

Effects of acute consumption of *garcinia kola* on hepatic enzymes in apparently well Nigerian youths.

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Abstract

Introduction: *Garcinia kola* belongs to the Family Clusiaceae guttiferae and contains a complex mixture of biflavonoids, prenylated benzophenones and xanthone¹. Its seeds, popularly called 'Bitter Kola', form an integral part of the herbal preparations used in traditional African medicine. A lot of studies have been done in animals to look at the effects of *Garcinia kola* on their organs, very few have been done in human beings.

Objective: This study was done to look at the effect of acute consumption of *Garcinia kola* on hepatic enzymes in apparently well Nigerian youths.

Methodology: The response of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) following the consumption of about 100 mg/kg of body weight of *Garcinia kola* was measured in 28 apparently well University of Ilorin medical students. The rise in the level of AST, ALT and ALP was studied from the plasma of the subjects. The basal level of the enzymes pre-consumption of *Garcinia kola* serves as control for the ones collected after 2 hours of *Garcinia kola* consumption.

Results: After consumption of *Garcinia kola*, the result shows that the level of AST rose from 90.6 ± 43.6 u/L to 120.9 ± 42.6 u/L which was significant at $p=0.001$, the level of ALT rose from 63.4 ± 56.3 u/L to 86.8 ± 51.6 u/L which was significant at $p=0.001$, and the ALP level rose from 101.1 ± 75.4 u/L to 139.5 ± 89.9 u/L which was significant at $p=0.001$. The De-Ritis ratio was calculated and was found to decreased from 7.3 ± 1.81 to 1.8 ± 1.0 which was significant at $p<0.041$ respectively. Pre-consumption of *Garcinia kola*, there was a weak negative correlation between AST and ALT at 'r' value of -0.310 and 'p' value of 0.108; so also between AST and ALP at 'r' value of -0.310 and 'p' value of 0.018 but positive correlation between ALT & ALP at 'r' value of 0.425 and 'p' value 0.024. Post-consumption of *Garcinia kola*, there was a stronger but still weak negative correlation between AST and ALT at 'r' value of -0.151 and 'p' value of 0.442; but positive one between AST and ALP at 'r' value of 0.205 and 'p' value of 0.296 but positive correlation between ALT and ALP at 'r' value of 0.321 and 'p' value 0.096.

Conclusion: The clinical significance of this study is that following the acute consumption of *Garcinia kola*, there was an increase in the plasma levels of AST, ALT and ALP, and a decrease in the calculated De-Ritis ratio. This shows that *Garcinia kola* is a hepatic enzymes inducer.

Recommendation: Therefore, extra care should be taken when interpreting the results of hepatic enzymes in habitual consumers of *Garcinia kola*. Also, those consuming it should take it with caution, or take it only when it is absolutely indicated in as much as its mechanism of induction is not known for now.

Key words: Acute Consumption, *Garcinia kola*, Hepatic Enzymes, Nigerian Youths.

Introduction

Early men were said to have gained some scientific knowledge by watching the effects produced by various plants when eaten by domestic animals. It is from this that they were able to arrive at dosages. The demand for the therapeutic drugs from natural products is on the increase in recent times.

This is traceable to possible realization that plant products contain active constituents that are capable of curing majority of man's diseases. It is observed that drugs of natural origin are the only widely used hepatoprotectives².

Garcinia kola belongs to the family Clusiaceae guttiferae and contains a complex mixture of biflavonoids, prenylated benzophenones and xanthone¹. Its seeds, popularly called 'Bitter Kola', form an integral

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part of the herbal preparations used in traditional African medicine. It has been confirmed to have anti-inflammatory, antimicrobial, pharmacological and antiviral properties³. The seeds of *Garcinia kola* have been employed in many herbal preparations in Nigeria for the treatment of ailments ranging from laryngitis, bronchitis to liver disorders⁴.

It is a popular agricultural produce available in large quantity in West Africa particularly in Nigeria and it is a tree that grows in the rain forests. It is found in the tropical rain region and given different names in Nigeria. It is known as Orogbo in Yoruba land, Namijin-goro among Hausa, and Akuilu in Iboland⁴. Like the kola nut, it is produced from a big tree however it is a monocotyledon. Although it is eaten widely for different purposes, it has nothing to do with the tradition of any known ethnic group. It has been identified as a potent antibiotic which could be effective in the treatment of many diseases. The fruit, seeds, nuts and bark of the plant have been used for centuries in folk medicine to treat ailments from coughs to fever. In the International market however, it is known as *Garcinia kola* which symbolizes its botanical name and it is used extensively in the preparation of herbal drugs either as stimulant supplement or as herbal remedies as well. As with any other herbs, you never consume *Garcinia kola* without first discussing its use and benefits with your physician, especially if you are currently being treated for other medical conditions or are on any medications. This had been the reasons for a nonstop demand for it and because, any products that have to do with human health will surely and always enjoy good patronage³.

It is considered as an effective agricultural produce in the treatment of cough, diarrhea, tuberculosis and other bacterial infections⁵. "When food is suspected to be contaminated by bacteria, chew bitter kola immediately after eating, it will prevent the development of any infection or poisoning. It is eaten mostly by the elderly people because of their belief that it could prolong life⁵. Researches done by scientists have revealed that *Garcinia kola* contains chemical compounds that will help the breakdown of glycogen in the liver and has other medicinal uses which account for its longevity property in man. The *Garcinia kola* extract exhibited dose-dependent antispasmodic effects on contractions

induced by acetylcholine, and dose-dependent spasmolytic effects on spasms of small intestine⁶.

Talking about the Chemistry of *Garcinia kola*, its extract gave the highest concentration of crude saponin when compared with the extract of other part of the plant. Alkaloids could not be detected in methanol and water extracts of the pulp and root. Neither was there any trace of alkaloid detected in the methanol extract of all the remaining part of the plant (seed, stem, leaves, and bark). However, there seemed to be a high concentration of alkaloidal substances in the water extract of the seed and stem⁴. Other chemical components *Garcinia kola* are: Tannis which were detected only in the methanol extract of the seed, stem, leaves and bark. Phlobatannin was detected in the methanol extract of all the part of the plant except the pulp. All the extract of the various part of the plant responded negatively to the test for free anthroquinone, and this suggests that the plant was probably devoid of any anthroquinone⁶. It is also confirmed that seeds of *Garcinia kola* contain energy-yielding nutrients (proteins, lipids, carbohydrates) and minute quantities of Kolaviron (consisting of biflavonoids GB-1, GB-2 and Kolaflavone, but lacks caffeine)³.

Despite the widespread increase in the rate of consumption of *Garcinia kola* in Nigeria not only among the elderly but even the youths for various reasons and purpose, very few literature are available on its biochemical effect on the liver. Hence, we thought it will be wise to have a look at the effect on the hepatic enzymes of youths involved acute consumption of *Garcinia kola*.

Aims and objectives

The aim of this study was to determine the effects *Garcinia kola* on the hepatic enzymes (aminotransferases {AST and ALT} and alkaline phosphatase {ALP}). The specific objectives were to determine plasma activities of AST, ALT and ALP both pre-and post consumption of *Garcinia kola* in apparently well Nigerian youths. De-Ritis ratio was determined from the AST and ALT plasma level.

Materials and Method

The subjects for this study comprised of 28 healthy University of Ilorin medical students (14 males and 14

females) by random selection method. Their age ranges from 19 to 28 years. The *Garciniakola* seeds used for this project were gotten from a *Garcinia kola* vendor at Baboko market in Ilorin, who got it from the same source. Criteria for Selection of Subjects

The following criteria were satisfied by each of the students before being accepted as a subject of the study:

- The well-being of the students was ascertained.
- Availability and ability to co-operate adequately throughout the duration of the study.
- No history of liver diseases.
- No form of inflammatory disorders.

Experimental Procedure

The age and sex of the subjects were recorded. All the tests were performed with the subjects comfortably seated. 3 mls of blood was collected from each of the subject by venepuncture using a needle and syringe and needle, and gently poured into the plain bottle. These serve as the control samples (i e before eating the *Garcinia kola*).

The subjects were then given 100 mg/kg of body weight of *Garcinia kola* to eat. After 2 hours, 3 mls of blood was collected and gently poured into the plain bottle. The plasma obtained before and after the consumption of *Garcinia kola* was then taken to the laboratory to analyze the levels of AST, ALT and ALP in each of the plasma samples collected.

Measurement of the analytes⁷

Measurement Principle for AST

α -ketoglutarate + L-Aspartate----->L-Glutamate + Oxaloacetate

NOTE: the reaction is catalyzed by AST.

The increase in oxaloacetate was an indicator reaction catalyzed by Malate dehydrogenase (MDH).

Oxaloacetate + NADH + H⁺-----> L-Malate + NAD⁺

NOTE: the reaction is catalyzed by MDY.

NADH is oxidized to NAD. The rate of the NADH decrease is directly proportional to the rate of formation of oxaloacetate and thus the AST activity.

Measurement of ALT⁷

Measurement Principle

α -ketoglutarate + L-Lactate-----> L-Glutamate + Pyruvate

NOTE: ALT catalyzes the reaction.

The increase in pyruvate is determined in an indicator reaction catalyzed by lactate dehydrogenase (LDH).

Pyruvate + NADH + H⁺-----> L-Lactate + NAD⁺

(NOTE: LDH catalyzes the reaction)

NADH is oxidized to NAD. The rate of the NADH decrease is directly proportional to the rate of pyruvate and thus the ALT activity.

Measurement of ALP⁸.

Measurement Principle

P-Nitro-phenyl phosphate+ H₂O-----> p-Nitrophenolate + Phosphate

NOTE: AP catalyzes the reaction

The p-Nitrophenol is present as yellow coloured p-Nitrophenolate. The increase of absorbance per minute at 450nm is proportional to the enzyme activity.

De Ritis Ratio is AST/ALT ratio and is more sensitive in most phases of hepatic disease⁹.

At the end of all measurement, each subject's age and sex were recorded. The level of AST, ALT, ALP and De-Ritis ratio in the plasma before and 2 hours after consumption *GarciniaKola* was recorded.

All analysis was done using SPSS (Statistical Package for Social Science Students) version 20. The mean of the subjects AST, ALT, ALP and De-Ritis ratio levels before and after consumption of *Garciniakola* was also calculated and recorded as \pm standard error of mean. While the students t-test was used to determined the difference between the means, p-values less than 0.05 (p<0.05) were taken as statistically significant.

Results

The results below show the effect of *Garciniakola* on Hepatic Enzymes and De-Ritis ratio before and 2 hours after consumption of the *Garcinia kola* which was studied in twenty-eight (28) apparently well Nigerian youths.

Table 1: Showing the descriptive variables of the parameters before and after *Garcinia kola* consumption

Parameters	Mean±SD (Pre- consumption of <i>G.kola</i>)	Mean±SD (Post- consumption of <i>G.kola</i>)	p-value
AST	90.6±43.6 u/l	120.9±42.6 u/l	0.001
ALT	63.4±56.3 u/l	86.8±51.6 u/l	0.001
ALP	101.1±75.4 u/l	139.5±89.5 u/l	0.001
DE-RITIS Ratio	7.3±1.81	1.8±1.0	0.041

The result shows that the level of AST rose from 90.6 ± 43.6 u/l to 120.9 ± 42.6 u/l, the level of ALT rose from 63.4 ± 56.3 u/l to 86.8 ± 51.6 u/l, the ALP level rose from 101.1 ± 75.4 u/l to 139.5 ± 89.9 u/l, and the De-Ritis ratio decreases from 7.3 ± 1.81 to 1.8 ± 1.0 respectively. The rise in AST, ALT and ALP levels, and the decrease in the De-Ritis ratio induced by consumption of *Garcinia kola* was significant at p <0.05.

Table 2: Showing Correlation studies between the hepatic enzymes before *Garcinia kola* consumption

Parameters	'r' value	p-value
AST vs ALT	-0.310	0.108
ALT vs ALP	0.425	0.024
AST vs ALP	-0.310	0.018

The table above shows that there was a negative correlation between AST & ALT and AST & ALP, but positive correlation between ALT & ALP respectively.

Table 3. Showing Correlation studies between the hepatic enzymes and De-Ritis ratio after *Garcinia kola* consumption.

Parameters	'r' value	p-value
AST vs De-Ritis Ratio	-0.094	0.634
ALT vs De-Ritis Ratio	-0.382	0.045
ALP vs De-Ritis Ratio	-0.101	0.609

The above table shows that there was negative correlation between the hepatic enzymes and the De-Ritis ratio.

Table 4: Showing Correlation studies between the hepatic enzymes after *Garcinia kola* consumption

Parameters	'r' value	p-value
AST vs ALT	-0.151	0.442
ALT vs ALP	0.321	0.096
AST vs ALP	0.205	0.296

The above table shows that there was negative correlation between AST and ALT, and positive correlation between ALT and ALP as well as AST and ALP respectively.

Table 5. Showing Correlation studies between the hepatic enzymes and De-Ritis ratio after *Garcinia kola* consumption.

Parameters	'r' value	p-value
AST vs De-Ritis Ratio	-0.245	0.209
ALT vs De-Ritis Ratio	-0.768	0.001
ALP vs De-Ritis Ratio	-0.258	0.185

The table above shows that there was negative correlation between the hepatic enzymes and the De-Ritis ratio respectively.

Figure 1 showing variation in hepatic enzymes pre and post *G. kola* consumption

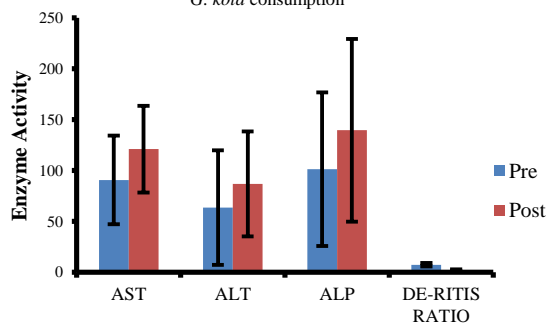
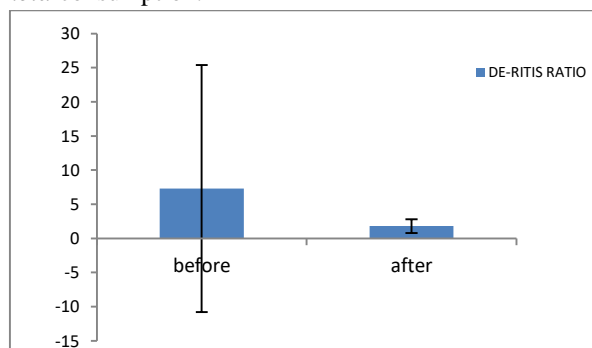


Figure 2 showing variation De-Ritis ratio pre and post *G. kola* consumption.



Discussion

In hepatocytes, 20% of AST is cytosolic, and 80% of AST is in the mitochondria. ALT is primarily found in the cytosol of hepatocytes and is also found in the mitochondria (ALT is more liver specific than AST). And a large percentage of ALT is found in the biliary canaliculi (an elevation of which is suggestive of biliary canaliculi dilatation, which is beneficial in patients with biliary obstruction). ALP is mostly found in the hepatobiliary portion of the liver.

This studies shows that *Garcinia kola* has potent effects on increasing the hepatic enzymes and decreasing De-Ritis ratio in human serum. Obviously, the elevated levels of these hepatic enzymes are a direct reflection of alterations in the hepatic structural integrity or induction of the hepatic enzymes production.

The decrease in the De-Ritis ratio post *Garcinia kola* consumption means that the rise in ALT level is higher than the equivalent rise in the AST level after *Garcinia kola* consumption (since De-Ritis ratio=AST/ALT). The reasons for this rise could be that: {a} *Garcinia kola* causes higher alteration in the genes coding for ALT than that of AST, (b) ALT is a better biomarker of hepatic damage than AST [since it is more liver specific than AST], or {c} there is higher mitochondria leakage of ALT than AST. This possible higher mitochondrial leakage might be due to differential variation in molecular masses of ALT and AST. If this is the case, then it is more likely that ALT is smaller in weight than AST.

Post consumption of *Garcinia kola*, it was noticed that the negative correlation between AST and ALT changes from negative to positive. However, there was a consistent maintenance of the negative correlation of the three hepatic enzymes and the De-Ritis ratio. Although, the values varied.

Cross-referencing is a bit more difficult as most studies done relating to hepatoprotective effects of *Garcinia kola* as well as hepatic biomarkers were mostly in animals than man. More so, most of them were based on toxicological studies.

In conclusion, consumption of *Garciniakola* increases hepatic enzymes in humans, which indicates that *Garciniakola* is a hepatic enzymes' inducer as shown by an increase in the plasma levels of AST, ALT and ALP,

and subsequent decrease in the calculated De-Ritis ratio. Therefore, extra care should be taken when interpreting the results of hepatic enzymes in habitual consumers of *Garciniakola*. Also, those consuming it should take it with caution, or take it only when it is absolutely indicated. It is also recommended that more studies of effects of *Garcinia kola* should be ventured into using humans at molecular level.

References

1. Terashima K., Takawa Y. and Niwa M. (2002) Powerful antioxidative agents based on Garcinonic acid from *Garcinia kola*. *Bio. Org. Med. Chm.* 10:1619-1625.
2. Hukkeri V.L., Jaiprakash B., Lavhale M.S., Karadi R.V. and Kuppast I.J. (2003) Hepatoprotective activity of *Ailanthusexcelsa* Roxb. Leaf extract on experimental liver damage in rats. *Pharmacognosy*11:1-2.
3. Iwu M.M., Igboko O.A., Onwuchekwu U. and Okunji C.O (1987) Evaluation of the antihepatotoxicity of the biflavonoids-Garcinia Kola seeds. *J. Ethnopharmacol.* 21:127-142.
4. Iwu M.M. (1982) Traditional Igbo Medicine. Institute of African studies, University of Nigeria, Nsukka, p.104.
5. Lin S.C., Chung T.C., Ueng T.H., Linn Y.H., Hsu S.H., Chiang C.L. and Lin C.C. (2000) The hepatoprotective effects of *Solnum alatummoench* on acetaminophene-induced hepatotoxicity in mice. *Am. J. Clin. Med.* 28:105-114.
6. Udia P.M., Braide V.B and Owu D.U (2009) Antispasmodic and spasmolytic effects of methanolic extract from seeds of *Garcinia kola* on isolated rat small intestine. *Nigerian Journal of Physiological Sciences* 24 (2): 111 -116.
7. Infusino I., Bonora R and Pateghini M. Traceability in Clin. Enzymology. (2007) *Clin Biochem Rev*: 28:155-61.
8. Tietz N.W., Shuey D.E., Rinker A.D and Shaw I.M (1983) IFCC methods for the measurement of catalytic concentration of enzymes. Part 5. IFCC methods for alkaline phosphatase (orthophosphoric-monoester phosphohydrolase, alkaline optimum EC 3.1.3.1. *Clin Chem Clin Biochem* 21:731-48
9. De Ritis F., Coltorti M and Giusti G (July 2006). "An enzymic test for the diagnosis of viral hepatitis: the transaminase serum activities. 1957". *Clin. Chim. Acta*369 (2): 148-52. doi:10.1016/j.cca.2006.05.