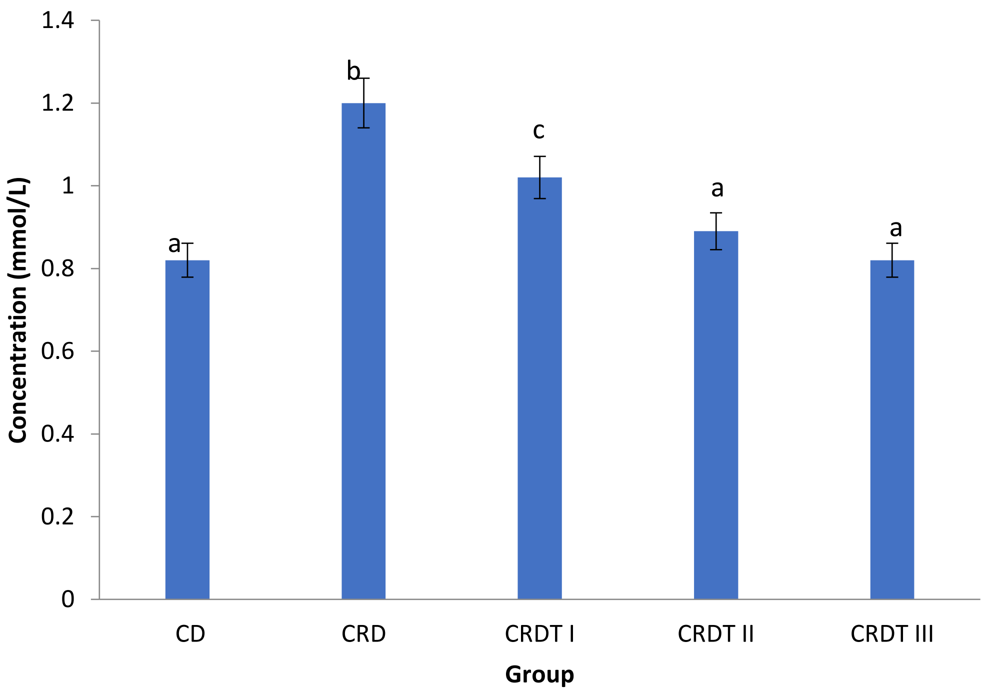

Figure 2: Effect of *T. occidentalis* leaf supplement on serum triglycerides of rats fed with cholesterol-rich diet. Bars with different letters indicate significant differences at $p < 0.05$. CD: Control diet, CRD: Cholesterol rich diet, CRDT I: Cholesterol rich diet + 3% of *T. occidentalis* leaves, CRDT II: Cholesterol rich diet + 6% of *T. occidentalis* leaves, CRDT III: Cholesterol rich diet + 9% of *T. occidentalis* leaves.

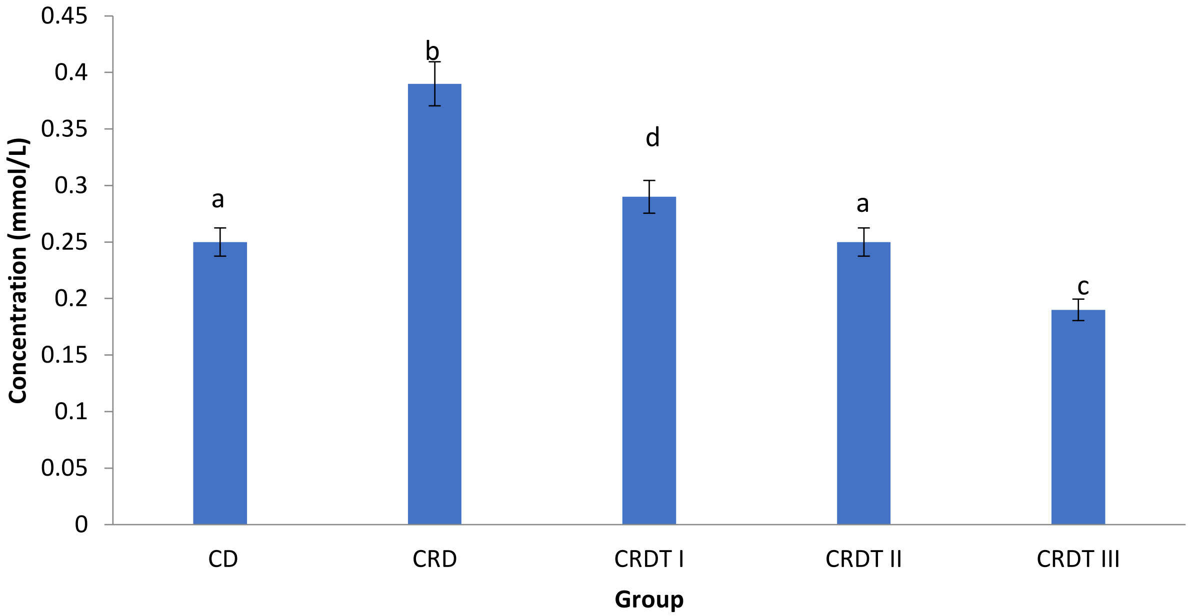

Figure 3: Effect of *T. occidentalis* leaf supplement on serum LDL-c of rats fed with cholesterol-rich diet. Bars with different letters indicate significant differences at p<0.05. CD: Control diet, CRD: Cholesterol rich diet, CRDT I: Cholesterol rich diet + 3% of *T. occidentalis* leaves, CRDT II: Cholesterol rich diet + 6% of *T. occidentalis* leaves, CRDT III: Cholesterol rich diet + 9% of *T. occidentalis* leaves.

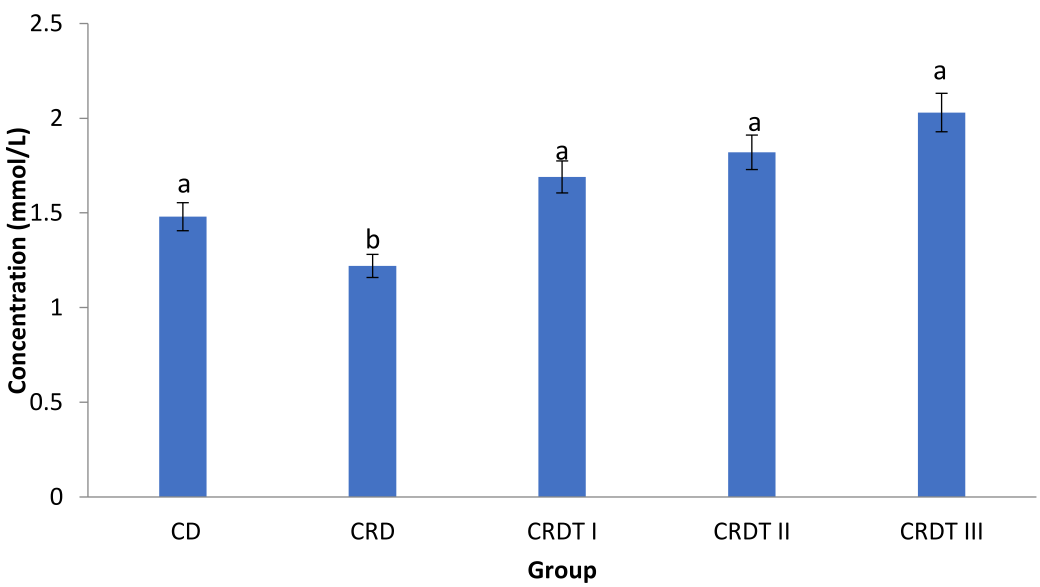

Figure 4: Effect of *T. occidentalis* leaf supplement on serum HDL-c of rats fed with cholesterol-rich diet. Bars with different letters indicate significant differences at p < 0.05. CD: Control diet, CRD: Cholesterol rich diet, CRDT I: Cholesterol rich diet + 3% of *T. occidentalis* leaves, CRDT II: Cholesterol rich diet + 6% of *T. occidentalis* leaves, CRDT III: Cholesterol rich diet + 9% of *T. occidentalis* leaves.

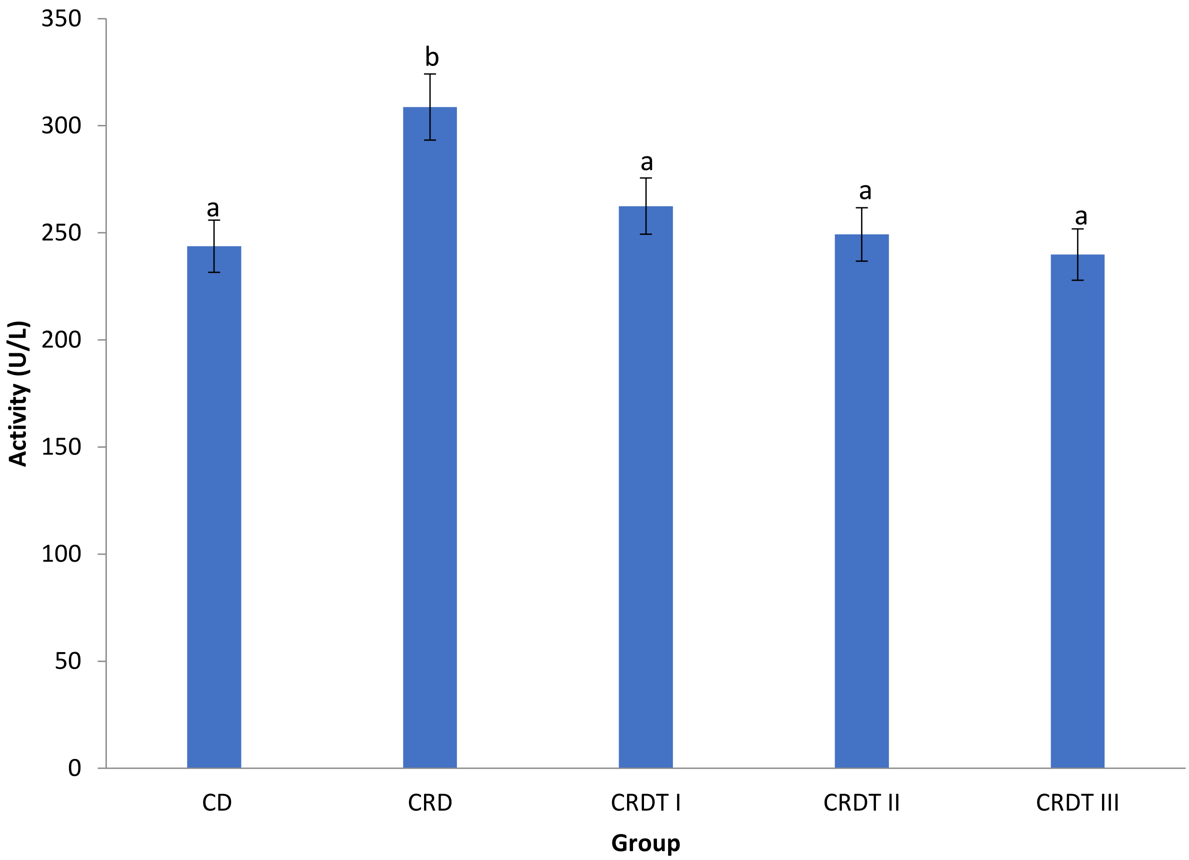

Figure 5: Effect of *T. occidentalis* leaf supplement on serum aspartate aminotransferase activity of rats fed with cholesterol-rich diet. Bars with different letters indicate significant differences at p<0.05. CD: Control diet, CRD: Cholesterol rich diet, CRDT I: Cholesterol rich diet + 3% of *T. occidentalis* leaves, CRDT II: Cholesterol rich diet + 6% of *T. occidentalis* leaves, CRDT III: Cholesterol rich diet + 9% of *T. occidentalis* leaves.

Activities of serum CK increased significantly ($p<0.05$) by 33.52% in rats fed cholesterol-rich diet when compared to rats fed normal basal diet (Figure 6). *Telfairia occidentalis* leaves supplement at the tested regimes 30, 60 and 90 g/kg to rats fed cholesterol-rich diet, significantly ($p<0.05$) decreased serum CK activity by 15.93, 24.58 and 25.14% when compared to rats fed cholesterol-rich diet (Figure 6).

The activities of LDH in the serum of cholesterol-rich diet-fed rats increased significantly ($p<0.05$) by 29.40% when compared to rats fed with basal diet (Figure 7). *Telfairia occidentalis* leaves supplement at the tested regimes 30, 60 and 90 g/kg to rats fed cholesterol-rich diet significantly ($p<0.05$) decreased serum LDH activity by 13.88, 22.48 and 24.30% when compared to rats fed cholesterol-rich diet as shown in Figure 7.

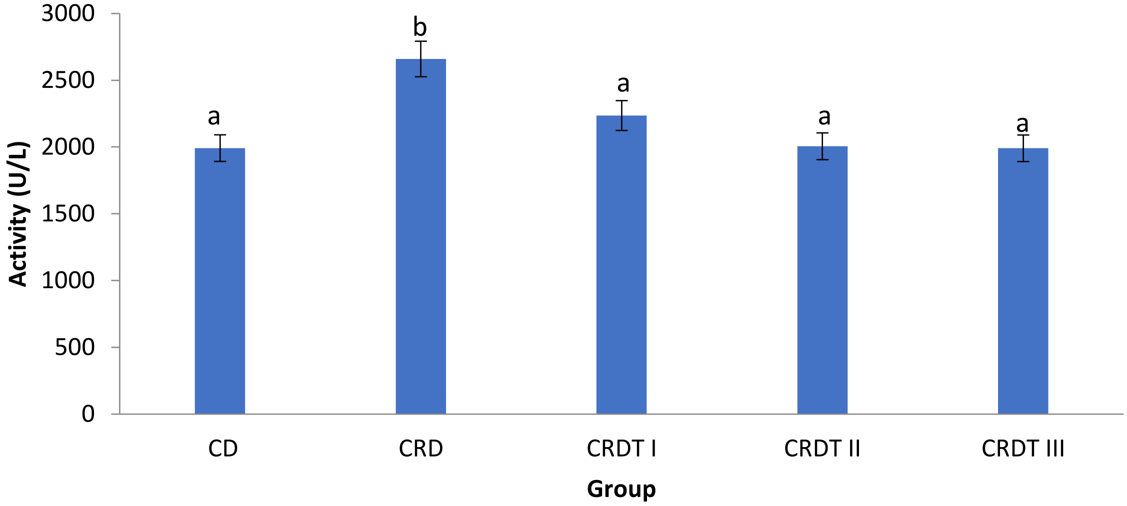

Figure 6: Effect of *T. occidentalis* leaf supplement on serum creatine kinase activity of rats fed with cholesterol-rich diet. Bars with different letters indicate significant differences at p<0.05. CD: Control diet, CRD: Cholesterol rich diet, CRDT I: Cholesterol rich diet + 3% of *T. occidentalis* leaves, CRDT II: Cholesterol rich diet + 6% of *T. occidentalis* leaves, CRDT III: Cholesterol rich diet + 9% of *T. occidentalis* leaves.

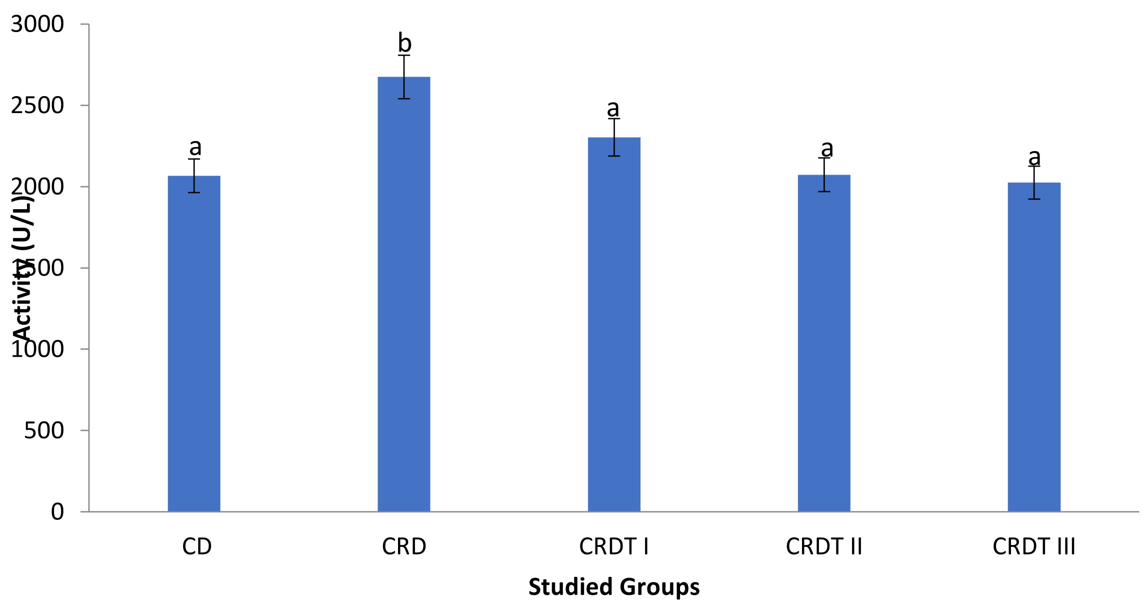

Figure 7: Effect of *T.* occidentalis leaf supplement on serum lactate dehydrogenase activity of rats fed with cholesterol-rich diet. Bars with different letters indicate significant differences at p<0.05. CD: Control diet, CRD: Cholesterol rich diet, CRDT I: Cholesterol rich diet + 3% of *T. occidentalis* leaves, CRDT II: Cholesterol rich diet + 6% of *T. occidentalis* leaves, CRDT III: Cholesterol rich diet + 9% of *T. occidentalis* leaves.

4. Discussion

This study presents the cardioprotective effect of *Telfairia occidentalis* leaves supplementation in rats fed cholesterol-rich diet. TC, TG, LDLc and HDLc are risk factors for the development of atherosclerosis and related cardiovascular diseases. The significant increase in serum levels of TC, TG and LDLc accompanied with a significant decrease in HDLc when compared with the control diet fed rats indicates protection. This agrees with previous studies on diet-induced cholesterolemia [35-40]. These results could be explained on the basis that feeding rats on atherogenic diets leads to an increase in cholesterol absorption and hence serum TC increment. It is apparent that the cholesterol-rich diet supplemented with *T. occidentalis* leaves lowered the serum TC level of rats in a concentration-dependent manner. Previous studies have shown that *T. occidentalis* has hypolipidemic effect in rats fed cholesterol-rich diet via a mechanism that is dependent on inhibition of the absorption of dietary cholesterol in the intestine or stimulation of the biliary secretion of cholesterol and cholesterol excretion in feaces [22,41].

The significant increase in serum HDLc concentration of rats supplemented with *T. occidentalis* leaves shows protective importance in CVD. The comparison of the effects showed that the diets prepared are regime dependent, although there was no significant difference. The protective role of HDLc against CVD has been suggested to occur in several ways [42]. Elevated HDLc level reduces the entry of cholesterol into the cell and increases cholesterol release from the cell. This is possible by promoting reverse cholesterol transport through scavenging excess cholesterol from peripheral tissues and subsequent esterification using lecithin cholesterol acyltransferase and deliverance to the liver and steroidogenic organs for bile acid and lipoprotein synthesis and eventual elimination from the body [43]. HDL-c also inhibits oxidation of LDL by virtue of its antioxidant and anti-inflammatory property [43,44]. The increase in HDLc may also be attributed to stimulation of pre-β HDLc and reverse cholesterol transport [45]. High serum level of LDLc is a risk factor for cardiovascular disease [43,46] and often accompany hypertension [47] while decrease in serum LDL-c has been considered to reduce risk of CVD. In this study, there is significant decrease in serum LDL-c concentration at the tested regimes which indicates possible cardio-protective effect of the leaf. This effect may be attributable to its flavonoid content as earlier reported that flavonoids lower LDL-c in both normolipidemic and hyperlipidemic rats [48].

AST, LDH and CK are marker enzymes for the assessment of myocardial injury. Increase in activities of these enzymes in the serum of cholesterol-rich diet-fed rats is an indication that hypercholesterolemia markedly increases myocardial infarction as evidenced by increased necrotic cell death and infarct size. Serum CK activity is a more sensitive indicator in early stage of myocardial ischemia while peak rise in lactate dehydrogenase is roughly proportional to the extent of the myocardial tissue [49]. This implies that excess and continuous consumption of cholesterol-rich diet may cause myocardial infarction, which correlates with previous findings [50,51]. From the results obtained, it is apparent that supplementation with *T. occidentalis* significantly lowered these biomarkers (LDH, CK and AST) indicating the likely cardio-protective property. The leaves of *T. occidentalis* may have exhibited cardiovascular protective activity due to their antioxidant property, which may be attributed to flavonoid content. It is evident from the data obtained from this study that *T. occidentalis* leaves exhibited cardio-protective property against atherosclerosis and cardiovascular diseases. This implies that the leaves may help in the management of dyslipidemic conditions.

5. Conclusion

From this study, it can be concluded that the leaves of *Telfairia occidentalis* can be used as oral remedy in the treatment of heart related disease induced by hypercholeterolemia. This has lend further credence to consumption of the vegetable especially by the locals.

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