Current Trends in Technology and Science
ISSN : 2279-0535. Volume : II, Issue : III

Anti-Hyperlipidemic Activity of Aqueous Extract of Carica Papaya Seed in Albino Rats fed with High Fat Diet

Nwangwa, E.K[1].
[1]Department of Physiology, Faculty of Basic Medical Science, College of Health Science, Delta State University, P.M.B 001, Abraka, Delta State, Nigeria. drezekingx@yahoo.com

Ekhoye, E.I.[1]
[1]Department of Physiology, Faculty of Basic Medical Science, College of Health Science, Delta State University, P.M.B 001, Abraka, Delta State, Nigeria. tareonline@yahoo.com

Abstract — The global prevalence of obesity is increasing rapidly and high dietary fat intake is a major risk factor for the development of obesity. The present study was undertaken to evaluate the effect of Carica papaya seed aqueous extract on serum lipid profile in Wistar rat fed with high fat diet (HFD) and to compare it with a standard hypolipidaemic drug simvastatin. Thirty healthy albino Wistar rats were randomized into 5 groups of 6 animals each. . The groups were treated as follows: Group A: normal diet (ND); Group B: HFD (vanaspati ghee + coconut oil mixture in ratio of 3:2 at 10 ml/kg/day); Group C: HFD+ C. papaya (200 mg/kg/day); Group D: HFD + C. papaya (300 mg/kg/day); Group E: HFD + simvastatin (1.8 mg/kg/day). Lipid profile was estimated after 5 weeks of treatment. Result show that aqueous extract of Carica papaya showed a significant ($p<0.05$) reduction in total cholesterol (g/dl), Triglyceride (g/dl), Low density lipoprotein (g/dl) levels and significant ($p<0.05$) increase in high density lipoproteins (g/dl) in hypercholesteromic rats. Therefore, aqueous extract of Carica papaya have lipid lowering potential and could be explored further for possible use in management of hypercholesterolaemia.

Keyword —Carica papaya, High fat diet, Lipid profile, Hyperlipidemia, Simvastatin

1. INTRODUCTION

The global prevalence of obesity is increasing rapidly among adults as well as among children and adolescents in places where high dietary fat intake is a major risk factor for the development of obesity [1]. Obesity is reaching epidemic proportions worldwide; it is correlated with various comorbidities, among which the most relevant are dyslipidemia [2], diabetes mellitus T2DM [3], fatty liver (which can later progress to nonalcoholic fatty liver disease [4], cardiovascular (CV) diseases such as heart failure (HF) and coronary heart disease (CHD) [5].

In recent times, focus on plant research has increased all over the world and a large body of evidence has to show immense potential of medicinal plants used in various traditional systems [6]. Fruits have been part of human diet and food supplement over the years. The rise in nutritional importance of fruit has been stimulated by range of degenerative disease prevalent in many part of the world. However, fruits are increasingly becoming popular in Nigerian diet [7]. Attention has been given to some tropical fruits that are of economic importance [8] among which Carica papaya is one. Carica papaya fruit is one of the most nutritional fruits grown and consumed in Africa. Studies had demonstrated the use of seed extract of Carica papaya as a tonic for the heart, analgesic and treatment for stomach ache [9] and have antioxidant properties [10]. It has offered some protection against oxidative damage to body tissues [11]. The antioxidant systems present in Carica papaya play a protective role against the production of reactive oxygen species and lipid peroxidation by-products. Recent reports have implicated Reactive Oxygen Species (ROS) in the pathogenesis of many human diseases [12]. Reactive Oxygen Species (ROS) are free radicals generated as byproducts of normal aerobic metabolism and also from reactions with drugs and toxins [13]. Excessive production of reactive oxygen species however, results in alteration in the balance between ROS and endogenous antioxidants and creates oxidative stress which is implicated in many pathological conditions such as diabetes [14], cardio vascular disease [13], cancer, Alzheimer's disease and ageing [15], atherosclerosis [16,17]. Some of these medicinal plants used in ethno medicine for the treatment and management of many of these diseases have been investigated for their antioxidative properties [18]. Many of the metabolites from these medicinal plants especially flavonoids exhibited potent antioxidant activity in vitro and in vivo [19,20,21]. In view the above background, the present study has been undertaken to evaluate the effect of Carica papaya on serum lipids in albino rats fed with high fat diet (HFD) and to compare it with a standard hypolipidaemic drug simvastatin.

2. MATERIALS AND METHODS

2.1 Plants Authentication and Extract Preparation:

Matured fresh C. papaya fruit was bought from a local market in Abraka, and was authenticated at the Botany Department, Delta State University, Abraka. The fruit was cut and the seeds were collected, air dried and later

grounded. The grounded C. papaya seed was weighed, 170g of the grounded seed was soaked in 2000ml of distill water for 72 hours and the residue was separated from the solvent. The solvent was concentrated to a paste like solid with a heating mantle yielding 36g. The extract was kept in a clean container and refrigerated until use.

2.2 Animal Handling:

Thirty male albinoWistar rats weighing between (173 – 305g) obtained from the animal house of the Faculty of Basic Medical Sciences, University of Benin, Benin City, were used for the study. They were kept in rat cages in a well-ventilated house, at the Animal House of the Faculty of Basic Medical Sciences, Delta State University and were exposed to 12 hours light and 12 hours darkness and they were fed with clean tap water and rat chow once daily (8.00am - 9.00am). They were allowed to acclimatize for fourteen (14) days prior to the experiment. The experiment was carried out for a period of 5 weeks. All the animals were taken care of under ethical consideration and the experimental protocol was duly approved by institutional ethic committee.

2.3 Method of Preparation of Simvastatin Suspension:

The stock solution was prepared by dissolving 20 mg of simvastatin in 70 ml of normal saline and used as a standard drug in a dose of 1.8 mg/kg body weight for the respective group. The daily dose of simvastatin for rats was calculated by extrapolation from the human dose (20 mg/day) as described by Gosh [22].

2.4 Method of Preparation of High Fat Diet:

Vanaspati ghee and edible coconut oil were procured from the market and a mixture of the two was prepared in a ratio of 3: 2 respectively v/v as per method of Shyamala et al. [23]. Hyperlipidemia was induced in the rats by single daily oral dose of 10m/kg body weight in addition to normal diet for the entire experimental period.

2.5 Experimental Design:

A total of thirty (30) Wistar albino rats were randomly divided into five groups of six rats each.

Group A: (Normal Control): Male rat treated with normal saline.

Group B: (Hyperlipidaemic Control Group): Male rat fed with High fat diet

Group C: Male rat fed High fat diet, and then received a dose of 200mg/kg of aqueous extract of C. papaya seed.

Group D: Male rat fed High fat diet, and then received a dose of 300mg/kg of aqueous extract of C. papaya seed.

Group E: Male rat fed High fat diet, and then received a dose of Simvastatin (1.8 mg/ kg/day).

The drugs were administered to the animals in the doses given above daily, by means of an orogastric cannula.

Collection of Samples: The rats were weighed weekly for five (5) weeks and mean weight was obtained and recorded after which they were sacrificed by decapitation after an overnight fast. Blood samples were collected from the heart by cardiac puncture in clean specimen bottles and the serum was immediately separated and stored until used for analysis of lipid profile. This was done twenty four (24) hours after the last treatment.

2.6 Lipid Profile Analysis:

After separation of serum from blood, the various parameters of lipid profile were estimated; they include Total Cholesterol (TC), Triglycerides, (TG), Low Density Lipoprotein Cholesterol (LDL), High Density Lipoprotein Cholesterol (HDL). Serum LDL was estimated by calculation based on Friedwald et al. [24]

LDL mg/dl = Total cholesterol – HDL - TG/5.

2.7 Statistical Analysis- Data was represented as mean ± SEM, and subjected to One-way Analysis of Variance (ANOVA) using Statistical software SPSS 17. A level of $p<0.05$ was considered as statistically significant.

3. RESULTS

This study showed the changes on the serum level of total cholesterol, triglycerides, high density lipoprotein and low density lipoprotein; due to the effect of Carica papaya. Simvastatin was used as a standard for improving the lipid profile. The charts below show the effect of C. papaya on total cholesterol, triglyceride, high density lipoprotein and low density lipoprotein.

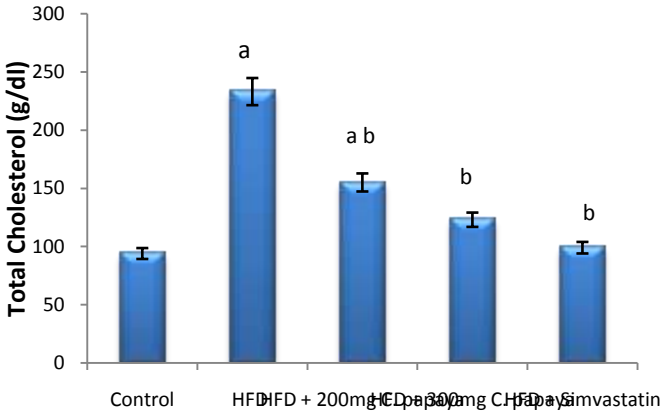

Fig 1 Effect of Carica papaya on Total Cholesterol (n=6): a: $p < 0.05$ when compared with Normal Control Group; b : $p < 0.05$ when compared with Hyperlipidaemic Control Group

Current Trends in Technology and Science
ISSN : 2279-0535. Volume : II, Issue : III

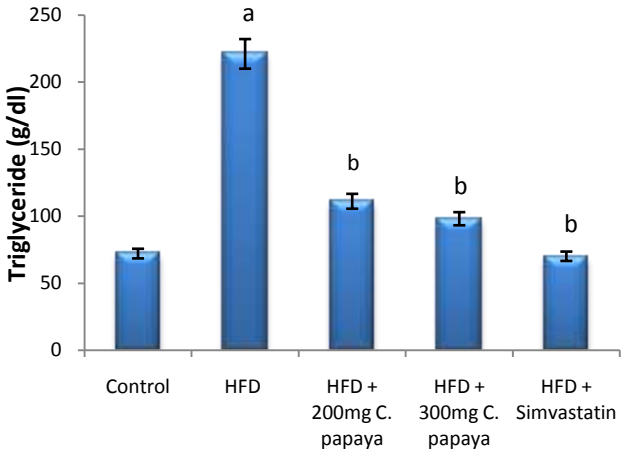

Fig 2 Effect of Carica papaya on Triglyceride (n=6):
a: $p < 0.05$ when compared with Normal Control Group; b : $p < 0.05$ when compared with Hyperlipidaemic Control Group

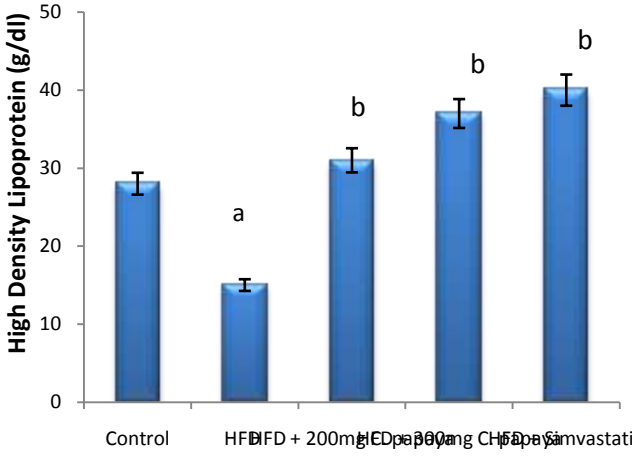

Fig 3 Effect of Carica papaya on High Density Lipoprotein (n=6):
a: $p < 0.05$ when compared with Normal Control Group; b : $p < 0.05$ when compared with Hyperlipidaemic Control Group

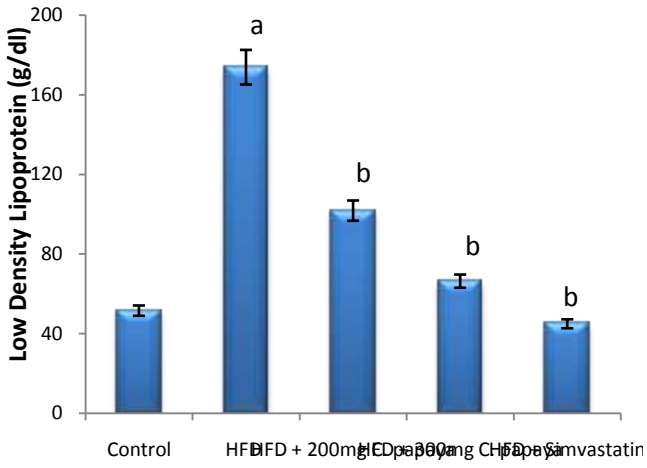

Fig 4 Effect of Carica papaya on Low Density Lipoprotein (n=6):
One Way ANOVA.a: $p < 0.05$ when compared with Normal Control Group; b : $p < 0.05$ when compared with Hyperlipidaemic Control Group

The results showed that there was a significant increase in all the lipid parameters ($p < 0.05$) except HDL after the administration of high fat diet when compared to control group. It also showed that concomitant administration of the C. papaya at a dose of 200 mg/kg and 300 mg/kg body weight along with HFD fed animals, showed a significant decrease in all the lipid parameters ($p < 0.05$) with a significant rise in HDL ($p < 0.05$) level as compared to hyperlipidemic control rats.
Standard drug simvastatin, at a dose of 1.8 mg/kg administered along with high fat diet, showed a significant decrease ($p < 0.05$) in all the lipid parameters while there was a significant ($p < 0.05$) increase in HDL level. The Hypolipidaemic activity of the aqueous extract of the plant was found to be less efficacious than that of the standard drug simvastatin in compared to the control.

4. DISCUSSION

Measurement of major lipids like cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides can give useful information about the functioning of the heart [25]. High concentrations of all lipids except the HDL are associated with an increased risk of atherosclerosis. High levels of triglycerides and LDLs are also associated with coronary artery disease [26].
Flavonoids.saponins and tannins which were present in the phytochemical analysis of the Carica papaya seed extract have been speculated to play significant roles in the metabolism of lipids [27]
In this study, the mean level of the total cholesterol, triglyceride and low density lipoprotein were significantly ($p<0.05$) decreased, the high density lipoprotein was significantly ($p<0.05$) increased due to the effect of Caricapapaya. This hypolipidemic effect of Carica papaya

could be related to its chemical composition, which shows the presence of alkaloids, flavonoids, saponin and cardiac glycosides. All these components are known to reduce serum lipid level in animals [28,29].

The reduction in the serum total cholesterol levels following the administration of the extract may be attributed to reduction in the concentration of acetyl CoA resulting from decreased β-oxidation of fatty acids since acetyl CoA is a key substrate in the biosynthesis of cholesterol [30]. The reduction observed in the serum triglyceride level can be adduced to inhibition of lipolysis [31]. It can also be attributed to the antioxidant activities of saponins which might have interfered with the oxidation of fatty acid [32]. The significant reduction in the LDL is understandable since a reduction in total cholesterol should normally result in reduction of LDL [33]. The increase in high density lipoprotein following the administration of aqueous extract of Carica papaya can be clinically beneficial. It has been demonstrated that an increase in the concentration of HDL correlates inversely with coronary heart disease [34]. This is because HDL removes cellular cholesterol and transports it to the liver where it is converted to bile acids and eventually excreted from the body [33]; and as such will reduce the risk of coronary artery disease.

5. Conclusion

Administration of Carica papaya produced a significant improvement in the lipid profile by lowering total cholesterol, LDL and triglycerides and by increasing HDL level thus helping in retarding the secondary complications. It has anti-lipidemic and anti-cholestrolemic activities and as such could be used in the management of hypercholesterolemic. This study thus, supports the acclaimed use of the plant in the management of hypertension.

Reference

[1] Canbakan B, Tahan V, Balci H, Hatemi I, Erer B, Ozbay G, Sut N, Nacibekiroglu M, Imeryuz N, Senturk H: Leptin in nonalcoholic fatty liver disease. Ann Hepatol, (2008). 7:249-54.

[2] Fried M, Hainer V, Basdevant A, Buchwald H, Dietel M, Finer N, Greve JW, Horber F, Mathus-Vliegen E, Scopinaro N, Steffen R, Tsigos C, Weiner R, Widhalm K. Interdisciplinary European guidelines on surgery for severe obesity. RozhlChir. (2008). 87:468-76.

[3] Pagotto U, Vanuzzo D, Vicennati V, Pasquali RG: Pharmacological therapy of obesity. G ItalCardiol (Rome). (2008). 9(4 Suppl 1):83S-93S.

[4] Marović D. Elevated body mass index fatty liver. SrpArhCelokLek, .(2008). 136:122-5.

[5] Lavie CJ, Artham SM, Milani RV, Ventura HO. The obesity paradox: impact of obesity on the prevalence prognosis of cardiovascular diseases. Postgrad Med, (2008). 120:34-41.

[6] Omotade O., Jeferson F., Daniel R., Joao R., Magareth A., Aline B. Antioxidative Properties of Ethyl Acetate Fraction of Unripe Pulp of Carica Papaya in Mice. Journal of Microbiology, Biotechnology and Food Sciences: (2011). 1 (3) 409-425.

[7] Dahanukar, S.A., Kulkarni, R.A. and Rege N.N. Pharmacology of medicinal plants and natural products; Indian Journal of Pharmacology. (2000); 32: S81 – S118.

[8] Glombitza, K.W., G.H. Mahran, Y.W. Mirhon, K.G. Michael and T.K. Motawi. Hypoglycemic and Antihyperglycemic Effects of ZizyplusSpinachristi in Rats.Planta.Med. (1993).pp: 244-247.

[9] GioveNakazawa, R.A. (1996). Traditional medicine in the treatment of enteroparasitosis.In Rev Gastroenterol Peru Journal, vol. 16, p .197–202.

[10] Rahmat, A., Abubakar, M.F., Faezah, N. Hambali, Z. The effect of consumption of guava (Psidiumguajaya) or Carica papaya on total antioxidant and lipid profile in normal male youth.In Asia Pacific Journal of Clinical and Nutrition, (2004).13, p.106.

[11] Indran, M., Mahmood, A.A. Kuppusamy, U.R. Protective Effect of Carica papaya L Leaf Extract against Alcohol Induced Acute Gastric Damage and Blood Oxidative Stress in Rats. In West Indian Medical Journal, (2008).vol. 57(4), p. 323-326.

[12] Repetto, M.G. - Llesuy,S.F. Antioxidant properties of natural compounds used in popular medicine for gastric ulcers.In Brazilian Journal of Medical and Biological Research, (2002). 35, p. 523-534.

[13] Singh Deveraj, U. Jialal, I. Vitamin E, oxidative stress and inflammation. In AnnualReview of Nutrition, (2005). 25, 151-174.

[14] Choi, E. - Hwang, J. Effects of some medicinal plants on plasma antioxidant system and lipid levels in rats.InPhytotherapy Research, (2005). 19, 382-386

[15] Surh, Y.Z. - Fergusson, L.R. Dietary and medicinal antimutagens and anticarcinogens: Molecular mechanisms and chemopreventive effects of selected dietary and medicinal phenolic substances.In Mutation Research Fundamental Molecular Mechanisms and Mutagenesis. (2003). 1-8,p. 523-524.

[16] Landmesser, U.- Drexler, H. Towards understanding superoxide dismutase regulation in atherosclerosis.In Arteriosclerosis Thrombosis Vascular Biology, (2002). 1(22), p.1367-1370.

[17] Shah, P.K. - Kaul, S. - Nilsson, J. Exploiting the vascular protective effect of high density lipoprotein and its apolipoproteins.In Circulation. (2001). 104, 2498-2502.

[18] Semiz, A. Sen, A. Antioxidant and chemoprotective properties of MomordicaCharantia(bitter melon) fruit extract.In Africa Journal of Biotechnology, (2007). 6: 273- 277.

[19] Usoh, I.F.-Akpan, E.J.- Etim, E.O.- Farombi, E.O. Antioxidant actions of dried flower extracts of Hibiscus sabdariffa L on Sodium arsenite-induced oxidative

stress in rats. In Pakistan Journal of Nutrition, (2005). 4: 135-141.

[20] Sofidiya, M.O. Odukoya, O.A. Familoni, O.B. Inya-Agha, S.T. Free radicals scavenging activity of some Nigerian medicinal plant extracts.In Pakistan Journal of Biology and Science. (2006). 9: 1438-1441

[21] Nwanjo, H.U. Free radicals scavenging potential of the aqueous extract of Viscum album (Mistletoe) leaves in diabetic wistar rats hepatocytes. In Internet Journal of Nutrition and Wellness. (2007).

[22] Ghosh MN. Fundamentals of experimental Pharmacology.Edn 3, Hilton and company, Calcutta, (2005): pp. 191-201.

[23] Shyamala MP, Venukumar MR, Latha MS. Antioxidant potential of the Syzygiumaromaticum (Gaertn) Linn (Cloves) in rats fed with high fat diet. Indian Journal of pharmacology. (2003). 35: 99-103.

[24] Friedwald WT, Levy RI, Frederickson DS.Estimation of LDL Cholesterol in plasma without preparation of ultracentrifuge.Clinical Chemistry.(1972). 18: 449-502.

[25] Chawla, R. Kidney Function Tests. In: Practical Clinical Biochemistry. Methods and Interpretation.2nd edition. JAYPEE Brothers Medical Publishers (P) Ltd., New Delhi, India. (1999). pp. 90-92.

[26] Chang, J., Chen, T., Chan, P., Chen, Y., Hsu, F., Lo, M. and Lin, J. The in vitro inhibitory effect of tannin derivatives on 3-hydroxyl-3-methyglutaryl-Coenzyme A reductase on vero cells.Pharmacology (2001). 62: 224-228.

[27] Abolaji, A. O., Adebayo, A. H. and Odesanmi, O. S. Effect of ethanolic extract of Parinaripolyandra (Rosaceae) on serumlipid profile and some electrolytes in pregnant rabbits. Research Journal of Medicinal Plants (2007). 1: 121-127

[28] Barry IA, Abdel-Hassan JA, Mohammed TS. The hypoglycaemic and antihyperglycaemic effect of Citrulluscolocynthis fruit aqueous extract in normal and alloxan diabetic rabbits. J. Ethnopharmacol. (2000). 71: 325-330.

[29] Ezekwe CI, Obidoa O. Biochemical effect of Vernoniaamygdalina on rats liver microsome. Niger. J. Biochem. Mol. Biol. (2001). 16: 1745-1798.

[30] Rang A.P., Dale M.M and Ritter J.M. Pharmacology. 3rd edition. Churchill Livingstone. New York. (1995). Pg 409.

[31] Owoyele, B.V., Yakubu, M.T., Alonge, F., Olatunji, L.A. and Soladoye, A.O. Effects of folic acid intake on serum lipid profile on apparently healthy young adult male Nigerians. African Journal of Biomedical Research.(2005). 8: 139-142.

[32] Rao, A.V Role of dietary sources of saponins in chemotherapy strategy of lowering the risk of human cancers. Medical Research publishers University of Toronto, Toronto. (1993). 219-225.

[33] Mayes, P. A. Lipid transport and storage. In: Harper's Biochemistry, 24th edition Murray, R.K., Granner, D.K; Mayes, P.A. and Rodwell, V.W. (eds). Prentice Hall International, Inc., USA. (1996). 254.

[34] Philip, D.M. Plasma enzymes in diagnosis. In: Clinical Chemistry in Diagnosis and Treatment. 6th edition.Arnold Publishers, London. (1995). 303-307.