

Effect Of Justicia Carnea Leaf Extract On The Liver Enzymes Of High-Fat Diet Fed Wistar Rats

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Abstract

There is a gradual shift from the traditional high residue, unprocessed or minimally processed 'African' diet to low residue highly processed diets which appear usually delicious and attractive. High-fat diet alters lipid metabolism thereby predisposing to cardio-metabolic disorders including hypertension, fatty liver disease, hyperlipidaemia and atherosclerosis. The present study investigated the effect of *Justicia carnea* (JC) leaf extract on the liver enzymes in high-fat diet fed wistar rats. The study involved a total of twenty-five wistar rats separated into five groups of five rats each. Group 1 served as control while groups 2 to 5 were fed with high-fat diet (HFD) throughout the period of the experiment. Group 2 remained untreated, Groups 3, 4 and 5 received respectively 200mg/kg, 500mg/kg and 1000mg/kg of JC leaf extract. The animals were fed with the extract for twenty-eight days and thereafter blood samples were collected for assessment of the liver enzymes using standard methods. Results showed that HFD did not cause any significant effect on the liver enzymes compared to control. Oral administration of 200mg/kg and 500mg/kg of JC extract caused significant increase in alkaline phosphatase (ALP) but no significant change in alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma-glutamyl transferase (GGT). However, consumption of 1000mg/kg of JC leaf extract significantly reduced the plasma levels of ALT but no significant changes in AST, ALP and GGT. This signifies a potential hepato-protective property of the extract, probably resulting from antioxidant and increased plasma lipid lowering effects reported in other studies. Conclusively, the present study suggests that JC leaf extract possesses possible hepato-protective potential when administered at higher concentrations in wistar rats.

Keywords: *Justicia carnea*, liver enzymes, high-fat diet.

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I. Introduction

In many cities, there is a gradual shift from the traditional high residue, unprocessed or minimally processed African diet to low residue highly processed diets (1). The highly processed flour or butter-based foods appear very delicious and attractive, hence its increased demand. A high-fat diet is one in which at least 35% of the caloric intake is derived from fats (2). Consumption of these high-fat diets (especially without commensurate increase in physical activity) has been well associated with rising prevalence of obesity and its complications even in animal models (1, 3, 4, 5). High-fat diet alters lipid metabolism thereby predisposing to cardiometabolic disorders including hypertension, fatty liver disease, hyperlipidaemia and atherosclerosis (6, 7, 8, 9, 10, 11). Some studies suggest that consumption of high-fat diet (HFD) triggers metabolic reactions in the mitochondria and endoplasmic reticulum leading to lipogenesis, inflammation and oxidative stress (12). This mechanism accelerates the development of non-alcoholic fatty liver disease (13). Previous studies have examined several modalities to ameliorate the effect of high fat diet including lifestyle modifications and use of plant products in human and animal experiments (14, 15, 16, 17; 18). Previous studies using animal models have proven some of the nutritional and therapeutic benefits of *Justicia carnea* including; lipid lowering effect (18), enhanced intestinal transit (19), hematinic property (20, 21) and antioxidant potential (22). The present study would investigate the effect of *Justicia carnea* leaf extract on the liver enzymes of high-fat diet fed wistar rats.

A significant increase in the levels of the transaminases [(alanine aminotransferase (ALT) and aspartate aminotransferase (AST)] characterizes the most typical abnormality in the liver function tests. Elevated level of these liver enzymes in plasma is commonly associated with hepatocellular liver injury, characterized by inflammation of the liver cells as well as damage to the liver cells themselves (23) as they tend

to leak into the circulation when the liver is damaged. ALT is a more specific indicator of liver inflammation than AST, which may be elevated in conditions affecting other organs.

II. Materials And Methods

The present study was conducted at the animal house of the department of Human Physiology, faculty of Basic Medical Sciences, University of Port Harcourt, Nigeria. Ethical approval was obtained from the university of Port Harcourt Research Ethics Committee with approval number; UPH/ CEREMAD/ REC/ MM82/030. The leaves of *Justicia carnea* used in this study were bought from an open market and identified in the Plant Science and Biotechnology department, University of Port Harcourt. Thereafter the leaves were processed to prepare the extract used for the study. A total of twenty-five male wistar rats were used for the research and allowed access to feed and water *ad libitum*. These were separated into five groups of five rats each; Group 1 (which served as control and received normal animal chows and distilled water), Group 2 (received High fat diet and water), Group 3 (received High fat diet + 200mg/kg of body weight of the extract), Group 4 (received High fat diet + 500mg/kg body weight of the extract) while Group 5 (received High fat diet + 1000mg/kg body weight of the extract). The daily dose of the extract was respectively administered orally to the animals for 28 days. Thereafter, each animal was anesthetized and blood samples collected to measure the liver enzymes; ALT, AST, alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) using standard methods.

Statistical package for social sciences (SPSS) version 22.0 was used for data analysis. Results were presented in tables. Continuous variables were expressed as mean \pm Standard error of mean (SEM). Statistical difference was determined using analysis of variance (ANOVA) and at $p < 0.05$.

III. Results And Discussion

Table 1: Effect of *Justicia carnea* leaf extract on liver enzymes

Group	ALT (IU/l)	AST (IU/l)	ALP (IU/l)	GGT (IU/l)
Control	6.48 \pm 0.26	21.60 \pm 1.12	37.40 \pm 0.75	9.92 \pm 0.93
HFD only	5.38 \pm 0.88	19.20 \pm 1.86	43.00 \pm 2.03	9.93 \pm 0.43
HFD + 200mg/kg of extract	5.42 \pm 0.32	18.80 \pm 1.24	62.60 \pm 2.48*#	9.08 \pm 0.96
HFD + 500mg/kg of extract	5.88 \pm 0.29	19.20 \pm 2.40	57.40 \pm 2.62*#	9.38 \pm 0.91
HFD + 1000mg/kg of extract	4.78 \pm 0.38*	19.40 \pm 1.69	44.20 \pm 3.60	8.78 \pm 0.82

* Significantly different compared to control,

Significantly different compared to HFD only

In some studies, administration of HFD has been used to induce non-alcoholic fatty liver disease (NAFLD) in animal models (9, 24, 25). Results of the present study showed that HFD did not cause any significant change in the concentrations of liver enzymes (ALT, AST, ALP and GGT) in wistar rats. This is probably because other studies suggest that over 50% of cases of NAFLD may have normal levels of AST and ALT (26). However, in another study involving high fat fructose diet, significant alterations of the liver oxidative enzymes were noted (27). In our study, daily oral administration of 200mg/kg and 500mg/kg of *Justicia carnea* (JC) leaf extract for 28 days had no significant effect on the ALT, AST and GGT concentrations compared to both the control and the HFD only groups as shown in the table above. However, these lower doses (200mg/kg and 500mg/kg) caused significant increases in the ALP concentrations compared to both the control and the HFD only groups. Although elevated serum ALP levels are often reported in liver and bone diseases, it can also result from other sites such as intestines and placenta and may occur without any underlying disease (28, 29, 30).

ALT is an enzyme found predominantly in the liver and indicates liver cell injury (31). A reduction in the levels of ALT from previously high levels could signify recovery of initially injured hepatocytes (32). Daily administration of 1000mg/kg of the JC leaf extract caused a significant reduction in ALT levels but no significant effects on the AST, ALP and GGT levels compared to the control group. JC leaf extract has been reported to contain flavonoids (33, 34) which are antioxidants (35). Studies have shown that antioxidants possess hepato-protective properties (36, 37). Also other studies showed that JC leaf extract increased intestinal motility and faecal lipid excretion (18, 19). These reported effects of JC thus, reduce the deleterious effects of high fat diet on the liver. This probably explains reduction in the ALT levels following consumption of 1000mg/kg of JC leaf extract. The result of the present study suggests that the hepato-protective potentials of JC on high-fat diet fed wistar rats are observed when consumed in high doses. Conclusively, JC leaf extract possesses hepato-protective potentials at higher doses probably due to its antioxidant potentials.

References

- [1] Wang, L., Wang, H., Zhang, B., Popkin, B. M., & Du, S. (2020). Elevated Fat Intake Increases Body Weight And The Risk Of Overweight And Obesity Among Chinese Adults: 1991-2015 Trends. *Nutrients*, 12(11), 3272.

- <https://doi.org/10.3390/Nu12113272>.
- [2] Qiao, J., Wu, Y., & Ren, Y. (2021). The Impact Of A High Fat Diet On Bones: Potential Mechanisms. *Food & Function*, 12(3), 963–975. <https://doi.org/10.1039/D0fo02664f>.
- [3] Nwafor, A., Mmom, F., Obia, O., Obiandu, C., Hart, V. O., & Chinko, B. C. (2015). Relationship Between Blood Pressure, Blood Glucose And Body Mass Index And Coexisting Prehypertension And Prediabetes Among Rural Adults In Niger Delta Region, Nigeria. *British Journal Of Medicine And Medical Research*. 9 (7), 1-12.
- [4] Konda, P. Y., Poondla, V., Jaiswal, K. K., Dasari, S., Uyyala, R., Surtineni, V. P., Egi, J. Y., Masilamani, A. J. A., Bestha, L., Konanki, S., Muthulingam, M., Lingamgunta, L. K., Aloor, B. P., Tirumalaraju, S., Sade, A., Ratnam Kamsala, V., Nagaraja, S., Ramakrishnan, R., & Natesan, V. (2020). Pathophysiology Of High Fat Diet Induced Obesity: Impact Of Probiotic Banana Juice On Obesity Associated Complications And Hepatosteatosis. *Scientific Reports*, 10(1), 16894.
- [5] Li, J., Wu, H., Liu, Y., & Yang, L. (2020). High Fat Diet Induced Obesity Model Using Four Strains Of Mice: Kunming, C57bl/6, Balb/C And Icr. *Experimental Animals*, 69(3), 326–335. <https://doi.org/10.1538/Expanim.19-0148>.
- [6] Wilde, D. W., Massey, K. D., Walker, G. K., Vollmer, A., & Grekin, R. J. (2000). High-Fat Diet Elevates Blood Pressure And Cerebrovascular Muscle Ca(2+) Current. *Hypertension (Dallas, Tex.: 1979)*, 35(3), 832–837. <https://doi.org/10.1161/01.Hyp.35.3.832>
- [7] Suk, M., & Shin, Y. (2015). Effect Of High-Intensity Exercise And High-Fat Diet On Lipid Metabolism In The Liver Of Rats. *Journal Of Exercise Nutrition & Biochemistry*, 19(4), 289–295. <https://doi.org/10.5717/Jenb.2015.15122303>
- [8] Duan, Y., Zeng, L., Zheng, C., Song, B., Li, F., Kong, X., & Xu, K. (2018). Inflammatory Links Between High Fat Diets And Diseases. *Frontiers In Immunology*, 9, 2649. <https://doi.org/10.3389/Fimmu.2018.02649>
- [9] Lian, C. Y., Zhai, Z. Z., Li, Z. F., & Wang, L. (2020). High Fat Diet-Triggered Non-Alcoholic Fatty Liver Disease: A Review Of Proposed Mechanisms. *Chemico-Biological Interactions*, 330, 109199. <https://doi.org/10.1016/J.Cbi.2020.109199>
- [10] Wali, J. A., Jarzewska, N., Raubenheimer, D., Simpson, S. J., Rodionov, R. N., & O'sullivan, J. F. (2020). Cardio-Metabolic Effects Of High-Fat Diets And Their Underlying Mechanisms-A Narrative Review. *Nutrients*, 12(5), 1505. <https://doi.org/10.3390/Nu12051505>
- [11] Guo, Z., Ali, Q., Abaidullah, M., Gao, Z., Diao, X., Liu, B., Wang, Z., Zhu, X., Cui, Y., Li, D., & Shi, Y. (2022). High Fat Diet-Induced Hyperlipidemia And Tissue Steatosis In Rabbits Through Modulating Ileal Microbiota. *Applied Microbiology And Biotechnology*, 106(21), 7187–7207. <https://doi.org/10.1007/S00253-022-12203-7>
- [12] Zheng, P., Ma, W., Gu, Y., Wu, H., Bian, Z., Liu, N., Yang, D., & Chen, X. (2023). High-Fat Diet Causes Mitochondrial Damage And Downregulation Of Mitofusin-2 And Optic Atrophy-1 In Multiple Organs. *Journal Of Clinical Biochemistry And Nutrition*, 73(1), 61–76.
- [13] Yang, R., Zhang, S., Kajander, H., Zhu, S., Koskinen, M. L., & Tenhunen, J. (2011). Ringer's Lactate Improves Liver Recovery In A Murine Model Of Acetaminophen Toxicity. *Bmc Gastroenterology*, 11, 125. <https://doi.org/10.1186/1471-230x-11-125>
- [14] Obia, O., Odum, J. E., & Chuemere, A. N. (2018). Nephroprotective And Antihyperlipidemic Activity Of Honey In Alloxan Induced Diabetic Wistar Rats. *International Journal Of Biochemistry Research And Review*. 22(1), 1-7.
- [15] Hussain, A., Cho, J. S., Kim, J. S., & Lee, Y. I. (2021). Protective Effects Of Polyphenol Enriched Complex Plants Extract On Metabolic Dysfunctions Associated With Obesity And Related Nonalcoholic Fatty Liver Diseases In High Fat Diet-Induced C57bl/6 Mice. *Molecules (Basel, Switzerland)*, 26(2), 302. <https://doi.org/10.3390/Molecules26020302>
- [16] Santos L. (2022). The Impact Of Nutrition And Lifestyle Modification On Health. *European Journal Of Internal Medicine*, 97, 18–25. <https://doi.org/10.1016/J.Ejim.2021.09.020>
- [17] Hoshide, S., Mogi, M. & Kario, K. (2023). The Importance Of Lifestyle Modification For Hypertension In Asia. *Hypertens Res* 46, 815–816. <https://doi.org/10.1038/S41440-023-01213-1>
- [18] Obia, O., & Eifuobhokhan, J. (2024). Effect Of Justicia Carnea Leaf Extract On Plasma And Fecal Lipid Profile In High-Fat Diet Fed Wistar Rats. *International Journal Of Health And Pharmaceutical Research*. 9(4), 64-70.
- [19] Eifuobhokhan, J., Obia, O., & Charles, C. (2024). Justicia Carnea Leaf Extract Improves Intestinal Transit In High-Fat Diet Induced Delayed Gut Motility In Wistar Rats. *European Journal Of Pharmaceutical And Medical Research*. 11(12), 50-54.
- [20] Onyeabo, C., Achi, N. K., Ekeleme-Egedigwe, C. A., Ebere, C. U., & Okoro, C. K. (2017). Haematological And Biochemical Studies On Justicia Carnea Leaves Extract In Phenylhydrazine Induced-Anemia In Albino Rats. *Acta Scientiarum Polonorum. Technologia Alimentaria*, 16(2), 217–230. <https://doi.org/10.17306/J.Afs.0492>
- [21] Orjiakor, C.A., Uroko, R.I., Njoku, O. U., & Ezeanyika, L.U.S. (2019). Nutritive Properties Of Aqueous Extract Justicia Carnea Leaves And Its Effects On Haematological And Some Biochemical Indices Of Anaemia Induced Male Wistar Albino Rats. *Biomedical Research*. 30 (4):645-654.
- [22] Anigboro, A. A., Avwioroko, O. J., Akeghware, O., & Tonukari, N. J. (2021). Anti-Obesity, Antioxidant And In Silico Evaluation Of Justicia Carnea Bioactive Compounds As Potential Inhibitors Of An Enzyme Linked With Obesity: Insights From Kinetics, Semi-Empirical Quantum Mechanics And Molecular Docking Analysis. *Biophysical Chemistry*, 274, 106607.
- [23] Kalas, M. A., Chavez, L., Leon, M., Taweesept, P. T., & Surani, S. (2021). Abnormal Liver Enzymes: A Review For Clinicians. *World Journal Of Hepatology*, 13(11), 1688–1698.
- [24] Dhibi, M., Brahmi, F., Mnari, A., Houas, Z., Chargui, I., Bchir, L., Gazzah, N., Alsaif, M. A., & Hammami, M. (2011). The Intake Of High Fat Diet With Different Trans Fatty Acid Levels Differentially Induces Oxidative Stress And Non-Alcoholic Fatty Liver Disease (Nafld) In Rats. *Nutrition & Metabolism*. 8(1), 65.
- [25] Recena Aydos, L., Aparecida Do Amaral, L., Serafim De Souza, R., Jacobowski, A. C., Freitas Dos Santos, E., & Rodrigues Macedo, M. L. (2019). Nonalcoholic Fatty Liver Disease Induced By High-Fat Diet In C57bl/6 Models. *Nutrients*, 11(12), 3067.
- [26] Nouredin, M., & Loomba, R. (2012). Nonalcoholic Fatty Liver Disease: Indications For Liver Biopsy And Noninvasive Biomarkers. *Clinical Liver Disease*, 1(4), 104–107.
- [27] Bayliak, M. M., Vatashchuk, M. V., Gospodaryov, D. V., Hurza, V. V., Demianchuk, O. I., Ivanochko, M. V., Burdyliuk, N. I., Storey, K. B., Lushchak, O., & Lushchak, V. I. (2022). High Fat High Fructose Diet Induces Mild Oxidative Stress And Reorganizes Intermediary Metabolism In Male Mouse Liver: Alpha-Ketoglutarate Effects. *Biochimica Et Biophysica Acta. General Subjects*, 1866(12), 130226. <https://doi.org/10.1016/J.Bbagen.2022.130226>
- [28] Sönmez, A. B., Arifoğlu, I., Yıldırım, A., & Tütüncüler, F. (2018). Benign Transient Hyperphosphatasemia In An Infant During Zinc Supplementation. *Turk Pediatri Arsivi*, 53(2), 120–123. <https://doi.org/10.5152/Turkpediatriars.2017.3158>
- [29] Shkalim Zemer, V., Hoshen, M., Levinsky, Y., Richenberg, Y., Yosef, N., Oberman, B., Cohen, M., & Cohen, A. H. (2023). Benign Transient Hyperphosphatasemia In Infants And Children: A Retrospective Database Study. *European Journal Of Pediatrics*, 182(7), 3211–3216. <https://doi.org/10.1007/S00431-023-04995-1>

- [30] Fernández-Gordón Sánchez, F. M., Gómez Labrador, C., Riado Mínguez, D., Agudo Fernández, S., & Castaño Milla, C. (2024). Persistently Elevated Alkaline Phosphatase Without Hepatopathy? Literature Review. *Revista Espanola De Enfermedades Digestivas*, 116(8), 447–448. <https://doi.org/10.17235/Reed.2023.9972/2023>
- [31] Moriles, K. E., Zubair, M., & Azer, S. A. (2024). Alanine Aminotransferase (Alt) Test. In *Statpearls*. Statpearls Publishing.
- [32] Yang, B., Luo, Q. L., Wang, N., Hu, Y. T., Zheng, W. X., Li, H., Maierziya, M., Gu, J., & Wang, Q. (2023). Hpf Modulates The Differentiation Of Bmcs Into Hlcs And Promotes The Recovery Of Acute Liver Injury In Mice. *International Journal Of Molecular Sciences*, 24(6), 5686. <https://doi.org/10.3390/Ijms24065686>
- [33] Ajuru, M., Kpekot, A.K., Omubo, J., & Morrison, I. (2021). Comparative Study Of Proximate And Phytochemical Analysis Of The Roots Of Justicia Carnea Lindl. And Justicia Carnea Secunda Vahl. *Nigerian Annals Of Pure And Applied Sciences*, 4(1), 28-34.
- [34] Arthur N. C., Marygisel N. U., Obia O., Oginma N. I. (2022). Gc-MS Analyzed Phytochemicals And Justicia Carnea Remediation Of Cadmium- Induced Oxidative Stress, Hyperglycemia And Hyperlipidaemia In Male Wistar Rats. *Himalayan Journal Of Applied Medical Sciences And Research*.3(1): 88-95.
- [35] Pei, R., Liu, X., & Bolling, B. (2020). Flavonoids And Gut Health. *Current Opinion In Biotechnology*, 61, 153–159.
- [36] Cordero-Herrera, I., Martín, M. A., Goya, L., & Ramos, S. (2015). Cocoa Flavonoids Protect Hepatic Cells Against High-Glucose-Induced Oxidative Stress: Relevance Of Mapks. *Molecular Nutrition & Food Research*, 59(4), 597–609. <https://doi.org/10.1002/Mnfr.201400492>
- [37] Obia, O., Chuemere, A. N., Chike, C.P.R., & Nyeche, S. (2017). Effect Of Supplementation Of Natural Honey On Serum Albumin And Total Protein Of Alloxan-Induced Diabetic Wistar Rats. *American Journal Of Phytomedicine And Clinical Therapeutics*. 5(3), 21.