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Hypoglycemic and Hypocholesterolemic Potential of *Persea americana* Leaf Extracts

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ABSTRACT The effect of aqueous and methanolic leaf extracts of *Persea americana* on plasma glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-CHOL), and high-density lipoprotein cholesterol (HDL-CHOL) in rats was investigated. Albino rats were fed a diet containing 20% groundnut oil, 0.5% cholesterol, and 0.25% cholic acid to induce hypercholesterolemia. They were then treated daily with aqueous or methanolic extract of *P. americana* leaf (10 mg/kg of body weight) for 8 weeks. There were no significant ($P > .05$) differences in the overall body weight gain of the hypercholesterolemic rats compared to normal control. Liver to body weight ratio, plasma glucose, total cholesterol (T-CHOL), and LDL-CHOL levels were significantly ($P < .05$) elevated in rats fed hypercholesterolemic diet compared to normal controls. The administration of aqueous and methanolic leaf extracts of *P. americana* induced reductions in plasma glucose (16% and 11%, respectively), T-CHOL (8% and 5%, respectively), and LDL-CHOL (19% and 20%, respectively) in the treated rats compared to the hypercholesterolemic controls. Also, plasma HDL-CHOL concentrations increased by 85% and 68%, respectively, in the aqueous and methanolic extract-treated rats compared to the hypercholesterolemic controls. These results suggest that aqueous and methanolic leaf extracts of *P. americana* lower plasma glucose and influence lipid metabolism in hypercholesterolemic rats with consequent lowering of T-CHOL and LDL-CHOL and a restoration of HDL-CHOL levels. This could represent a protective mechanism against the development of atherosclerosis.

KEY WORDS: • ***avocado*** • ***hypercholesterolemia*** • ***hypoglycemia*** • ***leaf extracts*** • ***rat***

INTRODUCTION

LIFE-STYLE CHANGES accompanying industrialization have a significant impact on the health of the people. In Nigeria, there appears to be a cultural transition toward a more westernized life-style. The traditional foods consisting mainly of roots, cereals, beans, tubers, and vegetables are giving way to fatty foods, sweet snacks, and drinks that are too calorie dense. These changes in dietary pattern among Nigerians, coupled with changes in physical activity patterns and increased use of tobacco products and alcohol, are possible causes of hyperlipidemia, which is becoming an important factor in the pathogenesis of chronic degenerative diseases such as cardiovascular diseases, diabetes, and cancer.

Recently, the use of alternative medicine and the consumption of plant materials have been on the increase in many countries in the world, mostly because plant-derived drugs and herbal formulations are commonly considered to be less toxic and freer from side effects than synthetic ones.[1–4] Avocado (*Persea americana* Mill.) is one of these plants that have been widely used in folk medicine. The bark, fruit, and leaf are used in traditional medicine in South America, West Indies, and Africa to provide remedies for various ailments.[5] The fruit is employed as a vermifuge and remedy for dysentery, the leaf juice has antibiotic activity, the aqueous extract of the leaves has a prolonged hypertensive effect, while the leaf decoction is taken as a remedy for diarrhea, sore throat, and hemorrhage and allegedly stimulates and regulates menstruation.[5]

The leaf extracts from *P. americana* have been shown also to have antiviral activity against herpes simplex type 1 virus,[6] human immunodeficiency virus 1,[7] and adenovirus.[6] It has anti-inflammatory activity[8,9] and antihypertensive activity.[10–12] Experimental and epidemiological studies have demonstrated that elevated levels of plasma cholesterol constitute a major risk factor for coronary heart disease.[13,14] The present study is aimed at investigating the effects of crude leaf extracts of *P. americana* on plasma glucose and lipid levels in the rat.

MATERIALS AND METHODS

Preparation of plant extracts

Fresh leaves of *P. americana* were air-dried and pulverized in a Waring blender, and the aqueous and methanolic extracts were prepared by Soxhlet extraction. The extracts

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TABLE 1. ORGAN TO BODY WEIGHT RATIO PERCENTAGES FOR RATS AFTER 8 WEEKS OF FEEDING

	Group			
Organ	*A*	*B*	*C*	*D*
Liver	2.97 ± 0.14[a]	4.89 ± 0.30[b]	4.41 ± 0.42[b]	4.64 ± 0.80[b]
Kidney	0.57 ± 0.02	0.58 ± 0.02	0.50 ± 0.02	0.53 ± 0.04
Heart	0.30 ± 0.01	0.35 ± 0.03	0.33 ± 0.02	0.36 ± 0.02
Lungs	0.48 ± 0.01	0.47 ± 0.02	0.52 ± 0.04	0.59 ± 0.06
Brain	0.90 ± 0.03	0.94 ± 0.06	0.97 ± 0.10	1.06 ± 0.24

Values are expressed as means ± SD for six rats. Diets were as follows: Group A, standard chow; Group B, hypercholesterolemic diet; Group C, hypercholesterolemic diet + 10 mg/kg of body weight *P. americana* aqueous extract; and Group D, hypercholesterolemic diet + 10 mg/kg of body weight *P. americana* methanolic extract.

Values not sharing a common superscript differ significantly at $P < .05$.

were evaporated to dryness in an oven at 40°C and stored in clean sterile vials until required.

Animal feeding

Male albino rats were divided into four feeding groups (A–D) of six rats per group. Group A was fed standard rat chow, and groups B, C, and D were fed a modified diet containing 20% groundnut oil, 0.5% cholesterol, and 0.25% cholic acid to induce hypercholesterolemia. Rats in groups C and D were orally treated with aqueous and methanolic extracts of *P. americana*, respectively, at a daily dose of 10 mg/kg of body weight. Rats in group B acted as hypercholesterolemic controls and received distilled water. The animals were observed daily and weighed weekly for 8 weeks.

At the end of the feeding period and after an overnight fast, blood was withdrawn via cardiac puncture when animals were rendered unconscious under pentobarbital anesthesia (100 mg/kg of body weight). The blood was collected in heparinized tubes followed by centrifugation at 3,000 *g* for 5 minutes at 4°C to separate the plasma. Total cholesterol (T-CHOL), high-density lipoproteins (HDL-CHOL), low-density lipoproteins (LDL-CHOL), and fasting blood glucose were measured using appropriate kits supplied by RANDOX Laboratories Ltd. (Crumlin, UK).

Statistical analysis

The results are expressed as mean ± SD values, and they were analyzed by two-way analysis of variance. They were statistically evaluated by Student's *t* test, and differences were considered statistically significant if the *P* value was $< .05$.

RESULTS

Table 1 shows the organ to body weight ratios of the different groups of animals. No significant differences were observed in body weight gain of rats, but liver weight and liver to body weight ratio were markedly increased ($P < .05$) in those animals fed the hypercholesterolemic diet compared to normal control rats. Also, brain to body weight ratio was higher in rats fed hypercholesterolemic diet compared to normal animals. However, organ to body weight ratios of kidney, lungs, and heart of hypercholesterolemic rats were not significantly ($P > .05$) different from normal control animals.

Plasma glucose concentrations of the experimental rats are shown in Figure 1. Plasma glucose was significantly ($P < .05$) higher in rats fed hypercholesterolemic diet compared to normal control rats. The administration of aqueous and methanolic leaf extracts of *P. americana* induced 16% and 11% reduction, respectively, in plasma glucose of the treated rats compared to the hypercholesterolemic control animals.

Plasma T-CHOL (Fig. 2) and LDL-CHOL (Fig. 3) levels were significantly ($P < .05$) increased in rats fed hypercholesterolemic diet compared to normal control. The administration of aqueous and methanolic leaf extracts of *P. amer-*

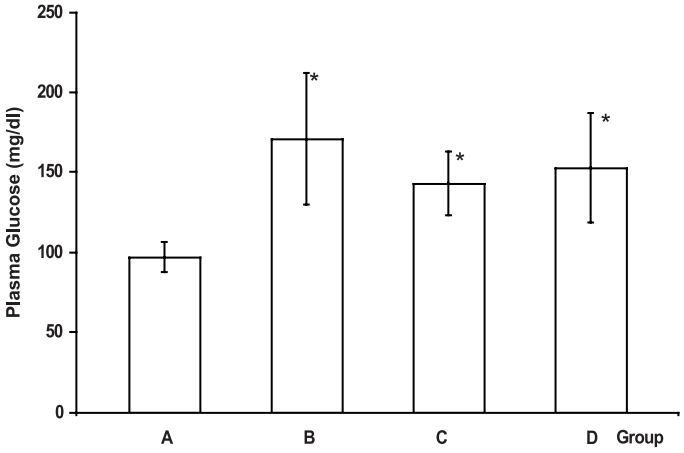

FIG. 1. Effect of aqueous and methanolic leaf extracts of *P. americana* on plasma glucose level in hypercholesterolemic rats. Values are expressed as means ± SD for six rats. Diets were as follows: Group A, standard chow; Group B, hypercholesterolemic diet; Group C, hypercholesterolemic diet + 10 mg/kg of body weight *P. americana* aqueous extract; and Group D, hypercholesterolemic diet + 10 mg/kg of body weight *P. americana* methanolic extract. *Significantly different from normal control at $P < .05$.

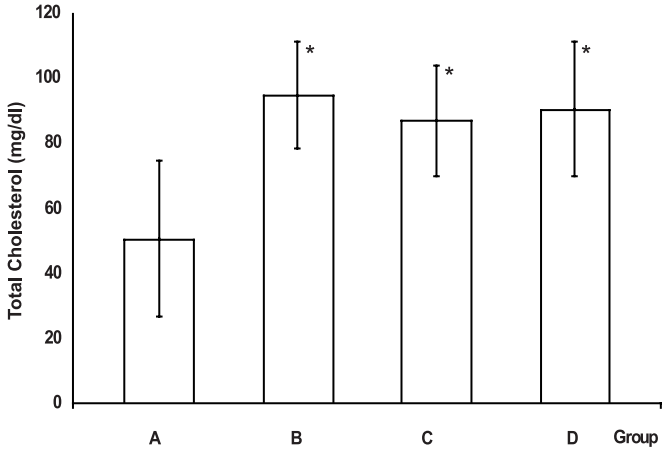

FIG. 2. Effect of aqueous and methanolic leaf extracts of *P. americana* on plasma T-CHOL concentration in hypercholesterolemic rats. Values are expressed as means ± SD for six rats. Diets were as follows: Group A = standard chow; Group B, hypercholesterolemic diet; Group C, hypercholesterolemic diet + 10 mg/kg of body weight *P. americana* aqueous extract; and Group D, hypercholesterolemic diet + 10 mg/kg of body weight *P. americana* methanolic extract. *Significantly different from normal control at $P < .05$.

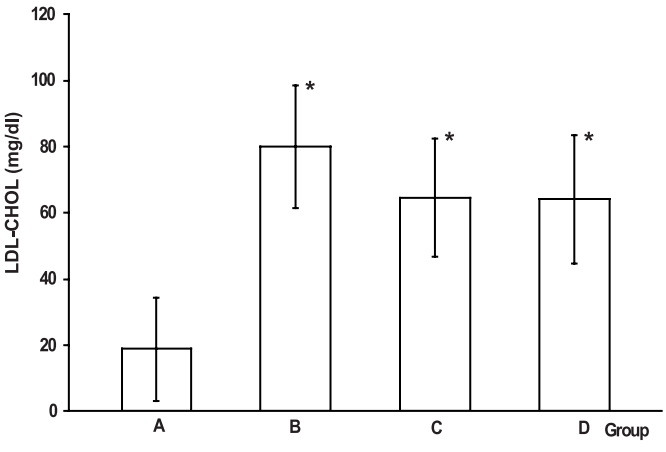

FIG. 3. Effect of aqueous and methanolic leaf extracts of *P. americana* on plasma LDL-CHOL concentration in hypercholesterolemic rats. Values are expressed as means ± SD for six rats. Diets were as follows: Group A, standard chow; Group B, hypercholesterolemic diet; Group C, hypercholesterolemic diet + 10 mg/kg body of weight *P. americana* aqueous extract; and Group D, hypercholesterolemic diet + 10 mg/kg of body weight *P. americana* methanolic extract. *Significantly different from normal control at $P < .05$.

icana caused 8% and 5% reduction, respectively, in T-CHOL levels and 19% and 20% decline, respectively, in plasma LDL-CHOL levels in the treated rats compared to the hypercholesterolemic control animals.

Feeding rats with hypercholesterolemic diet enriched with cholesterol and cholic acid produced a significant ($P < .05$) decrease in plasma HDL-CHOL in the hypercholesterolemic control rats compared to normal control animals (Fig. 4). However, plasma HDL-CHOL concentrations increased by 85% and 68%, respectively, in the aqueous and methanolic extract-treated rats compared to the hypercholesterolemic control and were close to the levels found in the normal control rats.

DISCUSSION

Aqueous and methanolic extracts of *P. americana* were investigated to determine whether they would lower hyperglycemia and hypercholesterolemia in the rat model. Based on the overall body weight gain, each group of animals tolerated the high cholesterol diet and the administration of the plant extracts. Body weight gain by the rats was not significantly different in the normal control and hypercholesterolemic groups. Liver weights were significantly elevated by feeding the hypercholesterolemic diet as compared to normal control rats, and this was accompanied by an increase in liver cholesterol concentration. This observation is similar to an earlier report that body weights were comparable but liver weights were significantly enhanced in a rat model by the intake of a hypercholesterolemic diet containing coconut oil, cholesterol, and cholic acid compared to control rats.[15] The higher liver weight in the hypercholesterolemic rats could be due to accumulation of lipids in the hepatocytes, and this may account for the marked elevation of liver to body weight ratio observed in rats fed the hypercholesterolemic diet compared to normal control rats.

It has previously been shown that elevations of saturated fatty acids are associated with increased endogenous glucose production in nondiabetic subjects.[16] Fasting plasma

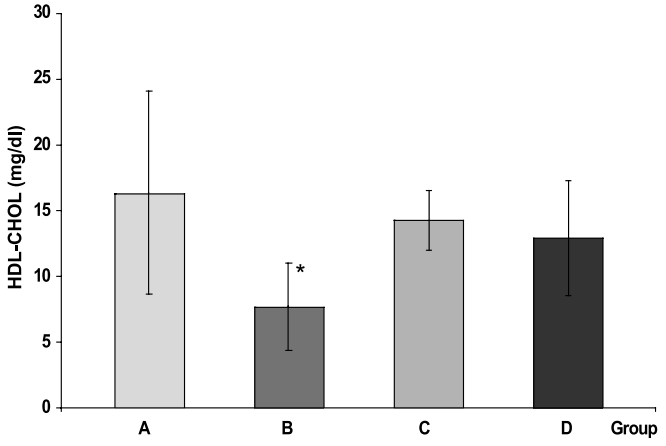

FIG. 4. Effect of aqueous and methanolic leaf extracts of *P. americana* on plasma HDL-CHOL concentration in hypercholesterolemic rats. Values are expressed as means ± SD for six rats. Diets were as follows: Group A, standard chow; Group B, hypercholesterolemic diet; Group C, hypercholesterolemic diet + 10 mg/kg of body weight *P. americana* aqueous extract; Group D, hypercholesterolemic diet + 10 mg/kg of body weight *P. americana* methanolic extract. *Significantly different from normal control at $P < .05$.

glucose was significantly raised in the hypercholesterolemic rats compared to controls. The increased glucose concentration in this study could be due to an increase of free glucose derived from either gluconeogenesis or glycogenolysis. However, administration of *P. americana* leaf extracts caused a reduction in the plasma glucose concentration in the treated animals.

The bark extract of *P. americana* has previously been reported to have antihyperglycemic and antidiabetic properties.[17] It has been suggested that the antihyperglycemic effects attributed to plants are due to their ability to restore the function of pancreatic tissues by causing an increase in insulin output or by inhibiting the intestinal absorption of glucose. Hence treatment with herbal drugs has an effect on protecting β-cells and smoothening out fluctuation in glucose level.[18] It is possible that *P. americana* leaf extract elicits its hypoglycemic action by stimulating secretion of insulin or by enhancement of blood glucose transport to peripheral tissues. A number of other plants have been reported to have antihyperglycemic and insulin stimulatory effects.[19,20]

Determinations of the lipid profile in plasma of rats fed the hypercholesterolemic diet containing groundnut oil, cholesterol, and cholic acid show increased levels of plasma cholesterol compared to normal controls. Also, there was an increase in LDL-CHOL and a decrease in HDL-CHOL. It has been reported that the activity of lecithin:cholesterol acyltransferase, the enzyme involved in the transesterification of cholesterol, the maturation of HDL, and the flux of cholesterol from cell membranes into HDL, tends to decrease in familial or diet-induced situations of hypercholesterolemia.[21,22] It is possible that lecithin:cholesterol acyltransferase activity was inhibited in the hypercholesterolemic rats in this study, resulting in a decreased level of HDL-CHOL. However, treatment of hypercholesterolemic rats with aqueous and methanolic leaf extracts of *P. americana* resulted in a decrease in T-CHOL and LDL-CHOL and a restoration of HDL-CHOL. These observations suggest that the leaf extracts of *P. americana* influence lipid metabolism in hypercholesterolemic rats (by a mechanism not yet known) with consequent lowering of T-CHOL and LDL-CHOL and a restoration of HDL-CHOL levels. It has been shown that HDL-CHOL has the ability to promote efflux of cholesterol from cells, a process that may minimize the accumulation of foam cells in the artery wall and thus protect against the development of atherosclerosis.[23–25]

The antihypercholesterolemic effect of *P. americana* leaf extract seen in this study could represent a protective mechanism against the development of atherosclerosis. It could therefore be concluded that aqueous and methanolic extracts of *P. americana* leaf lower plasma glucose, T-CHOL, and LDL-CHOL levels and increase HDL-CHOL concentrations in the rat, and this could account for its use in folk medicine for the treatment of diabetes and hypertension. However, our results showing the aqueous extract to be more beneficial should be studied further.

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