International Journal of Medicine and Biomedical Research
Volume 1 Issue 3 September – December 2012
www.ijmbr.com

Original Article

Gastroprotective potentials of the methanolic extract of *Garcinia kola* in rats

Ige S.F[1*], Akhigbe R.E[1], Olaleye S.B[2], Adeyemi J.W[1]

[1]Department of Physiology, College of Health Sciences, Ladoke Akintola University of Technology, Ogbomoso, Oyo state, Nigeria. [2]Department of Physiology, College of Medicine, University of Ibadan, Ibadan, Oyo state, Nigeria.

*Corresponding Author: funkeige2006@gmail.com
Received: 07.03.12; Accepted: 19.07.12

ABSTRACT

Background: There is a claim in the folklore medicine of the use of *Garcinia kola* (GK) seeds in the management of gastritis and gastric ulcer. However, there has not been any scientific evidence in the literature that substantiated or refuted this with regards to the management of gastritis and gastric ulcerations in association with gastric morphological damage and cytoarchitectural changes. **Aim**: This study aims at evaluating the efficacy of the methanolic extract of GK (mGK) in the management of gastritis and gastric ulcerations in rat model. **Methods**: Adult albino rats with comparable weight were randomized into six groups. Group A was administered 1ml/kg bw of distilled water three times daily. Group B and C were administered ethanol (0.2ml/23g bw of 80% v/v) two hours prior termination of experiment and 150mg/kg bw of mGK daily for three weeks respectively. Group D was pre-treated with mGK and then ethanol as in groups B and C. Group E was administered ethanol as in group B and post-treated with mGK as in group C. Group F was concomitantly treated with mGk as in group C and ethanol as in group B. **Results**: Ethanol induced gastritis and gastric ulceration. Treatment with mGK abrogated ethanol-induced gastric damage: it reduced the morphological damage score, ulcer score, gastric wall thickness, and lipid peroxidation ($p<0.05$), and also improved the cytoarchitecture of the gastric mucosa. **Conclusion**: This study substantiated the gastroprotective potentials of mGK. The mechanism of action could be associated with the anti-oxidative activities of the flavonoid constituents.

Key words: *Garcinia kola*, flavonoids, gastritis, ulcer, lipid peroxidation

INTRODUCTION

Gastric ulcers are breaches in the gastric mucosa that extends through the muscularis mucosae into the submucosa or deeper, which commonly occur in the form of peptic ulcer or acute gastric ulceration.[1] On the other hand, gastritis is the

inflammation of the gastric mucosa, which is basically diagnosed histologically.[1] There has been a remarkable increase in the contribution of knowledge in the treatment of these pathological conditions.

Folklore medicine has grown over the years following the discovery of bioactive agents of plants and scientific evidences to justify their uses in the management of various clinical conditions. The importance of phytotherapy cannot be over-emphasized as plants have been proven to be effective, less expensive, and safer.[2] The anti-ulcer activities of various plants have been investigated. Such plants include *Egletesviscosa,*[3] *Landolphiaowarensis,*[4] *Hedrantherabarteri,*[5] *Solanumnigrum*Linn,[6] and *Garcinia kola.*[7,8]

Garcinia kola seed, commonly known as bitter kola belongs to a family of tropical plants known as Guttifera.[9] In Nigerian languages, it is commonly called *Namiji*goro in Hausa, *Agbilu* in igbo, and *Orogbo* in Yoruba. *Garcinia kola* has economic values across West African countries where the seeds are commonly chewed and used for traditional ceremonies.[10] The seeds are also used in folk medicine in many herbal formulations and have potential therapeutic benefits due largely to the activity of their flavonoids and other bioactive compounds.[11-17]

The antiulcer effect of petroleum ether extract of *Garcinia kola* (GK) has been reported.[7] Similarly, the antiulcer effect of diet containing GK has been documented.[8] However, there is still dearth of information in the open scientific literature on the studies that evaluated the gastroprotective role of the methanolic extract of GK in the management of gastritis and gastric ulcerations in association with gastric morphological damage and cytoarchitectural changes. Therefore, we decided to provide information on the gastroprotective potentials of methanolic extract of GK (mGk) using rat model.

MATERIALS AND METHODS

Experimental animals

Male and female albino rats (*Rattus norvegicus*) of Wistar strain of comparable weights were used for the study. Rats were housed in clean standard metabolic cages with free access to rat chow and tap water free of contaminants. The cages were contained in a well-ventilated standard housing conditions (temperature: 25°C±2, photoperiod: 12h natural light/dark cycle; humidity: 50-55%)

Preparation of plant extract

The method described by Olaleye and Farombi [7] was used in the preparation of the extract with some modifications. Briefly, the outer coats were removed and the seeds were cuts into pieces and air-dried. The air-dried seeds were grounded to fine powder and methanolic extraction was done by Soxhlet extraction. The yield was concentrated to a solid.

Animal grouping and treatment

Thirty albino rats of both sexes were randomized into six groups (A-F). Treatment was as follow:
Group A: received orally 1ml of distilled water daily for 3 weeks (control group).
Group B: received ethanol (0.2ml/23g body weight of 80% v/v) two hours before the animals were sacrificed to induce gastric ulceration.
Group C: received mGK (150mg/kg p.o) daily for three weeks.
Group D: received mGK (150mg/kg p.o)for three weeks and ethanol (0.2ml/23g body weight of 80% v/v) two hour before the animals were sacrificed; mGK pre-treated
Group E: received ethanol (0.2ml/23g body weight of 80% v/v) at the start of the administration, then mGK (150 mg /kg p.o) was given throughout the experiment; mGK post-treated.
Group F: received mGK(150 mg /kg p.o) for two weeks & four days, then ethanol (0.2ml/23g body weight of 80% v/v) was given once orally , after which they received mGK(150 mg /kg p.o) for the rest three days of that week; mGK concomitant treatment

Induction of gastric ulceration

Gastric ulceration was induced by administering 0.2ml/23g body weight of 80% v/v ethanol. The animals to be given the ethanol were fasted for 24 hours. 80 % v/v ethanol was prepared and given to these animals using an oral cannula which was connected to a hypodermic syringe. The oral cannula was position at the back of the pharynx of the rats into their oesophagus to prevent inflammation of the tongue and the lining of the rats mouth by the ethanol, then, the ethanol was steadily administered at the dosage of 0.2ml/23g body weight.

Morphological damage score, ulcer score, and thickness of the gastric wall

Morphological damage was scored as described by Zheng *et al.*[18] With the aid of a magnifying lens, hyperemia was examined and scored. Also, the inflammation developed was scored whether it was

linear or multiple as follows: no hyperemia, no inflammation=0, hyperemia without inflammation=1, hyperemia with linear inflammation=2, hyperemia with multiple inflammation=3. Ulcer score was determined as described by Rao *et al.*[3] Gastric wall thickness was measured using a vernier caliper which was zeroed before use.

Determination of lipid peroxidation status

Animals were sacrificed after the experimental period, and the stomach of each rat was dissected. The stomach tissues were homogenized in phosphate buffer with the aid of a homogenizer, and then centrifuge at 4000 revolution / minute for ten (10) min. After wards, the supernatant layer was then collected for the biochemical analyses. Malondialdehyde (MDA), catalase (CAT), and superoxide dismutase (SOD) were determined as described in previous studies.[19-22]

Histological processing and examination

Small section of stomach were taken from two distinct areas from each stomach and placed in 10% formalin for histological examination. The stomach was fixed, cut into 5 µm sections, stained with hematoxylin and eosin.

Ethics

Animals received humane care in adherence with the guideline of the institution and as stated in the National Institute of Health Guidelines for the Care and Use of Laboratory Animals.

Statistical analysis

Data are presented as mean±SEM (n=5). Statistical analyses were done using one-way analysis of variance (ANOVA) to account for the different treatments and were complemented with unpaired t-test. Differences were considered statistically significant at $p<0.05$.[23]

RESULTS

Effect of the extract on morphological damage score, ulcer score, and thickness of the gastric wall

Ethanol administration induced gastric damage and ulcer in rats. Treatment with mGK significantly ($p<0.05$) ameliorated this effect in a manner suggestive that post-treatment and concomitant treatment with mGK produced a better result than mGK pre-treatment (figure 1 and 2). Similarly, mGK treatment significantly ($p<0.05$) prevented increase in the gastric wall thickness (figure 3).

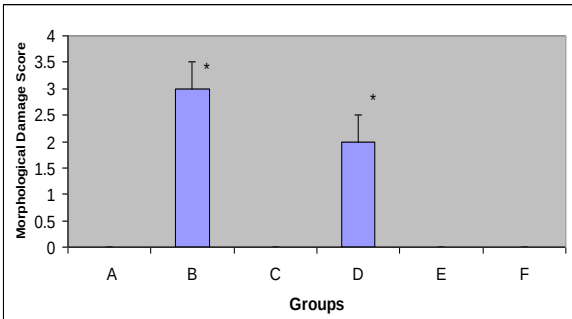


Figure 1: Effect of *Garcinia kola* extract on morphological damage score of gastric tissue
***p<0.05 vs group A**

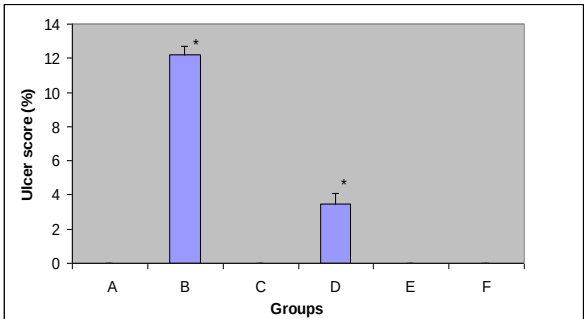


Figure 2: Effect of *Garcinia kola* extract on ulcer score of gastric tissue
***p<0.05 vs group A**

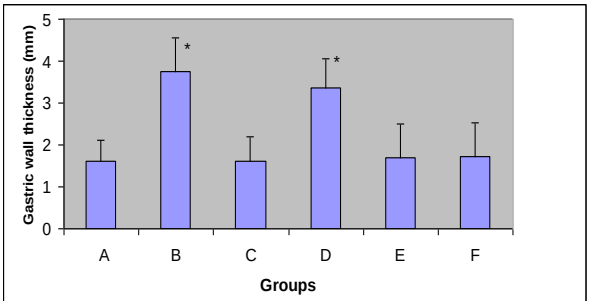


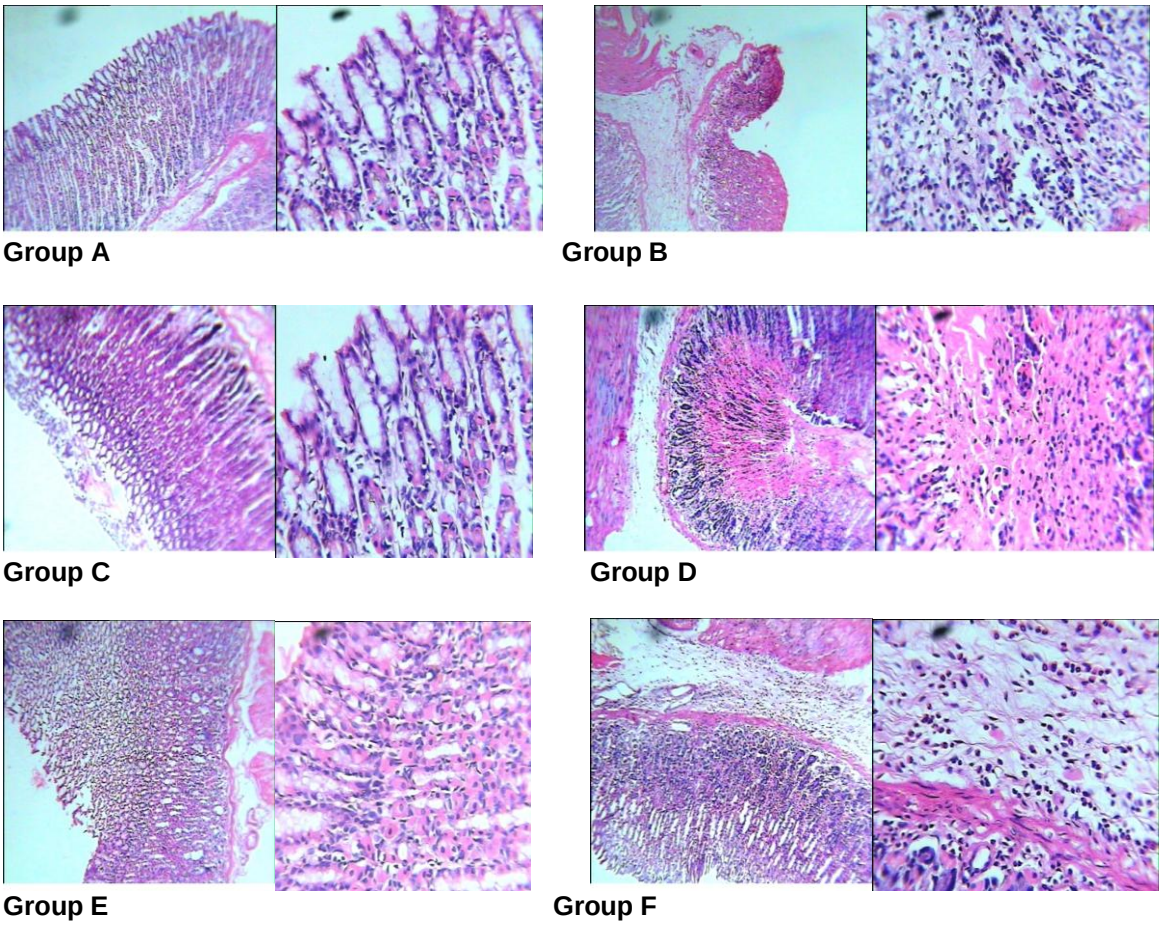
Figure 3: Effect of *Garcinia kola* extract on gastric wall thickness
***p<0.05 vs group A**

Effect of the extract on lipid peroxidation status

Table 2 shows that mGK treatment significantly ($p<0.05$) enhanced lipid peroxidation status by reducing MDA, and increasing CAT and SOD.

Effect of the extract on histological examination

Histological studies also revealed that mGK maintained the cytoarchitecture of the gastric tissue by preventing gastric ulceration and infiltration of the mucosa by inflammatory cells.



Group A **Group B**

Group C **Group D**

Group E **Group F**

Group A: The diagram above shows that the whole thickness of the stomach wall in the control animal group is intact with absence of inflammatory cells in the mucosa layer of the stomach wall. **Group B:** The above diagram shows the ulceration of the mucosa layer through the muscularis mucosa, resulting in the exposure of the submucosa layer with infiltration of the mucosa layer of the stomach tissue with dense number of inflammatory cells. **Group C:** The diagram above reveals that G*arcinia kola* extract maintains the normal histology of gastric tissue. The gastric layers are intact and there are no infiltrative cells. **Group D:** The above diagram shows ulceration of the gastric mucosa with preservation of some part suggesting the ameliorating effect of *Garcinia kola*. There is less dense population of the inflammatory cells. **Group E:** The above diagram shows regeneration of the gastric mucosa with few infiltrative cells. This is suggestive of the alleviating effect of *Garcinia kola*. **Group F:** The diagram above shows intact gastric mucosa with few infiltrative cells.

Figure 4: Histological examination of the effect of *Garcinia kola* extract on gastric tissue

DISCUSSION

Since many people now depend on herbal medicine for health care, possibly because other treatments modalities are becoming more expensive and often carry serious side effects,[24] it is now necessary to investigate options in folklore medicine for the management of diseases. Several natural products including *Garcinia kola* have been documented to have antiulcerogenic effect.[3-8] However, none of these studies has reported the gastroprotective effect of the methanolic extract of *Garcinia kola*, as commonly used in the folklore medicine, in the management of gastritis and gastric ulcerations in association with gastric morphological damage and cytoarchitectural changes. This study thus provides scientific information on the therapeutic efficacy of *Garcinia kola* in cases of gastritis and gastric ulcerations.

Table 1: Effect of *Garcinia kola* extract on Lipid peroxidation status of stomach tissue

Groups/Variables	MDA (IU/g tissue)	Catalase (IU/g tissue)	SOD (IU/g tissue)
Group A	**0.82±0.9**	**0.00175±0.33**	**0.49±0.34**
Group B	**1.43±1.3***	**0.00100±0.41***	**0.16±0.23***
Group C	**0.58±0.75***	**0.00190±0.29***	**0.95±0.09***
Group D	**1.19±1.22***	**0.00130±0.5***	**0.40±0.29***
Group E	**0.42±0.99***	**0.00210±0.28***	**1.4±0.53***
Group F	**0.25±0.44 ***	**0.00250±0.32***	**1.7±0.44***

***p<0.05 vs. group A**

MDA: Malondialdehyde

Esimone *et al.*[25] documented the phytochemical constituents of *Garcinia kola* seeds to include saponins, tannins, flavonoids, proteins, glycosides, reducing sugar, starch, sterols and triterpenoids, with flavonoids predominating. Flavonoids have been implicated as possible bioactive agents responsible for antiulcerogenic and anti-inflammatory effects.[26-30]

The significant ($p<0.05$) decrease in the ulcerogenic indices (morphological damage score, ulcer score, and gastric wall thickness) seen in this study are indications of the ulcerogenic potentials of *Garcinia kola* extract. Similarly, the maintenance of the cytoarchitecture of the gastric mucosa with little or no infiltration of inflammatory cells as seen in histopathological examinations are pointers to the anti-inflammatory (anti-gastritis) activities of the *Garcinia kola*. This is in tandem with previous studies that documented the antiulcer and anti-inflammatory effects of flavonoids in various plant extracts.[7,8,29,30]

It has been documented that gastritis and gastric ulcers are related with stress,[1] possibly by inducing lipid peroxidation. This study reveals that *Garcinia kola* extract prevented lipid peroxidation by increasing the enzymatic anti-oxidants (catalase and superoxide dismutase) levels and reducing malondialdehyde (lipid peroxidation index). *Garcinia kola* extract has previously been shown to improve oxidative status.[31-33] Flavonoids have been reported to inhibit isoforms of inducible nitric oxide synthase (iNOS) and of cyclooxygenase (COX-2) which are responsible for the synthesis of prostaglandins and nitric oxide, as well as reactive C protein and adhesion molecules, mediators of inflammation.[34] The anti-inflammatory activities of flavonoids is also complemented by their ability to activate NF-E2related factor 2 (Nrf2), thus increasing anti-oxidant defenses.[34] The antiulcerogenic and anti-inflammatory effects of *Garcinia kola* extract might be associated with its anti-oxidative potentials. The administration of the extract which led to enhancement of lipid peroxidation status may be responsible for the

significant improvements on ulcerogenic and inflammatory indices.

Studies have implicated the flavonoid constituents of plants in enhancing ulcerogenic and inflammatory indices due to its anti-oxidative effect.[30] The flavonoids present in the methanolic extract of *Garcinia kola* might have helped in enhancing the oxidative defense mechanisms which led to significant reduction in the ulcerogenic and inflammatory indices. This study also suggests that post-treatment and concomitant treatment with *Garcinia kola* is more efficacious.

In conclusion, results of this study provide scientific evidence which lend credence to the use of *Garcinia kola* extract in the folklore medicine in the management of gastritis and gastric ulcerations.

REFERENCES

1. Kumar V, Abbas A, and Fausto N. Stomach. In: Pathologic Basis of Diseases. 8th Ed. Elsevier Saunder 2007.
2. Yakubu MT, Akanji MA, and Nafiu MO. Anti-diabetic activity of aqueous extract of *Cochlospermum planchonii* root in alloxan-induced diabetic rats. Cameroon J Expt Biol 2010;6:91-100.
3. Rao VNS, Santos FA, Sobreira TT, Souza MF, Melo CL and Silveira ER. Investigation on the gastroprotective and antidiarhoeal properties of tematin, a tetramethoxyflavone from Egletsviscosa. Planta Med 1996;63:146-149.
4. Olaleye SB, Owoyele BV, and Odunkoni AO. Antiulcer and gastric antisecretory effects of Landolphiaowariensis extracts in rats. Nig J Physiol Sci 2008;23:23-26.
5. Onasanwo SA, Singh N, Olaleye SB, Mishra V, Palit G. Anti-ulcer and antioxidant activities of Hedrantherabarteri {(Hook F.) Pichon} with possible involvement of H+, K+ ATPase inhibitory activity. Indian J Med Res 2010;132:442-449.
6. Saravanan S, Dhasarathan P, Indira V and Venkatraman R. Gastro Protective and Antioxidant Activity of *Solanumnigrum*Linn. against Aspirin and Cold Restraint Stress induced Ulcerated Rats. Res J Immunol 2011;4:1-11.
7. Olaleye SB, and Farombi EO. Attenuation of Indomethacin- and HCl/Ethanol-Induced Oxidative Gastric Mucosa Damage in Rats by Kolaviron, A Natural Biflavonoid of *Garcinia kola* Seed. Phytother Res 2006;20:14-20.
8. Ibironke GF, Olaleye SB, Balogun O and Aremu DA. Antiulcerogenic effect of diet containing seeds of Garcinia kola (Heckel). Phytother Res 1997;11:312 - 313.
9. Plowden CC. A manual of plants names. 3rd ed. London. George Ltd. 1972; Pp239.
10. Eleyinmi AF, Bressler DC, Amoo IA, Sporns P, Oshodi AA. Chemical composition of Bitter Cola (Garcinia kola) seed and hulls. Pol J Food Nutr Sci 2006;15/56:395–400.
11. Akintonwa A, Essien AR. Protective effects of *Garcinia kola* seed extract against paracetamol-induced hepatotoxicityin rats. J Ethnopharmacol 1990;29:207–211.
12. Adegoke GO, Kumar MV, Sambaiah K, Lokesh BR. Inhibitory effect of *Garcinia kola* on the lipid peroxidation in rat liver homogenate. Indian J Exp Bio 1998;36:907–910.
13. Tona L, Ngimbi NP, Tsakala M, Mesia K, Cimanga K, Apers S, De Bruyne T, Peiters L, Totte J, Vlietinck AJ. Antimalarial activity of 20 crude extracts from nine African medicinal plants used in Kinshasa, Congo. J Ethnopharmacol 1999;68:193–203.
14. Farombi EO, Tahnteng JG, Agboola AO, Nwankwo JO, Emerole GO. Chemoprevention of 2-acetylaminofluorene-induced hepatotoxicity and lipid peroxidation in rats by kolaviron – a *Garcinia kola* seed extract. Food Chemical Toxicol 2000;38:535–541.
15. Farombi EO, Akanni OO, Emerole GO. Antioxidant and scavenging activities of flavonoid extract (kolaviron) of *Garcinia kola* seeds *in vitro*. Pharm Biol 2002;91:129–134.
16. Farombi EO. African indigenous plants with chemotherapeutic potentials and biotechnological approach to the production of bioactive prophylactic agents. African J Biotech 2003;2:662–671.
17. Okunji CO, Ware TA, Hicks RP, Iwu MM, Skanchy DJ. Capillary electrophoresis determination of biflavanones from *Garcinia kola* in three traditional African medicinal formulations. Planta Med 2002;68:440-444.
18. Zheng L, Gao ZO, and Wang SX. A chronic ulcerative colitis model in rats. World J Gastroenterol 2000;6:150-152.
19. Fridovich I and Misra HP. The role of superoxide anion in the auto-oxidation of epinephrine and a simple assay for superoxide dismutase. J Biol Chem 1972;247:3170-3175.
20. Jiang ZY, Woolland ACS, Wolff SP. Hydrogen peroxide production during experimental protein glycation. FEBS Letters 1990;268:69–71.
21. Varshney R, Kale RK. Effects of calmodulin antagonists on radiation-induced lipid peroxidation in microsomes. Int J Radiat Biol 1990;58:733-43.
22. Ige SF, Akhigbe RE, Adewale AA, Badmus JA, Olaleye SB, Ajao FO, Saka WA, Owolabi OQ. Effect of Allium cepa (onion) extract on cadmium-induced nephrotoxicity in rats. Kidney Res J 2011;1:41-47.
23. Akhigbe RE, Olatunji LA, Soladoye AO, Oyeyipo IP. Effect of angiotensin 1-converting enzyme inhibitor, captopril, on body weight, and food and water consumption in oral contraceptive-treated rats. Am J Biochem Mol Biol 2011;1:95-100.
24. Yakubu MT, Akanji MA, Oladiji AT. Aphrodisiac potentials of the aqueous extract of Fadogiaagrestis (Schweinf. Ex Hiern) stem in male albino rats. Asian J Androl 2005;7:399-404.
25. Esimone CO, Adikwu MU, Nworu CS, Okoye FBC, and Odimegwu DC. Adaptogenic potentials of Camellia sinensis leaves, Garcinia kola and Kola nitida seeds. Sci Res Essays 2007; 2:232-237.

26. Alarcón de la Lastra C, Martín MJ, La Casa C, Motilva V. Antiulcerogenicity of the flavonoid fraction from Bidensaurea: comparison with ranitidine and omeprazole. J Ethnopharmacol 1994;42:161-168.
27. Izzo AA, Carlo GD, Mascolo N, Capasso F and Autore G. Antiulcer effect of flavonoids: Role of endogenous PAF. Phytother Res 1994;8:179–181.
28. Reyes M, Martín C, Alarcón de la Lastra C, Trujillo J, Toro MV, Ayuso MJ. Antiulcerogenicity of the flavonoid fraction from Erica andevalensisCabezudo-Rivera. Z Naturforsch 1996;C51:563-569.
29. Kim HP, Son KH, Chang HW, Kang SS. Anti-inflammatory plant flavonoids and cellular action mechanisms. J Pharmacol Sci 2004;96:229-245.
30. Landberg R, Sun Q, Rimm EB. Selected dietary flavonoids are associated with markers of inflammation and endothelial dysfunction in US Women. J Nutr 2011;141:618-25.
31. Adaramoye O A. Comparative effects of vitamin E and kolaviron (a biflavonoid from Garciniakola) on carbon tetrachloride-induced renal oxidative damage in mice. Pak J Biol Sci 2009;12:1146-51.
32. Adaramoye OA, Awogbindin I, Okusaga JO. Effect of kolaviron, a biflavonoid complex from Garcinia kola seeds, on ethanol-induced oxidative stress in liver of adult wistar rats. J Med Food 2009;12:584-90.
33. Okoko T. In vitro antioxidant and free radical scavenging activities of Garcinia kola seeds. Food ChemToxicol 2009;47:2620-2623.
34. González-Gallego J, Sánchez-Campos S, Tuñón MJ. Anti-inflammatory properties of dietary flavonoids. Nutr Hosp 2007;22:287-93.

doi: http://dx.doi.org/10.14194/ijmbr.133

How to cite this article: Ige S.F, Akhigbe R.E, Olaleye S.B, Adeyemi J.W. Gastroprotective of the methanolic extract of *Garcinia kola* in rats. Int J Med Biomed Res 2012;1(3):172-178

Conflict of Interest: None declared