www.ajbrui.org

Afr. J. Biomed. Res. Vol. 21 (September, 2018); 231- 236

Mini Review

The Potential Protective Effects of Selected Medicinal Plants on Liver Function and Integrity

Oguntibeju O.O.

Phytomedicine and Phytochemistry Group, Oxidative Stress Research Centre, Department of Biomedical Sciences, Faculty of Health & Wellness Sciences, Cape Peninsula University of Technology, Bellville 7535, South Africa.

ABSTRACT

The use of herbal plants or their preparations in the management of various diseases including liver diseases has been practiced for several decades and its extension in current dispensation is recognized. It has been shown that the effect of medicinal plants is somehow related to belief, tradition and culture of the community. The correct usage and dosage of each medicinal plant as recommended by the traditional practitioner or as supported by scientific evidence for the specific disease/ailment is believed to be related to the anticipated benefits. Liver diseases form significant causes of morbidity and mortality in humans and animals globally. Therefore a healthy liver is important for the overall health and wellbeing of both humans and animals. Different studies have reported on the anti-diabetic, anti-inflammatory and antioxidant activities of various medicinal plants in various animal models. However, this review examines the hepato-protective potentials of selected medicinal plants.

Keywords: *Vernonia amygdalina, essential oil, Vitamin E, Rutin, antioxidant, reactive oxygen species*

*Author for correspondence: *E-mail*: *oguntibejuo@cput.ac.za, bejufemi@yahoo.co.uk Tel: +27210538495.*

Received: May, 2018; Accepted: August, 2018

Abstracted by:

Bioline International, African Journals online (AJOL), Index Copernicus, African Index Medicus (WHO), Excerpta medica (EMBASE), CAB Abstracts, SCOPUS, Global Health Abstracts, Asian Science Index, Index Veterinarius

INTRODUCTION

The liver is a large organ located in the upper region of the abdominal cavity, below the diaphragm, lying to the right of the stomach. It is important to note that most compounds absorbed by the intestine pass through the liver, making the liver to function as a control center that integrates various metabolic processes and regulating the traffic of biological fuel molecules such as the carbohydrates (Zakin et al., 2002; Naaz et al., 2007; Wang et al., 2012).

Before examining the hepato-protective effects of selected medicinal plants in this paper, it is important, to briefly state key functions of the liver. The liver is the key organ regulating homeostasis in the body. It is involved with various biochemical pathways related to growth, fight against disease, nutrient supply, energy provision and reproduction. The liver is expected not only to perform physiological functions but also to protect against hazards of harmful drugs and chemicals. The metabolic activities of the liver are vital for providing biological fuel to the brain, muscle and other peripheral organs. The liver can produce glucose for release into the blood by breaking down its store of glycogen and by carrying out gluconeogenesis. The main precursors for gluconeogenesis are lactate and alanine from muscle, glycerol from adipose tissue, and glucogenic amino acids from the diet. The liver also plays a central role in the regulation of lipid metabolism and plays a vital function in dietary amino acid metabolism, absorbing the majority of amino acids and primarily use of amino acids for protein synthesis (Hall, 2010; Shi et al., 2014).

In spite of significant scientific advancement in the field of medicine in the last decades, liver problems or diseases seem to be on the rise and have become recognized as public health challenges globally. Many scientists are of the opinion that modern orthodox medicine has very little to offer in the treatment of liver diseases, therefore many medicinal plants are being explored for their possible hepato-protective activities in the treatment and management of liver diseases. For instance in India, over 87 medicinal plants are used in different combinations as herbal medicines for treating liver diseases (Hikino & Kiso (1988; Sharma et al., 1991; Wang et al., 2012; Shi et al., 2014). The principle of using medicinal plants to treat various diseases including liver diseases is also common in African countries and other developing countries. Interestingly, the use of medicinal plants in treating various ailments including liver disease is now gaining ground even in

developed countries. In this review, the following plants and their hepato-protective activities are examined.

Bitter Kola seeds *(Garcinia kola)*

Different studies have investigated the health benefits of extracts of bitter kola seeds in animal models and have reported on its antioxidant, anti-diabetic and anti-inflammatory effects in chemically-induced diabetes or toxicity (Iwu et al., 1987; Orie & Ekon, 1993; Farombi et al., 2002; Adaramoye et al., 2005; Adaramoye 2012). In a recent study in our laboratory, we examined the hepato-protective activity of kolaviron-a Garcinia biflavonoid complex in hypeglycaemic-mediated hepatic injury (Ayepola et al., 2013). In this study, fresh seeds of Garcinia kola were purchased from a market in Ibadan, Nigeria and authentication was done at the Department of Botany, University of Ibadan. Garcinia kola seeds were sliced, air-dried and kolaviron was isolated according to the method of Iwu et al., 1987; Adaramoye, 2012). The extract was concentrated and its concentrated ethylacetate golden yellow solid form was obtained. In this randomized study, adult male Wistar rats weighing between 240-290 g were divided into 4 groups (10 animals per group) and were chemically induced with diabetes using streptozotocin. Following treatment with kolaviron, our results showed that kolaviron administration to diabetic rats significantly reduced serum levels of liver enzymes such as ALT and AST compared to diabetic control (group without kolaviron treatment). Interestingly, treatment of diabetic group with kolaviron significantly reduced IL-6 and alpha-TNF when compared with both normal control and diabetic control rats and also prevented liver hypertrophy.

Plate 1
Bitter kola

In a study conducted by Oze et al (2010), the hepato-protective effect of aqueous extract of Garcinia kola was examined in sixty male and female rats. The rats were grouped into six groups (10 animals per group) and in the experimental design' animals in group 1 were given physiological saline, groups 2 and 3 received 100 and 200 mg/kg of the plant extract in that order. Group 4 was administered 10mg/kg methamphetamine (MAM) subcutaneously. On the other hand, groups 5 and 6 received 100 and 200mg/kg of the extract in that order prior to the induction of neurotoxicity using 10mg/kg methamphetamine. Following sacrifice of animals, serum levels of AST, ALT, ALP, total bilirubin and its conjugated metabolites were used to assess liver damage. It was reported that 50% of the animals in group 4 died, 30% of died in group 5 and none died in 6 after 10-30 min interval of MAM administration. It was reported that the serum levels of some of the marker enzymes and bilirubin were reduced significantly in group 4 at 200mg/kg of the plant extract. The result suggests a possible hepato-protective potential of the kola viron and perhaps its local applications in the management of hepatic dysfunction. Although the mechanism by which kola viron could effect hepato-protection in the presence of toxins is not fully understood, it could possibly be connected to the ability of kola viron to cause membrane stabilization through arrest of free radical reaction in relation to its antioxidant activity (Adaramoye et al., 2005; Oze et al., 2010; Adaramoye, 2012).

The effects of gavage treatment with Garcinia kola seeds on biochemical markers of liver function in diabetic rats were evaluated by Udenze et al., 2012). In this study, 30 male albino rats were randomly divided into 6 groups (n=5). The non-diabetic control and non-diabetic treated groups received by gavage normal saline and 600mg/kg of Garcinia kola seed powder suspended in normal saline in that order. In the last 4 groups, diabetes was induced by intraperitoneal injection of alloxan (diabetic control received normal saline while 3 groups received 300mg/kg, 600mg/kg and 900mg/kg of Garcinia kola in that order) and Garcinia kola was administered twice daily for 21 days. The results showed that treatment with Garcinia kola attenuated serum glucose, ALT, AST, ALP and urea levels of diabetic rats suggesting that the extract is hypoglycaemic and hepato-protective.

Different parts of Garcinia kola have found useful applications in medicinal/traditional purposes. Galam investigated the effects of aqueous extract of Garcinia kola seed on the liver histology (Galam et al., 2013). The results indicated that the treated sections of the liver showed no evidence of degenerative changes or cytoarchitecture distortions of the hepatic parenchyma and it was concluded from the study that intake of Garcinia kola does not cause any acute morphological changes in the liver. At the University of Port Harcourt, Wegwu and Didia reported that Garcinia kola may be acting as a natural antioxidant that prevents hepatic oxidative stress induced by CCI4 (Wegwu & Didia, 2007; Adaramoye, 2012).

Rooibos *(Aspalathus linearis)*

Rooibos is a herbal African tea found in the Cederberg mountain range part of the Western Cape Province, South Africa. It is known to be rich in phenols (antioxidants). In a recent study, Ayeleso et al examined lipid profiles, antioxidant status and liver hispathology in male Wistar following supplementation with rooibos (Ayeleso et al., 2013). The outcome of the study showed that consumption of rooibos improved antioxidant status and preserved liver architecture and that there was a significant increase in liver glutathione levels compared with control group. In another study, Ajuwon et al (2013) examined the protective effects of rooibos supplementation on tert-butyl hydroperoxide-induced oxidative hepatotoxicity in Wistar rats. In this study, 80 pathogen-free male Wistar rats weighing 240 g on the average were randomly divided into eight groups. Oxidative stress was induced by intraperitoneal injection of tert butyl

hydroperoxide for the last two weeks of the 8-week study. Results indicated that supplementation with rooibos significantly decreased conjugated dience, MDA levels in the liver as well as ALT, AST and LH in the liver. The study concluded that rooibos supplementation was capable of alleviating tert-butyl hydroperoxide-induced oxidative hepatotoxicity and that the mechanism of this protection may involve inhibition of lipid peroxidation and modulation of antioxidant enzymes and glutathione status. The protective biochemical function of naturally occurring antioxidants is gaining more attention and this study therefore provides biological evidence supporting the role of rooibos as an adjuvant therapy in the prevention and treatment of liver disorders/diseases.

There has been a rise in the application of natural dietary products as health and wellness promoting agents against excess free radicals. Hepatic tissue is widely exposed to oxidative stress due to its vital role in the regulation of different physiological and biochemical processes. In a more recent laboratory-based study, Canda et al (2014) investigated the effects of consumption of rooibos and rooibos-derived commercial supplements on hepatic tissue injury by tert-butyl hydroperoxide in Wistar rats. The authors reported that rooibos herbal tea is a good dietary antioxidant source and in conjunction with its various other components offers a significant enhanced antioxidant status of the liver especially in induced oxidative stress situation.

Red palm Oil *(Elaeis guineensis)*

Red palm oil, obtained from the fruit of oil palm (Elaeis guineensis) originates from the rain forest area of West Africa and is mainly used for cooking (Oyewole & Amosu, 2010; Falade et al., 2016). It contains the highest known concentrations of natural antioxidants such as carotenes and Vitamin E. Consequently, due to its rich antioxidant contents, palm oil is beneficial in preventing skin aging, fat oxidation, reduction of blood pressure and thrombotic tendency of platelets (Mukherjee & Mitra, 2009; Edem, 2002; Oguntibeju et al., 2010).

Plate 2
Red palm oil

In 2013, Ayeleso et al examined the impact of dietary red palm oil on liver architecture and antioxidant status in the liver of male Wistar rats and reported that red palm oil up-regulated the levels of antioxidant enzymes, preserved liver architecture, therefore its consumption could help in boosting antioxidant status and in promoting general well-being (Ayeleso et al., 2013). Ajuwon et al (2013) also showed that red palm oil supplementation in a chemically-induced oxidative stress was capable of reverting hepatic injury.

Phyllanthus amarus

This plant which is believed to have originated from Malaysia is a small tropical herb and occurs commonly in India and southern Nigeria as well as other West African countries such as Equatorial Guinea and Ghana. Different laboratory-based studies have examined its health benefits however, there seem to be a resurgence of interest in its hepato-protective and antidiabetic activities (Adedapo et al., 2014). In a study performed in Nigeria, Adedapo et al examined the antidiabetic/hepato-protective activities of the aqueous leaf extract of Phyllanthus amarus in laboratory animals where the animals were induced with diabetes using alloxan (70mg/kg). Phytochemical screening of the leaves of the plant demonstrated the presence of alkaloids, tannins, flavonoids, and saponin. In the acute toxicity testing, none of the animal died in all the groups. When the anti-diabetic/hepato-protective activity of the extract was examined, there was a significant reduction in glucose level. Also, chronic administration of the extract significantly reduced the total cholesterol and triglyceride levels. Microscopic examination of the liver section of the diabetic extract-treated group showed normal arrangement of hepatocytes with clear broad liver cells compared with diabetic control group without extract treatment (Adedapo et al., 2014).

Plate 3:
Rooibos

In another study, ethanolic extract of Phyllanthus amarus (0.3kg/kgbw) were given to all groups of animals with the exception of the control group after 30 minutes of alloxan administration. Phyllanthus amarus was found to show hepato-protective effect by reducing the concentration of thiobarbituric acid reactive substances (TBARS) and enhancing reduced glutathione level and antioxidant enzymes such as glutathione peroxidae, glutathione-S-transferase, superoxide dismutase and catalase (Naaz et al., 2007). Interestingly, other species such as P emblica, P polyphyllus, P reticulates have also been reported to demonstrate hepatoprotection in CCl4-induced oxidative stress and

toxicity (Pramyothin et al., 2006; Das et al., 2008). Yanagi et al (1989) observed the effect of P.amarus against hepatitis B virus and reported that extracts of P.amarus inhibited the viral DNA polymerase and hepatitis B virus. The aqueous extract of dried plant of P.amarus did not elicit any chronic toxicity in mice at 0.2mg in a daily dose for ninety days as evaluated by biochemical, pharmacological, histopathological and physiological parameters (Jayaram et al., 1987; Lee et al., 2006). P.niruri form parts of traditional medicine with several formulations in the treatment of jaundice. In a clinical trial on chronic hepatitis B virus carriers, hepatitis B surface antigen clearance in a P.amarus treated group was 59% against 4% in the placebo (Jayanthi et al., 1988). In a separate study, treatment with P.amarus significantly improved liver function in both acute hepatitis A and B with a higher rate clearance (Geetha et al., 1992; Lee et al., 2006; Wang et al., 2012).

Other Plants with Hepatoprotective Activities

Sangameswaran et al (2008) in a study on Andrographis linenta extracts in CCl4-induced liver injury in rats reported that male Wistar rats with chronic liver damage induced by subcutaneous injection of 50% v/v CCl4 in liquid paraffin at a dose of 3ml/kg on alternate days for a period of four weeks and treated with methanol and aqueous extracts of A.linenta orally at a dose of 845mg/kg per day preserved the liver architecture and reverse elevated liver enzymes following treatment. The hepato-protective effects of Morinda citrifolia has also been investigated and report showed that it significantly reduced liver enzymes and cholesterol, triglyceride and LDL-cholesterol and appears to protect the liver against exogenous CCl4 exposures (Wang et al., 2008). The hepato-protective property of the ethanol extract of the leaf of Ptrospernum acerifolium was investigated in rats. After the administration of the extract and following the sacrifice and sample collection, physiological and biochemical parameters were determined according to standard procedures. In the ethanol extract-treated animals, hepatotoxicity of CCl4 was curtailed significantly by restoration of serum bilirubin and liver enzymes compared to the normal group and standard drug silymarin-treated group (Kharpate et al., 2007; Wang et al., 2008; Wang et al., 2012). Sultana et al (1995) reported that the presence of plant extracts of Solanum nigrum and Cichorium intybus protected hepatic DNA against oxidative damage to its deoxyribose sugar moiety in dose-dependent pattern. The authors suggested that the observed hepato-protective of these plants may be related to their ability to suppress oxidative degradation of DNA.

Ahsan and colleagues studied the methanol extracts of seven medicinal plants for their hepato-protective activity in Swiss albino rats with liver damage induced by CCl4. It is a common knowledge that results of histopathological studies provide supportive evidence for biochemical analysis (Ahsan et al., 2009). In the study of Ahsan and colleagues (2009), histology of the liver section of normal control animal showed normal hepatic cells each with well-defined cytoplasm, prominent nucleus and nucleolus. However, that of CCl4 treated group animal demonstrated total loss of hepatic architecture with centrilobular hepatic necrosis, fatty changes, vacuolization and congestion of sinusoids, kupffer cell hyperplasia and crowding of central vein and apoptosis. Interestingly, treatment with methanol extract of the following plants: Casuarium equisetifolia, Cajanus cajan and Gycosmis pentaphylla at a dose of 500mg/kgbwt indicated moderate to weak activity in protecting the liver cells from CCl4 injury. However, treatment with Bixa orellana extract reversed the hepatic injury to normal showing strong hepato-protective activity.

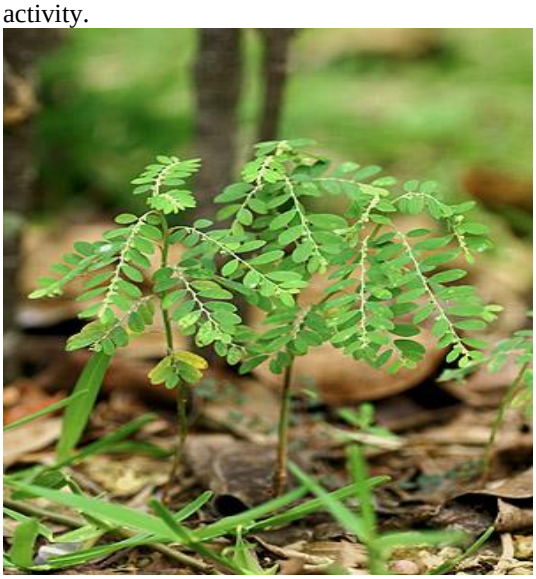

Figure 4
Phyllanthus amarus

The damage to the structural integrity of the liver is commonly assessed by detrmining serum aminotransferases (ALT and AST) activities (Ohta et al., 1997). In an animal study performed by Amin and Hamza, after treatment with azathioprine (AZP), levels of serum ALT and AST were significantly increased when compared to control group (Amin & Hamza, 2005). In contrast, pretreatment with water extract of Hibiscus sabdariffa (HS), Rosmarinus officinalis (RO) and Salvia officinalis (SO) blocked the AZP-induced elevation of serum ALT and AST activities. Pretreatment with HS or SO completely abated the increase of serum ALT activity (100% protection) and the increase of AST was decreased by 37% and 95% respectively. Pretreatment with RO prevented the AZP-induced elevation of serum ALT and AST activities by 73%. It was observed that pretreatment with the three plants completely reversed elevation of hepatic MDA associated with AZP treatment alone and that pretreatment with HA, RO or SO prevented the necrotic changes along with histopathological changes induced by AZP treatment.

Conclusion

From the activities of the selected medicinal plants discussed in this paper, it can be seen that the contribution of medicinal plants to the treatment and management of various diseases in general and hepatic injury in particular cannot be underestimated. It is important to note that the application of medicinal plants is fast entering the domain of conventional medicines. This should stimulate government to invest more funds into medicinal plants research with the aim of discovering more potent active ingredients, explore new potential medicinal plants and to standardize its use at different levels in the society. It is also vital to state at this point that caution must be exercised in the use of medicinal

plants especially those perceived to have hepato-protection since their careless and unsupervised use may pose serious problem to the liver specifically and to human health and wellbeing generally.

Acknowledgement
The author will like to thank the National Research Foundation (NRF) and Cape Peninsula University of Technology for financial support for this work.

REFERENCES

Adaramoye OA, Farombi EO, Adeyemi EO, Emerole GO (2005). Comparative study on the antioxidant properties of flavonoids of Garcinia kola seeds. Pak J Med Sc 21: 1-2.

Adaramoye OA (2012). Antidiabetic effect of kolaviron, a iflavonoid complex isolated from Garcinia kola seeds, in Wistar rats. Afri Health Sci 12 (4): 498-506.

Adedapo A, Ofuegbe S & Oguntibeju O (2014). The antidiabetic activities of the aqueous leaf extract of Phyllanthus amarus in some laboratory animals.in: Antioxidant-antidiabetic agents and human health (ed OO Oguntibeju). InTech, Croatia pp 115-137.

Ahsan R, Islam KM, Haque E (2009). Hepatoprotective activity of methanol extract of some medicinal plants against carbon tetrachloride induced hepatotoxicity in albino rats. Global J Pharmacol 3: 116-122.

Ajuwon OR, Katengua-Thamahane E, Van Rooyen J, Oguntibeju OO & Marnewick JL (2013). Protective effects of rooibos (*Aspalathus linearis*) and/or red palm oil (Elaeis guineensis) supplementation on tert-butyl hydroperoxide-induced oxidative hepatoxicity in Wistar rats. Evidence-Based Compl & Alt Med 2013: 1-19.

Amin A & Hamza AA (2005). Hepatoprotective effects of Hibiscus, Rosmarinus and Salvia on azathione-induced toxicity in rats. Life Sciences 77: 266-278.

Ayeleso AO, Brooks NL & Oguntibeju OO (2013). Impact of dietary red palm oil (Elaeis guineensis) on liver architecture and antioxidant status in the blood and liver of male Wistar rats. Med Tech SA 27:18-22.

Ayeleso AO, Oguntibeju OO & Brooks NL (2013). Assessment of lipid profiles, antioxidant status and liver hispathology in male Wistar rats following dietary intake of rooibos (Aspalathus linearis). Int J Pharmacol 9: 348-357.

Ayepola OR, Chegou NN, Brooks NL & Oguntibeju OO (2013). Kolaviron, a Garcinia biflavonoid complex ameliorates hyperglymia-mediated hepatic injury in rats via suppression of inflammatory response. BMC Compl & Alt Med 13: 363-369.

Canda BD, Oguntibeju OO & Marnewick JL (2014). Effects of consumption of rooibos (*Aspalathus linearis*) and a rooibos-derived commercial supplement on hepatic tissue injury by tert-butyl hydroperoxide in Wistar rats. Oxid Med & Cell Long 2014: 1-9.

Das BK, Bepary S, Datta BK, Chowdhury AA, Ali MS, Rouf AS (2008). Hepaprotective activity of Phyllanthus reticulates. Pak J Pharma Sc 21: 333-337.

Edem DO (2002). Palm oil: biochemical, physiological, nutritional, haematological and toxicological aspects: a review. Plant Foods Hum Nutr 57: 319-341.

Falade AO, Oboh G & Okoh AI (2016). Potential health implications of the consumption of the thermally-oxidised cooking oils-a review. Polish J Food & Nutr Scis 67 (2): 11-30.

Farombi EO, Akani OO, Emerole GO (2002). Antioxidants and scavenging activities of flavonoids extract (kola viron) of Garcinia kola seeds in vitro. Pharm Boil 40: 107-116.

Galam NZ, Gambo IM, Habeeb AA & Sgugaba AI (2013). The effect of aqueous extract of Garcinia kola seed on the liver histology. J Nat Sci Res 3:8-87.

GeethaJ, Manjula R, Malathi S (1992). Efficacy of essential phospholipid substance of soya bean oil and Phyllanthus niruri in acute viral hepatitis. J Gen Med 4: 53-54.

Hall JH (2010). Guy and Hall textbook of medical physiology 12th Edition Elsevier pp 1-32.

Hikino H and Kiso Y (1988). Natural products for liver diseases. In: Economic and medicinal plant research Vol 2. London: Academic Press pp 39-72.

Iwu MM, Onwuchekwa UA, Okuni CO (1987). Evaluating the antihepatoprotective active ingredients of bioflavonoidsd of Garcinia kola seed. Pharm Biol 4): 107-116.

Jayanthi V, Madanagopalan N, Thyagarajan SP, Balakumar V, Parimalam S, Malathi S (1988). Value of herbal medicines, Phyllanthus niruri, eclipta alba, piper longus, thyippili and combination of Phyllanthus niruri and Ricinus communis in acute viral hepatitis. J Gastero & Hepatol 3: 533-554.

Jayaram S, Thyagarajan SP, Panchanadam M, Subramanian S (1987). Antihepatitis B virus properties of Phyllanthus niruri. Biomedicine 7: 9-16.

Kharpate S, Vadnerkar G, Jain D, Jain S (2007). Hepatoprotective activity of the ethanol extract of the leaf of Ptrospermum acerifolium. Ind J Pharma Sc 69: 850-852.

Lee CY, Peng WH, Cheng HY, Chen FN, Lain MT & Chiu TH (2006). Hepatoprotective effect of Phyllanthus in Taiwan on acute Liver damage induced by carbon tetrachloride. Am J Chin Med 34 (3): 471.

Mukherjee S, Mitra A (2009). Health effects palm oil. J Hum Ecol 26: 197-203.

Naaz F, Jayed S, Adbin MZ (2007). Hepatoprotective effect of ethanol extract of Phyllanthus amarus on aflatoxin B1-induced liver damage in mice. J Ethnopharmacol 113: 503-509.

Oguntibeju OO, Katengua ET, Esterhuyse & Truter AJ (2010). Modulation of erythrocyte antioxidant enzyme levels by red palm oil supplementation in male Wistar rats. J Food Agri & Environ 8: 250-255.

Ohta Y, Nishida K, sasaki E, Kongo M, Ishiguro I (1997). Attentuation of disrupted hepatic active oxygen metabolism with the recovery of acute liver injury in rats intoxicated with carbon tetrachloride. Res Comm Mol Pathol & Pharmacol 95: 191-207.

Orie NN & Ekon EU (1993). The bronchodialator effect of Garcinia kola. East Afri Med J 70: 143-145.

Oyewole OE & Amosu AM (2010). Public health nutrition concerns on consumption of red palm oil (RPO): the scientific facts from literature. Afri J Med Med Sci 39: 255-562.

Oze G, Okoro I, Obi A & Nwoba P (2010). Hepatoprotective role of Garcinia kola (heckle) nut extract on methamphetamine: induced neurotoxicity in mice. Afri J Biochem Res 4: 81-87.

Pramyothin P, Samosorn P, Poungshompoo S &

Chaichantipyuth C (2006). The protective effects of Phyllanthus emblica extract on ethanol induced rat hepatic injury. J Ethnopharmacol 107: 361-364.

Sangameswaran B, Reddy RC, Jayakar B (2008). Hepatoprotective effect of leaf extracts of Andrographis linenta nees on liver damage caused by carbon tetrachloride in rats. Phytotherar Res 22: 124-126.

Sharma A, Shing RT, Sehgal V, Handa SS (1991). Antihepatotoxic activity of some plants used in herbal formulations. Fitoterapia 62: 131-138.

Shi J, Li CJ, Yang JZ, Ma J, Wang C, Tang J, Li Y, Chen H and Zhang DM (2014). Hepatoprotective coumarins and secoiridoids from Hydrangea paniculata. Fitoterapia 96:138-145.

Sultana S, Perwaiz S, Igbal M, Athar M (1995). Crude extracts of hepatoprotective plants, Solanum nigrum and Cichorium intybus inhibit free radical-mediated DNA damage. J Ethnopharmaol 45: 189-192.

Udenze EC, Braide VB, Okwesilieze, Akuodor & Odey MO (2012). The effects of gavage treatment with Garcinia kola seeds on biochemical markers of liver functionality in diabetic rats. Ann Biol Res 3: 4601-4608.

Wang MY, Anderson G, Nowicki D, Jensen J (2008). Hepatic protection by noni fruit juice against CCl4-induced chronic liver damage in female SD rats. Plant Foods Hum Nutr 63: 141-145.

Wang BS, Leeb CP, Chenc ZT, Yud HM and Duhb PD (2012). Comparison of the hepatoprotective activity between cultured Cordyceps militaris and natural Cordyceps sinensis. J Funct Foods 4:489-495.

Wegwu MO & Didia BC (2007). Hepatoprotective effects of Garcinia kola seed against hepatotoxicity induced by carbon tetrachloride in rats. Biokem 19: 17-21.

Yanagi M, Unoura M, Kobayashi K (1989). Inhibitory effect of an extract from Phllanthus niruri on reaction of endogenous HBV-DNA polymerase and other DNA synthetases. In: Abstracts of papers presented at the 1989 meeting on Hepatitis B viruses, Cold Spring Harbor, New York: Cold Spring Harbor Laboratory 77S5-8.

Zakin A, Boyer D & Thomas D (2002). Hepatology: a textbook of liver disease 14th Edition ISBN 9780721690513 pp 1-40