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**Alteration of Plasma Lipid Profile and Atherogenic Indices of Cholesterol Loaded Rats
by *Tridax Procumbens* Linn: Implications for the Management of Obesity and
Cardiovascular Diseases**

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Abstract

The effect of the administration of 20mg/100g aqueous extract of the leaves of *Tridax procumbens* on the packed cell volume (PCV), daily weight gain, plasma lipid profiles and atherogenic indices of rats fed 1g/100g cholesterol, was investigated. The mean daily weight gain and plasma concentrations of triglyceride, LDL-, VLDL- and total cholesterol, as well as the atherogenic indices [Cardiac Risk Ratio (CRR), Atherogenic Coefficient (AC) and Atherogenic Index of Plasma (AIP)] of the treated animals were all significantly lower ($p < 0.05$) than those of the test control and control. The PCV and plasma HDL-cholesterol level of the treated animals was significantly higher ($p < 0.05$) than that of the test control, although lower than that of the control. These results suggest a possible protective role of the extract against the development of cardiovascular diseases, as well as dyslipidemic conditions, whether primary or secondary to diabetes mellitus, hypertension and obesity

Keywords: Hypertension, hypocholesterolemia, lipid profile, obesity, *Tridax procumbens*

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INTRODUCTION

About 80% of the world's population depends on plants to treat many common ailments, and 30% of modern conventional drugs are derived from plant sources. Herbs have been used safely and effectively for many centuries, and are free of most of the side effects associated with synthetic drugs¹. *Tridax procumbens* Linn (compositae), a grass commonly found in tropics is traditionally used in the South Eastern and South Western Nigeria, for stopping bleeding, treating diarrhea, malaria and stomachache, and reducing blood pressure^{2,3}. Edeoga *et al.*² demonstrated the hypotensive effect, while Hemalatha⁴ demonstrated the antihepatotoxic and antioxidant defense potential of aqueous extracts of the leaves of *Tridax procumbens* on rats.

Dyslipidemia is associated with hypertension, diabetes mellitus and obesity, and is one of the major risk factors for the development of cardiovascular disease⁵⁻⁹. Therefore, the present study was designed to investigate the effect of aqueous extracts of *Tridax procumbens* on the plasma lipid profile of cholesterol-loaded rats with a view to finding any possible cue to the molecular basis of its antihypertensive action.

MATERIALS AND METHODS

Collection of Animals and Preparation of the Leaves

Albino rats were collected from the animal house of the Department of Biochemistry, University of Port Harcourt, Port Harcourt, Nigeria. The plants were collected from behind the Ofrima Hall Complex of University of Port Harcourt, Port Harcourt, Nigeria. After due identification at the Herbarium of the Department of Plant Science and Biotechnology, University of Port Harcourt, Nigeria, their leaves were collected, rid of dirt, oven dried at 55°C and ground into powder. The resultant powder was soaked in boiled distilled water for 12h, after which the resultant mixture was filtered and the filtrate, hereinafter referred to as the aqueous extract was stored for subsequent use. A known volume of this extract was evaporated to dryness, and the weight of the residue used to determine the concentration of the filtrate,

which was in turn used to determine the dose of administration of the extract to the test animals.

Experimental Design and Composition of Diet

The rats were randomly sorted into three groups of five animals each, so that the average weight difference was $\pm 1.8g$. The animals were individually housed in plastic metabolic cages. After a one-week acclimatization period on guinea growers mash (Bendel Feed and Flour Mills Ltd., Ewu, Nigeria), the treatment commenced and lasted for a week. The test received daily by intra-gastric gavages, 1g/100g body weight of cholesterol and 20mg/100g body weight of the extract; the test-control received daily by intra-gastric gavages, 1g/100g body weight of cholesterol; while the control group received appropriate volumes of water by the same route. The dosage of administration of the extract was adapted from Bhagwat *et al.*¹⁰. The animals were allowed food and water *ad libitum*. At the end of the treatment period the rats were weighed and anaesthetized by intra-peritoneal injection of 5mg/kg body weight of 25% Urethane saline solution. While under anesthesia blood was collected from each rat via heart puncture and transferred into heparin sample bottles after which they were painlessly sacrificed.

Determination of the Plasma Lipid Profiles/Indices

Plasma total cholesterol (TC), HDL-cholesterol (HDLC) and triglyceride (TG) were assayed enzymatically with commercial test kits (Randox Laboratories, Crumlin, England). Plasma LDL-cholesterol was calculated using the Friedewald equation¹¹, as follows:

$$LDLC = TC - HDLC - TG/2.2.$$

$$VLDLC = TG/2.2.$$

The atherogenic indices were calculated^{8,12-14} as follows:

$$\text{Cardiac Risk Ratio (CRR)} = TC/HDLC$$

$$\text{Atherogenic Coefficient (AC)} = (TC - HDLC)/HDLC$$

$$\text{Atherogenic Index of Plasma (AIP)} = \log(TG/HDLC)$$

Statistical Analysis of Data

All values are quoted as the mean \pm SD. The values of the various parameters for the control, test control and test groups were analyzed for statistical significant differences using the student's *t*-test. $P < 0.05$ was assumed to be significant.

RESULTS

Table 1 shows the effect of aqueous extracts of *Tridax procumbens* on the mean daily weight gain and PCV of cholesterol loaded rats. The mean daily weight gain of the test animals was significantly lower ($p < 0.05$) than that of the test control and the control groups. The PCV of the animals in the test group was significantly higher ($p < 0.05$) than that of the test control, and significantly lower than that of the control. The effect of the aqueous extract of *Tridax procumbens* on plasma lipid profiles of cholesterol loaded rats is shown in Table 2.

The plasma total triglyceride, LDL-, VLDL- and total cholesterol levels of the treated animals was significantly lower ($p < 0.05$) than those of the test control and control. The plasma HDL-cholesterol levels of the treated

animals was significantly lower ($p < 0.05$) than that of the test control, although significantly lower than that of the control. The atherogenic indices: cardiac risk ratio (CRR), atherogenic coefficient (AC) and atherogenic index of plasma (AIP), of the treated animals was significantly lower ($p < 0.05$) than those of the test control and control animals (Table 3).

DISCUSSION

The PCV of the animals in the test group was significantly higher than that of the test control, and significantly lower than that of the control (Table 1). This implies that the extract significantly protected the animals against the hypercholesterolemia induced lowering of PCV, even though it could not restore it to normal level. Weight loss helps improve and control coronary risk incidence, diabetes mellitus, dyslipidemia, hypertension, obesity and physical functioning¹⁵⁻¹⁸, and is one of the strategies for increasing low HDL-C levels¹⁹, as well as improving the insulin resistance¹⁸. Therefore, the significantly low mean daily weight gain produced by the extract, in the test animals implies that it may be useful in the management of hypertension, obesity and dyslipidemia.

Table 1: Effect of aqueous extract of *Tridax procumbens* on the PCV and mean daily weight gain of cholesterol loaded rats.

Parameter	Control	Test-control	Test
PCV (%)	40.59 \pm 4.71 ^a	34.13 \pm 1.12 ^b	37.26 \pm 2.85 ^c
Mean daily weight gain (g/day)	6.07 \pm 1.92 ^a	6.71 \pm 1.01 ^a	4.29 \pm 0.58 ^b

Values are means \pm SD, n=4 per group. Entries with different superscripts are significantly different at $p < 0.05$.

Table 2: Effect of aqueous extract of *Tridax procumbens* on the plasma lipid profile of cholesterol loaded rats.

Parameter	Concentration (mmol/L)		
	Control	Test-control	Test
Plasma triglyceride	1.81 \pm 0.36 ^a	3.71 \pm 0.65 ^b	1.59 \pm 0.69 ^a
Plasma total cholesterol	6.15 \pm 1.05 ^a	8.18 \pm 0.71 ^b	6.37 \pm 0.45 ^a
Plasma HDL cholesterol	2.49 \pm 0.02 ^a	2.21 \pm 0.04 ^b	2.49 \pm 0.06 ^a
Plasma VLDL cholesterol	0.82 \pm 0.16 ^a	1.69 \pm 0.30 ^b	0.72 \pm 0.31 ^a
Plasma LDL cholesterol	2.83 \pm 0.91 ^a	4.29 \pm 0.63 ^b	3.16 \pm 0.20 ^a

Values are means \pm SD, n=4 per group. Entries with different superscripts are significantly different at $p < 0.05$.

Table 3: Effect of aqueous extract of *Tridax procumbens* on the atherogenic indices of cholesterol loaded rats.

Parameter	Control	Test-control	Test
Cardiac risk ratio	2.47 \pm 0.43 ^a	3.89 \pm 0.98 ^b	2.57 \pm 0.25 ^a
Atherogenic coefficient	1.47 \pm 0.43 ^a	2.89 \pm 0.98 ^b	1.57 \pm 0.25 ^a
Atherogenic index of plasma	-0.15 \pm 0.09 ^a	0.23 \pm 0.16 ^b	-0.23 \pm 0.18 ^a

Values are means \pm SD, n=4 per group. Entries with different superscripts are significantly different at $p < 0.05$.

High plasma concentrations of triglyceride is both an independent and synergistic risk factor for cardiovascular diseases^{8,14,20} and is often found in hypertension⁵, abnormal lipoprotein metabolism, obesity, insulin resistance and diabetes mellitus^{6,9,18,20}. In this study, the extract produced a significantly lower plasma triglyceride level. Another well-established and recognized risk factor for developing atherosclerosis and other cardiovascular diseases is increased plasma total cholesterol level²¹. It is often found in hypertension⁵. It therefore follows that a reduction in plasma total cholesterol level will reduce the risk of cardiovascular diseases. Thus, the significantly lower plasma total cholesterol levels produced by the extract, connotes the ability of the extract to protect against cardiovascular diseases.

High plasma concentrations of LDL and VLDL cholesterol is a risk factor for cardiovascular disease^{21,22} and is often found in diabetes mellitus^{6,7,9}, hypertension⁵ and obesity¹⁸. Decreases in plasma LDL cholesterol have been considered to reduce risk of coronary heart disease⁷. In this study, we observed a significantly lower plasma LDL and VLDL cholesterol levels in the treated animals.

Another major and well-established risk factor for the development of cardiovascular diseases is decreased plasma concentrations of HDL cholesterol^{7,8,13,22}. It often accompanies diabetes mellitus^{6,7,9}, hypertension⁵, and obesity¹⁸. Clinical data show that increase in plasma HDL cholesterol concentration decreases cardiovascular risk^{7,9,13,19}.

High HDL exerts a protective effect by decreasing the rate of entry of cholesterol into the cell via LDL and increasing the rate of cholesterol release from the cell²³ by enhancing reverse cholesterol transport by scavenging excess cholesterol from peripheral tissues followed by esterification through lecithin: cholesterol acyltransferase and delivering it to the liver and steroidogenic organs for subsequent synthesis of bile acids and lipoproteins and eventual elimination from the body^{19,21}; and inhibiting the oxidation of LDL as well as the atherogenic effects of oxidized LDL by virtue of its antioxidant^{19,21,24} and anti-inflammatory property²¹.

In this study, the extract produced an increased plasma HDL cholesterol concentration.

Atherogenic indices are powerful indicators of the risk of heart disease: the higher the value, the higher the risk of developing cardiovascular disease and vice versa^{8,12-14,25}. In this study, we observed that the extract significantly reduced atherogenic indices CRR, AC and AIP. Low atherogenic indices are protective against coronary heart disease²⁵.

In conclusion, our results suggest a possible protective role of the extract against the development of atherosclerosis and coronary heart disease, as well as the dyslipidemic conditions that characterize diabetes mellitus, hypertension, metabolic syndrome and obesity. It also suggests that the extract can help manage the dyslipidemic conditions²⁶ that accompany the administration of thiazide diuretics.

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