treated groups. The three doses of *A. gangetica* juice showed no significant difference ($P > 0.05$) when compared with the nondiabetic control and the glibenclamide-treated group.

Figure 2 depicts the ratio of plasma total cholesterol:HDL-cholesterol in the experimental animals. The diabetic control group has the highest value, which was over 300% higher than that of the normal control. Glibenclamide returned this ratio to a level not signifcantly ($P > 0.05$) different from that of the normal control, but significantly ($P < 0.05$) higher than all the groups treated with *A. gangetica* juice.

The influence of the treatments on plasma bicarbonate concentration was represented in Figure 3. *A. gangetica* juice lead to a further significant ($P < 0.05$) increase in plasma bicarbonate in the diabetic rats.

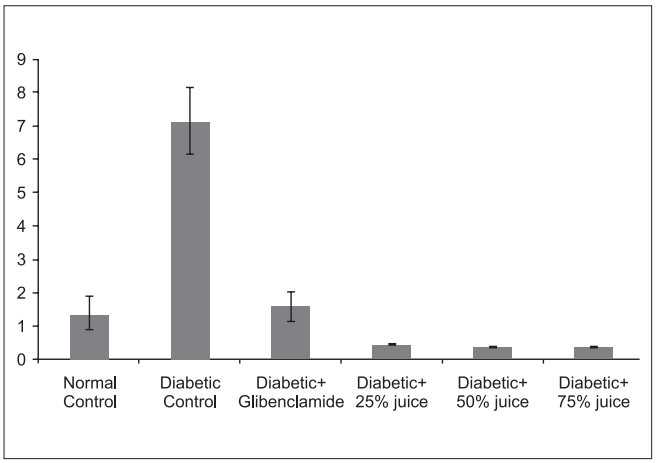

Figure 2: Effect of *A. gangetica* juice on total cholesterol:HDL-cholesterol ratio in the experimental rats (bars represent mean ± SEM)

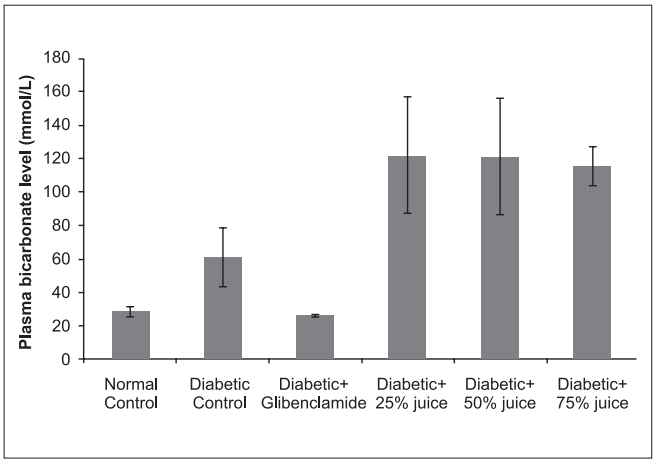

Figure 3: Effect of *A. gangetica* juice on plasma bicarbonate level in the experimental rats (bars represent mean ± SEM)

DISCUSSION

The rise in blood glucose was accompanied by reduction in body weight, an observation that has been reported in other studies.[4,22] In Lee *et al*.'s[22] study, phytic acid was reported to reverse the diabetic-induced wasting. Hence, phytic acid, which is found in very high concentration in vegetables, may be responsible for the hypoglycemic effect of *A. gangetica* juice. It is well recognized that gastrointestinal autonomic neuropathy associated with disordered gastrointestinal motor and sensory function occurs frequently in diabetes.[23] This may contribute to a decrease in the food intake and an eventual weight loss, as observed in this study.

Hyperglycemia induces both oxidative stress (glucose autooxidation and advanced glycosylation end products) and a reductive stress through pseudohypoxia with NAD(P)H in the intima.[22] This redox stress overwhelms the endogenous antioxidants and initiates an oxidative destruction of membrane lipids, leading to increase in TBARS. This indirect biomarker of oxidative stress has been reported to be consistently high in diabetes.[4] The findings of this study show that *A. gangetica* juice as much as glibenclamide reversed the hyperglycemia-induced lipid peroxidation.

The mechanism by which vegetable juice exerts a protective effect appears to be related to a variety of bioactive compounds that can reduce oxidative stress.[12,24] Vegetable juice contains many antioxidants, including carotenoids, tocopherols, ascorbic acid and polyphenols, which is able to quench reactive oxidants (free radicals) and reduce oxidative damage to cell structures. Ezike *et al*.[13] reported the presence of flavonoid in *A. gangetica*. Flavonoids, apart from being antioxidants, have been reported to inhibit sodium-dependent vitamin C transporter 1 (SVCT1) and glucose transporter isoform 2 (GLUT2), the intestinal transporters for vitamin C and glucose, leading to a decrease in the intestinal absorption of glucose.[25]

Hyperglycemia and dyslipidemia as well as oxidative stress generally coexist in diabetic subjects. Dyslipidemia, which includes not only quantitative but also qualitative abnormalities of lipoproteins, plays a significant role in the proatherogenesis of vascular complications in diabetes.[2,26] It is worth nothing that *A. gangetica* juice reduced dyslipidemia and the risk of cardiovascular disease, as indicated by the reduced level of total cholesterol:HDL-cholesterol ratio. In man at least, this ratio is considered to increase the risk of coronary heart disease.[27]

Many dietary factors have been reported to contribute to

the ability of herbs to improve dyslipidemia.[28] Saponin, among other secondary metabolites, is reported to be present in the leaves of *A. gangetica*.[9] This may be responsible for the lipid-lowering effect of this juice on blood lipid. Saponins may lower cholesterol by binding with cholesterol in the intestinal lumen, preventing its absorption, and/or by binding with bile acids, causing a reduction in the enterohepatic circulation of bile acids and increase in its fecal excretion.[28] Increase bile acid excretion is offset by enhanced bile acid synthesis from cholesterol in the liver and consequent lowering of the plasma cholesterol.[26] Kumarappan *et al*.[29] reported that administration of polyphenol to alloxan-induced diabetic rats reversed hyperlipidemia, and they attributed this to a reduction in the activity of hepatic HMG-CoA reductase. The antidyslipidemic effect of *A. gangetica* juice can therefore be linked to the synergistic action of these phytochemicals.

Diabetes-induced hyperlipidemia is attributable to excess mobilization of fat from the adipose due to underutilization of glucose.[28] The lack of insulin and elevations of the counter-regulatory hormones lead to activation of enzymes that stimulate lipolysis in the adipose tissue and ketogenesis in the liver. During the process of ketogenesis, free fatty acids are transformed into acetoacetate and β-hydroxybutyrate. Acetone, the least-abundant ketone body, is generated by spontaneous decarboxylation of acetoacetate. Diabetic ketoacidosis is characterized by elevated ketone bodies in the blood and metabolic acidosis, as characterized by a high level of bicarbonate.[28,30] Glibenclamide, a sulphonylurea, produces hypoglycaemia by increasing the secretion of insulin from pancreas.[31] Therefore, the inability of the juice to reduce ketoacidosis suggests that the reduction of plasma glucose might be a consequence of reduced intestinal absorption rather than an increase in the uptake and/or utilization by glucose-sensitive tissues due to an increased insulin secretion from β-cells of islets of Langerhans or because of the insulin-like actions of some components of the herb. Hence, the increase in diabetic acidosis in the diabetic rats is a point of concern in using the juice of *A. gangetica* to manage diabetes.

REFERENCES

1. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025; Prevalence, numerical estimates and projections. Diabetes Care 1998;21:1414-20.
2. Sobngwi E, Mauvais-Jarvis F, Vexiau P, Gautier JF. Diabetes in Africans: epidemiology and clinical specificities. Diabetes Metab (Paris) 2001;27:628-34.
3. Rotimi CN, Dunson GM, Berg K, Akinsete O, Amoah A, Owusu A. In search of susceptibility Genes for Type 2 diabetes in West Africa: The design and results of the first phase of the AADM study. Ann Epidemiol 2001;11:51-8.
4. Rotimi SO, Olayiwola I, Ademuyiwa O, Adamson I. Inability of legumes to reverse diabetic-induced nephropathy in rats despite improvement in blood glucose and antioxidant status. J Med Food 2010;13:163-9.
5. Ajgaonkar SS. Herbal drugs in treatment of diabetes mellitus: a review. Int Diabetes Fed Bull 1979;24:10-9.
6. Marles RJ, Fanis-Worth WR. Antidiabetic plants and their active constituents. Phytomedicine 1994;2:93-9.
7. Gill LS. Ethnomediacal uses of plants in Nigeria. Benin City: Uniben Press; 1992. p. 33.
8. Marim R. Ethnobotanical investigation among tribes in Madurai district of Tamil Nadu (India). J Ethnobiol Ethnomed 2006;2: 25-32.
9. Akah PA, Ezike AC, Nwafor SV, Okoli CO, Enwerem NW. Evaluation of anti-asthmatic property of *Asystasia gangetica* leaf extracts. J Ethnopharm 2003;89:25-36.
10. Soladoye MO, Sonibare MA, Nadi AO, Alabi DA. Indigenous angiosperm biodiversity of Olabisi Onabanjo University permanent site. Afr J Biotech 2002;4:554-62.
11. Yeoh HH, Wong PF. Food value of lesser utilized tropical plants. Food Chem 1993;46:239-41.
12. Okudu HO. Effect of drying on the nutrient contents of some Nigerian green leafy vegetable. Nig J Nutri Sci 2008;29:232-6.
13. Ezike AC, Akah PA, Okoli CO. Bronchospasmolytic activity of the extract and fractions of *Asystasia gangetica* leaves. Int J App Res Nat Prod 2008;1:8-12.
14. Daziel JM. The useful Plants of West Tropical Africa. Apapa, Lagos: Nigeria National Press Limited; 1968. p. 232-3, 56.
15. Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Ann Clin Biochem 1969;6:24-31.
16. Biggs HG, Erikson TA, Moorehead WR. A manual colorimetric assay of triglyceride in serum. Clin Chem 1975;21:47.
17. Zlatkis A, Zak B, Boyle AJ. A new method for the direct determination of serum cholesterol. J Lab Clin Med 1953;41: 486-92.
18. Gidez LI, Miller GJ, Burstein M, Slagle S, Eder HA. Separation and quantitation of subclasses of human plasma high density lipoproteins by simple precipitation procedure. J Lipid Res 1982;23:1206-23.
19. Friedewald WT, Levy RE, Frederickson DS. Estimation on the concentration of low density lipoprotein cholesterol in plasma without use of the ultracentrifuge. Clin Chem 1972;18:499-502.
20. Forrester RL, Wataji LJ, Silverman DA, Pierre KJ. Enzymatic method for the determination of CO2 in serum. Clin Chem 1976;22:243-50.
21. Buege JA, Aust SD. Microsomal lipid peroxidation. Methods Enzymol 1978;52:302-5.
22. Lee S, Park H, Cho A, Jung H, Cho S, Cho Y, *et al*. Effects of dietary phytic acid on serum and hepatic lipid levels in diabetic KK mice. Nutr Res 2005;25:869-76.
23. Schmidt RE. Neuropathology and pathogenesis of diabetic autonomic neuropathy. Int Rev Neurobiol 2002;50:257-92.
24. Kawashima A, Madarame T, Koike H, Komatsu Y, Wise JA. Four week supplementation with mixed fruit and vegetable juice concentrates increased protective serum antioxidants and folate and decreased plasma homocysteine in Japanese subjects. Asian Pac J Clin Nutr 2007;16:411-21.
25. Song J, Kwon O, Chen S, Daruwala R, Eck P, Park JB, *et al*. Flavonoid Inhibition of Sodium-dependent Vitamin C Transporter 1 (SVCT1) and Glucose Transporter Isoform 2 (GLUT2), intestinal transporters for vitamin c and glucose. JBC 2002;277:15252-60.

26. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology and management. JAMA 2002;287:2570-81.
27. Ademuyiwa O, Ugbaja RN, Rotimi SO. Plasma lipid profile, atherogenic and coronary risk indices in some residents of Abeokuta in south-western Nigeria. Biokemistri 2008;20:85-91.
28. Nimenibo-Uadia R. Effect of aqueous extract of *Canavalia ensiformis* seeds on hyperlipidaemic and hyperketonaemia in alloxan-induced diabetic rats. Biokemistri 2003;15:7-15.
29. Kumarappan CT, Rao TN, Mandal SC. Polyphenolic extract of *Ichnocarpus frutescens* modifies hyperlipidemia status in diabetic rats. J Cell Mol Biol 2007;6:175-85.
30. Sefedini E, Prašek M, Metelko Ž, Novak B, Pinter Z. Use of capillary β-hydroxybutyrate for the diagnosis of diabetic ketoacidosis at emergency room: our one-year experience. Diabetologia Croatica 2008;37:73-8.
31. Singh M, Balamurugan M, Gupta A, Yadav S, Sharma A, Acharya AY, *et al*. Antidiabetic activity of glibenclamide loaded liposomes in alloxan induced diabetic. Ars Pharm 2007;48:31-6.

Source of Support: Nil, **Conflict of Interest:** None declared