British Journal of Pharmacology and Toxicology 2(4): 199-204, 2011
ISSN: 2044-2467

Submitted: June 30, 2011 Accepted: August 27, 2011 Published: October 25, 2011

Toxicological Aspects of *Cola acuminata* Nut Extracts

[1]Shama I.Y. Adam, [1]Ahmed A.N. Yahya, [1]Wala M.M. Salih and [2]Warda S. Abdelgadir
[1]Department of Biochemistry, Faculty of Science and Technology, School of Biochemistry, El Neelain University, Sudan
[2]Food Research Centre, P. O. Box 213, Khartoum North, Sudan

Abstract: The multipurpose medicinal plant, *Cola acuminata*, was chosen for this investigation. Prominent effects on body weight and weight gain was observed. The toxicity on liver, kidney and heart was correlated with changes in the activity of Aspartate Transaminase (AST) and Alanine Transaminase (ALT), and the concentration of cholesterol, albumin and urea in serum. There was an increase in the neutrophils and decrease in lymphocytes in the blood of all the tested groups and an increase of WBC of two groups only. Cytoplasmic fatty vacuolation or necrosis of the centrilobular hepatocytes catarrhal enteritis with minute erosions of the intestinal epithelium with lymphocytic infiltration in the lamina propria and hemosidrin deposition, shrinkage of the glomerular tufts and dilatation of the proximal convoluted tubules were also seen. In group 3 there were lymphocytic infiltrations, glomerular packing, degeneration or necrosis of the epithelial cells of the renal convoluted tubules. No significant lesions were observed in the heart of the test rats. The vital organs of the control rats remained healthy.

Key words: *Cola acuminata*, hematology, pathological findings, serum chemistry, toxicity

INTRODUCTION

The therapeutic utility and toxicity of plants is according to their chemical constituents, and toxicity occurs when these plants are taken in large quantities. Cola (Kola) is a member of the genus of tree belongs to the family Sterculiaceae (Purseglove, 1968), which are native to central and western Africa most notably Sierralione, Liberia, Ivory Coast and Nigeria, and may also be found in Gabon and in the Congo River Basin and Sudan. The most commonly known species are *C. acuminata*, *C. verticillata* and *C. nitida*, with the latter two having the greatest economic importance (Lovejoy, 1980).

Traditionally, the leaves, twigs, flowers, fruit follicles and the bark of *C. acuminata* was used to prepare a tonic as a remedy for gout, dysentery, coughs, diarrhea, vomiting (Ayensu, 1978), chest complaints, various ailments including parasitic diseases (Ebana *et al.*, 1991), and for the management of sexual impotence and erectile dysfunction (Mugish and Origa, 2005). In Benin the *Cola acuminata* fruits are mixed with other plants to treat primary and secondary sterility, and also used as diuretic and laxative when administered orally (Neuwinger, 1996). The Caffeine content in *Cola nuts* may also be helpful in easing migraine headaches because the Caffeine and Theobromine act as cerebral vasodilator. *Cola nuts* are also thought to relieve the pain of neuralgia (Hirt and M´pia, 2001).

Cola acuminata proanthocyanidin is a class of anti-trypansomal compound effective against *Trypansoma bruci*. *In vitro* this compound induced growth arrest and lyses of blood stream form trypanosomes (Kubata *et al.*, 2004).

Chewing of *Cola nuts* is a wide spread habit in the Sub-Saharan Countries of Africa, especially in Northern Nigeria and Sudan to enhance mental alertness (Benjamin *et al*., 1991), and it has been used in folk medicine as an aphrodisiac and appetite suppressant (Mugish and Origa, 2005), and to treat morning sickness. The astringent effect of *Cola nut* can be useful in treating wound and inflammation when applied directly to the skin (Michael, 1995).

In Europe, the roasted seeds are used in the treatment of different disorder and as strong stimulant (Hirt and M´pia, 2001). The council of Europe and the US Food and Drug Administration have approved *Cola nut* as a food additives.

A well-planned experiment was design, for the first time, to obtain information on the effect of various oral doses (75 and 300 mg/kg/day) of methanol and aqueous extracts of *Cola acuminata* on male Wistar rats dosed for two weeks. Emphasis was put on changes in growth, lesions, and alteration in haematology and serobiochemical constituents of treated rats.

Corresponding Author: Warda S. Abdelgadir, Food Research Centre, P.O.Box, 213, Khartoum North, Sudan

MATERIALS AND METHODS

Cola acuminata nuts were purchased from a local market in Khartoum, authenticated by the scientists at the Aromatic and Medicinal Plants Research Institute. The plant tissues were cleaned, shade-dried and ground using a mechanical grinder. The entire experiment was carried out at the premises of the Aromatic and Medicinal Plants Research Institute.

Extract preparation: An accurately weighed 50 g of the powdered plant was extracted with petroleum ether (60-80ºC) for 2 h in a Soxhlet apparatus. The extract was then evaporated by a Buchi Rota evaporator under reduced pressure. The extracted plant material was air-dried, repacked in Soxhlet and extracted again with methanol at 99˚C for 2 h. The extract was similarly evaporated, air dried and the yield was recorded.

In a conical flask, the plant residue was further extracted with distilled water over night at room temperature (25-30ºC), filtered and freeze dried.

Experimental design: Thirty, two weeks old male Wistar rats were obtained and housed within the premises of the Medicinal and Aromatic Plant Research Institute, National Centre for Research, Khartoum. They were fed starter diet and provided free access to water for 2 weeks (adaptation period). The rats were then allotted at random to five groups each of 6 rats. Group 1 rats served as control and fed the starter diet, group 2 and 3 were given the methanol extract of the seeds at 75 and 300 mg/kg/day via the oral rout respectively. The rats of group 4 and 5 were given the aqueous extract of the seeds at 75 and 300 mg/kg/day via the oral rout respectively. All rats were dosed their designated experimental oral doses for 2 weeks.

Average body weight and body weight gain were estimated weekly for each group and the clinical signs were recorded. Lots of three rats from each group were anaesthetized with diethyl ether and humanely slaughter at the end of week one and week 2. Blood sample were collected at slaughter. At necropsy, all rats were examined to identify gross lesions and specimen of the liver, heart, kidney, spleen and intestine were immediately fixed in 10% neutral buffered formalin and processed for histopathology.

Haematological parameters: Blood samples were collected into dry test tubes containing heparin and examined for Haemoglobin (Hb) concentration, Packed Cell Volume (PCV), Red Blood Cell (RBC) counts, White Blood Cell (WBC) and differential WBC counts, Mean Corpuscular volume (MCV), Mean Corpuscular Haemoglobin (MCH), and Mean Corpuscular Haemoglobin Concentration (MCHC), according to the method described by Schalm *et al.* (1975).

Serobiochemical parameters: Sera were analyzed for the activities of aspartate transaminase (AST), alanine transaminase (ALT), and the concentration of total protein, albumin, globulin, bilirubin, cholesterol and urea using the commercial kits (Biosystem Chemicals, Barcelona, Spain) according to the manufacturer instructions.

Histopathological methods: Post- mortem finding were recorded and specimens of tissues (liver, heart, kidney, spleen and intestine) were collected immediately after slaughter of rats, fixed in 10% neutral buffered formalin and embedded in paraffin wax, sectioned at 5µm and stained with Haematoxylin and Eosin (H and E).

Statistical methods: The significance of significance between means was compared at each time point using Duncan's multiple range tests after ANOVA for one-way classified data (Snedecor and Cochran, 1989).

RESULTS

Effect on growth: These data are shown in Table 1. After the first week of the experiment, all the test groups showed significant decrease ($p<0.05$) in body weight gain. At the end of the experimental period, rats given 75 mg/kg/day of *C. acuminata* aqueous extract (group 4) showed significant increase ($p<0.05$) in body weight gain, whereas the test groups 2 and 5 showed depression in body gain ($p<0.05$). None of the rats died during the 2 weeks period.

Haematological changes: These data are summarized in Table 2. After one week of dosing, there were significant decreases ($p<0.05$) of PCV value and neutrophils count and a significant increase ($p<0.05$) of lymphocytes count of rats given *C. acuminata* methanol extract at 75 mg/kg/day (group 2). The WBC count of groups 3 and 4, and the lymphocytes count of group 3 were lower ($p<0.05$) than the control rats.

At the end of the experimental period, the values of Hb and PCV of group 5 given aqueous extract at 300 mg/kg/day) and the lymphocyte count of all the test groups were lower ($p<0.05$) than the controls (group 1), whereas the counts of WBCs of groups 2 and 3 and the neutrophils of all the test groups were higher ($p<0.05$) than the rats of group 1 (controls).

Serobiochemical changes: These data are presented in Table 3. At the first week of the experiment, there was an increased activity of AST in all the test groups. The ALT

Table 1: Body weight and body weight gain in rats orally given *C. acuminata* extracts for 2 weeks

	Parameters		
Treatment groups	Body weight (g) 0 Week	Body weight gain (g) 1 week	Body weight gain (g) 2 week
Control (normal diet)	86.7±7.9	17.1±3.4	13.0±4.3
75 mg/kg/day (per os) Methanolic extract	87.5±2.1	4.7±5.1*	8.7±3.8*
300 mg/kg/day (per os) Methanolic extract	87.5±4.4	0.7±9.7*	12.4±9.9^{NS}
75mg/kg/day (per os) Aqueous extract	86.6±5.7	1.8±5.1*	15.4±8.1*
300mg/kg/day (per os) Aqueous extract	86.5±4.7	3.5±2.3*	11.0±2.8*

Values are expressed as mean±S.E; NS: not significant; *: Significant: (p>0.05)

Table 2: Haematological changes in rats given methanol and aqueous extract of *cola acuminata* nuts

	Groups				
	1	2	3	4	5
Parameters	Control	Meth extract 75 m/kg/day	Meth. extract 300 m/kg/da	Aque extract 75 m/kg/day	Aque. extract 300 m/kg/da
One week					
Hb	11.9±0.2	10.5±1.0^{NS}	11.4±0.7 ^{NS}	11.1±2.0 ^{NS}	12.5±0.1^{NS}
RBC 9×10^6 mm^3)	6.8±0.2	6.0±0.6 ^{NS}	6.2±0.2 ^{NS}	6.5±1.3 ^{NS}	17.1±0.1 ^{NS}
PCV (%)	37.4±0.7	32.3±3.2*	34.3±1.8 ^{NS}	34.6±6.5 ^{NS}	39.0±0.4 ^{NS}
MCH (m^3)	54.7±1.2	55.0±0.9 ^{NS}	55.1±0.9 ^{NS}	53.3±0.4 ^{NS}	54.9±0.4 ^{NS}
MCH (pg)	17.5±0.3	17.8±0.4 ^{NS}	18.3±0.5 ^{NS}	17.0±0.3 ^{NS}	17.6±0.1 ^{NS}
MCHC (%)	31.9±0.2	32.4±0.3 ^{NS}	33.10.4± ^{NS}	32.0±0.4 ^{NS}	32.1±0.2 ^{NS}
WBC(×10^6 mm^3)	6.0±0.2	4.9±2.5 ^{NS}	4.4±0.9*	3.2±0.5*	5.0±0.8 ^{NS}
Neutrophils (%)	44.1±2.3	38.6±3.7*	58.1±5.7*	43.6±14.3^{NS}	41.0±4.7 ^{NS}
Lymphocytes (%)	55.5±2.3	61.5±3.7*	41.9±5.7*	56.4±14.3^{NS}	59.0±4.7 ^{NS}
Two weeks					
Hb	1 1.2±0.3	11.3±0.3^{NS}	11.1±0.2^{NS}	10.8±0.7 ^{NS}	9.2±1.2*
RBC (×10^6 mm^3)	6.1±0.3	6.2±0.1^{NS}	6.1±0.1^{NS}	6.0±0.3 ^{NS}	5.1±0.6 ^{NS}
PCV (%)	35.2±1.4	35.5±0.9 ^{NS}	34.9±0.5 ^{NS}	35.1±2.2 ^{NS}	29.4±2.6*
MCV (m^3)	58.1±0.7	57.2±0.8^{NS}	57.3±0.4 ^{NS}	58.5±1.1 ^{NS}	57.9±0.2 ^{NS}
MCH (pg)	18.4±0.4	18.1±0.3 ^{NS}	18.4±0.2 ^{NS}	18.1±0.8 ^{NS}	18.2±0.2 ^{NS}
MCHC (%)	31.4±0.3	31.7±0.1 ^{NS}	31.9±0.1 ^{NS}	30.9±0.8 ^{NS}	31.4±0.3 ^{NS}
WBC(×10 ^{6}mm^3)	6.9±1.1	10.9±1.6*	9.5±2.0*	6.2±1.8 ^{NS}	6.5±2.3 ^{NS}
Neutrophils (%)	35.0±1.0	49.6±2.6*	54.4±4.2*	51.9±2.3*	58.7±2.8*
Lymphocytes (%)	65.0±1.0	50.4±2.6*	45.6±4.2*	48.1±2.3*	41.3±2.8*

Values are mean±SE; NS: Not significant; *: Significant : (p>0.05); Meth: Methanol; Aque: aqueous

Table 3: Serobiochemical changes in rats given methanol and aqueous extract of *cola acuminata* nuts

	Groups				
	1	2	3	4	5
Parameters	Control	Meth. extract 75 m/kg/day	Meth. extract 300 m/kg/day	Aque. extract 75 m/kg/day	Aque. extract 300 m/kg/day
One week					
AST (iu)	179.0±8.5	217.3±9.8*	228.3±9.9 *	216.7±8.5*	262.3±3.3*
ALT (iu)	38.3±8.8	34.0±1.7^{NS}	34.3±3.8 ^{NS}	32.7±3.7 ^{NS}	52.3±5.2*
Total protein (g/dL)	6.4±0.5	6.9±0.1 ^{NS}	6.7±0.3 ^{NS}	6.2±0.3^{NS}	7.2±0.1*
Albumin (g/dL)	4.2±0.2	4.8±0.1^{NS}	4.7±0.3^{NS}	3.5±0.7^{NS}	5.1±0.1*
Globulin (g/dL)	2.1±0.5	2.1±0.2^{NS}	1.9±0.9^{NS}	2.7±0.4 ^{NS}	2.1±0.1^{NS}
Bilirubin (mg/dL)	1.0±0.0	0.1±0.0^{NS}	0.1±0.0 N S	0.1±0.0 ^{NS}	0.1±0.0 ^{NS}
Cholesterol (mg/dL)	79.0±7.6	82.3±2.3 ^{NS}	78.0±7.6^{NS}	93.0±1.5*	86.3±3.2*
Urea(mg/dL)	49.3±4.6	62.8±4.4*	59.0±3.1*	51.7±3.3*	66.7±4.8*
Two Weeks					
AST(iu)	148.0±8.0	219.0±9.7*	147.0±3.0^{NS}	191.5±1.5*	182.5±2.5*
ALT(iu)	58.0±1.0	72.0±3.5*	55.5±1.5*	51.0±1.0*	52.0±2.0*
Total protein (g/d)	7.1±0.1	7.1±0.2^{NS}	6.6±0.2^{NS}	6.5±0.4^{NS}	6.8±0.2 ^{NS}
Albumin (g/dL)	4.6±0.1	4.3±0.3^{NS}	4.0±0.4^{NS}	3.9±0.2 ^{NS}	3.8±0.2^{NS}
Globulin (g/dL)	2.5±0.1	2.8±0.1^{NS}	2.6±0.2^{NS}	2.9±0.1^{NS}	3.0±0.0 ^{NS}
Bilirubin (mg/dL)	0.1±0.0	0.1±0.0^{NS}	1.0±0.0 ^{NS}	0.1±0.0 ^{NS}	0.1±0.0^{NS}
Cholesterol (mg/dL)	87.5±0.5	82.7±1.5 *	89.5±0.5 *	87.5±1.2 ^{NS}	72.5±2.5*
Urea (mg/dL)	60.5±2.5	67.7±2.2*	63.0±1.0 *	52.0±2.0*	66.0±2.0*

Values are mean±SE; NS: Not significant; *: Significant: (p>0.05); Meth: Methanol; Aque: Aqueous

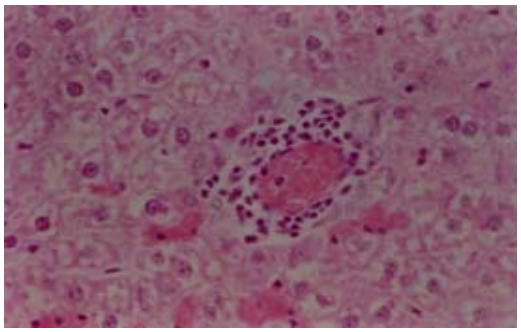
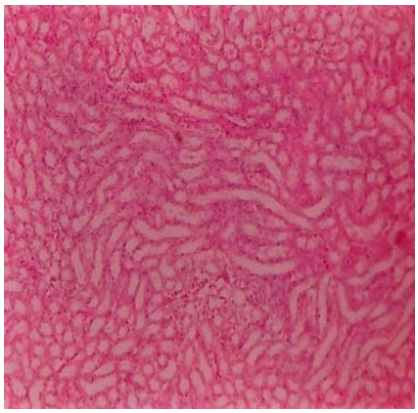
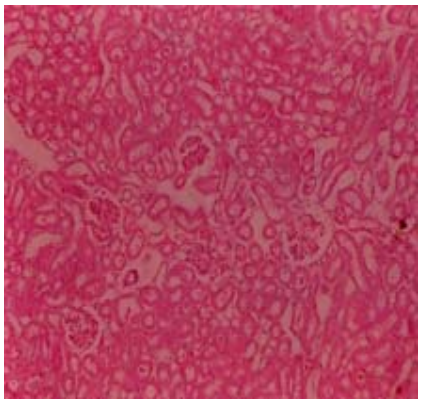


Fig. 1: Liver of rats receiving methanol extract at 75 mg/kg for two weeks shows fatty changes, hemorrhage, necrosis and lymphocytic infiltration H&E. X100



(a)



(b)

Fig. 2: (a) Kidney of rats receiving aqueous extract at 75 mg/kg for one week shows fatty change, necrosis, segmentation and degeneration of glomeruli and (b) dilatation of renal tubules and necrosis H&E. X 100

activity, concentration of the total protein and albumin of group 5, cholesterol of groups 4 and 5 and the urea concentration of all tested groups were higher ($p<0.05$) than the controls of group 1.

After two weeks the activity of AST of groups 2, 4 and 5, and ALT activity of group 2 were higher ($p<0.05$) than the controls. There was a significant decrease ($p<0.05$) in ALT activity of groups 3, 4 and 5, cholesterol concentration of groups 2 and 5, and urea concentration of group 4. An increase in cholesterol concentration of group 3 and urea concentration of groups 2, 3 and 5 was also detected.

Histopathological findings: After 2 weeks of treatment with daily oral doses of *C. acuminata* seeds extracts, group 4 showed consistent lesions that included cytoplasmic fatty vacuolation or necrosis of the centrilobular hepatocytes (Fig. 1). Catarrhal enteritis with minute erosions of the intestinal epithelium with lymphocytic infiltration in the lamina propria and hemosidrin deposition, shrinkage of the glomerular tufts and dilatation of the proximal convoluted tubules were also seen. In group 3 there were lymphocytic infiltrations, glomerular packing, degeneration or necrosis of the epithelial cells of the renal convoluted tubules (Fig. 2a, b). No significant lesions were observed in the heart of the test rats. The vital organs of the control rats (Group 1) showed no lesion throughout the two weeks experimental period.

DISCUSSION

There is a lack of information about the toxicity of *Cola acuminata* nuts to animals. The administered doses were chosen at 75 and 300 mg/kg/day because the aqueous and methanol extracts at this level were toxic to Wistar rats in *Rhanterium epapposum* and *Trichodesma africanum* aerial parts (Adam and Adam, 2008). The results indicated that the plant extracts are toxic and lethal to rats by whatever route (Oral or I.M) they were given.

The toxicity of the plant material seems dependent of the types of active principles, the concentration added to the diet and the rate of their metabolic conversion in the liver to metabolites and their consequent excretion.

Phytochemical investigations Cola nut have demonstrated the presence of alkaloid such as caffeine, theobromine (Moloney, 1970), phenolic compound (Van Buren, 1970), tannin, oxalate, saponin, cyanogenic and cardiac glycosides (Monago and Uwakwe, 2005), proanthocyanidin (Kubata *et al*., 2004). Proanthocyanidin, tannins, catechin have been used extensively for reducing inflammation and excessive secretion such as bleeding, mucous and diarrhea (Loeb *et al*., 1989) because of their ability to protect and dry out mucous membrane or

wounds (Khanna *et al*., 2002). In addition, proanthocyanidins are known for their antiviral (Mantani *et al*., 2001), anti bacterial (Foo *et al*., 2000; Ho *et al*., 2001) and anti leishmanial activities (Kiderlen *et al*., 2001).

The major alkaloids present in *Cola* species are caffeine, theobromine and theophylline. Some studies have, however, found that exposure to caffeine is related to poor neuromuscular development and significant increases in breech presentation of fetuses (Barr and Streissguth, 1978). Caffeine and theobromine can penetrate the placental barrier quite easily (Kimmel *et al*., 1984) and so affect the developing fetus. Consumption of caffeine during pregnancy leads to changes in the levels of brain chemicals such as DNA, Zinc, c.AMP, protein and alkaline phosphatase (Concannon *et al*., 1978; Huges and Beveridge, 1991). Theophylline has been used in therapeutics for bronchodilation, for acute ventricular failure and for long term control of bronchial asthma.
The growth change is due to mal absorption of the intestines due to intestinal disquamination or damage in other vital organs.

In present study the rats given methanol and aqueous extracts of *Cola acuminata* seeds at the concentrations of 75 and 300 mg/kg showed a decrease in the activity of ALT and the concentration of albumin which might be attributed to the damage and necrosis in the liver resulting in an inability of the hepatocytes to synthesize the enzyme and albumin or due to the renal dysfunction and over excretion in urine. The increase in the activity of AST is attributed to the damage in liver and heart (Chazquileres and Robert, 1996). Increase in the concentration of urea is due to renal insufficiency and inability of renal tubule to excrete the waste products.

The presence of haemosiderin deposits in the red pulp of the spleen might have resulted from slight destruction of RBCs by unknown substances. In group 5 fed *Cola acuminata* seed aqueous extract at 300 mg/kg, the anaemia was due to the decreased levels of Hb and PCV levels (Kimber *et al*., 1965). The type of anaemia is normocytic normochromic (normal MCV, normal MCHC).

We concluded that the study demonstrated a significant toxicity for male Wistar rats of *Cola acuminata* seeds at concentrations of 75 and 300 mg/kg administered by oral route. Consumption of *Cola acuminata* seeds cause damage of vital organs exemplified by necrosis, fatty changes, haemorrhage and congestion.

In spite of the several uses of plant in developing countries especially rural areas there is no standardized doses system in traditional medicine practice we suggest that further researches might be carried safety dosage to avoid the toxicity, and isolation of plant constituents and determine their mode of action.

ACKNOWLEDGMENT

Authors are greatly indebted to all who have provided them with invaluable assistance, advice and encouragement throughout the course of this work.

REFERENCES

Adam, S.I.Y. and S.E.I. Adam, 2008. Evaluation of Toxicity *Rhanterium epapposum* in Wistar rats. J. Pharm. Toxicol., 3(2): 134-140.

Ayensu, E.S., 1978. Plants for medicinal uses with special references to arid zones. Proceedings of the International Arid Lands Conference on Plant Resources, 1978, Lubbock, Texas, pp: 117-178.

Barr, H.M. and P. Streissguth, 1978. Caffeine use during pregnancy and child outcome: A seven years protective study. Neurotox Teratol., 13: 441-448.

Benjamin, L.T., A.M. Rogers and A. Rosenbaum, 1991. Coca-cola, caffeine, and mental deficiency: Harry Hollingworth and the chattanooga trial of 1911. J. History Behav. Sci., 27(1): 42-55.

Chazquileres, O. and A. Robert, 1996. Percentage of International Normalze Ratio. Laboratorie Central d' Hematologie et d' Immunology. Paris, France.

Concannon, I.T., J.M. Branughler and M.D. Chechter, 1978. Pre and post- natal effects of caffeine on brain biogenic amines, cyclic neucleotides and behavior in developing rats. J. Pharm. Exp. Ther., 220: 673-679.

Ebana, R.U.B., B.E. Madunagu, E.D. Ekpe and I.N. Otung, 1991. Microbiological exploitation of cardiac glycosides and alkaloids from *Garcinia kola*, *Borreria ocymoides*, *Cola nitida* and *Citrus aurantifolia*. J. Appl. Bacteriol., 71: 398-401.

Foo, L.Y., L.Y. Howell and A.B. Vorsa, 2000. The structure of cran berry proanthocyanidins which inhibit adherence of urophathogenic *P. fimbriated E. coli in vitro*. Phytochem., 54: 173-181.

Hirt, H.M. and B. M´pia, 2001. Natural Medicine in the Tropics, 2nd Edn., Drucherei Bauer, Winnenden.

Ho, K.Y., C.C. Tsai, J.S. Huang, C.P. Chen, T.C. Lin and C.C. Lin, 2001. Antimicrobial activity of tannin components from *Vaccinium vitisidaea* L. J. Pharm. Pharm., 53: 187-191.

Huges, R.N. and I.J. Beveridge, 1991. Behavioral effects of exposure to caffeine during gestation, lactation or both. Neurotoxical Teratol., 13: 641-647.

Khanna, S., M. Venojarvi and S. Roy, 2002. Dermal wound healing properties of redox-active grape seed proanthocyanidins. Free Radic. Biol. Med., 33:1096.

Kiderlen, A.F., O. Kayser, D. Ferreira, H. Kolodziej, 2001. Tannins and related compounds: Killing of amastigotes of *leishmania donovani* and release of nitric oxide and tumer necrosis factor α in macrophage *in vitro*. Z. Naturforsch., 56: 444-454.

Kimber, C., R.S. Oliver and A.H. Aster, 1965. The mechanism of anemia in chronic liver disease. Am. J. Med., 38: 767.

Kimmel, C.A., G.L. Kimmel, C. White, T.E. Grasto, J.F. Young and G.J. Neison, 1984. Blood flow changes and conceptual development in pregnant in response to caffeine. Fund Appl. Toxicol., 4: 240-247.

Kubata, B.K., K. Nagamune and N. Muramkami, 2004. *Cola acuminate* proanthocyanidins: A class of anti-trypansomal compounds effective against *Trypansoma brucii*. Int. J. Parasitol., 35: 91-103.

Loeb, H., Y. Vendenplas, P. Wursch and P. Guersy, 1989. Tannin-rich carob pod for the treatment of acute-onset diarrhea. J. Pediatr. Gastroenterol. Nutr., 8: 480-485.

Lovejoy, P.E., 1980. Kola in the History of West Africa (La kola dans l'histoire de l'Afrique occidentale) Cahiers d'Études Africaines, Cahier, 20(77-78): 97-134.

Mantani, N., N. Imanish, H. Kawamata, N. Terasawa and H. Ochiai, 2001. Inhibitory effect of (+) catechin on the growth of influenza A/PR/8 virus in MPCK cells. Planta Med., 67: 240-243.

Michael, C., 1995. The healing Herbs the Ultimate Guide to the Curative Power of Nature's Medicines, Bantam Books, New York.

Moloney, A., 1970. Sketch of the Forestry of West Africa. Sampson Low, London. Van Buren J. Fruit Phenolic. In: Hulme, A.C., (Ed.), The biochemistry of Fruits and their Products. Academic Press, London, 1: 269-304.

Monago, C.C. and A.A. Uwakwe, 2005. Tannin, Oxalate, Saponin, Cyanogeni and Cardiac glycosides contents of *Cola nitida* and *Cola acuminata*. Global J. Pure Appl. Sci., 11(4): 501-504.

Mugish, M. K. and H.O. Origa, 2005. Traditional herbal remedies used in the management of sexual impotence and erectile dysfunction in Western Uganda. Afri. Health Sci., 5(1): 40-49.

Neuwinger, H.D., 1996. African Enthobotany-Poisons and Drugs: Chemistry, Pharmacology and Toxicology. Chapman and Hall, London.

Purseglove, J.W., 1968. Tropical crops: Dicotyledons. Long-mans Green and Co. Ltd. London.

Schalm, O.W., N.C. Jain and G.H. Carroll, 1975. Veterinary Haematology, 3rd Edn., Philadelphia, Lea and Febiger, USA.

Snedecor, G.W. and W.C. Cochran, 1989. Statistical Methods, 8th Edn., Iowa state University Press-Ames. Iowa.

Van Buren, J., 1970. Fruit Phenolic. In: Hulme, A.C. (Ed.), The biochemistry of Fruits and their Products. Academic Press, London, (1): 269-304.