Effect of *Garcinia kola* Seed Ethanolic Extract on Renal Function Indices in Male Wistar Rats

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ABSTRACT

This study seeks to evaluate the effect of *Garcinia kola* seed ethanolic extract on renal function parameters of male Wistar rats. Thirty (30) male Wistar rats weighing 150.42 ± 3.98 g were divided into three groups (I, II and III) comprising ten animals each. Animals in group I (control) received 0.5 ml of distilled water while those in groups II and III were administered 100 and 200 mg/kg body weight of the extract respectively once daily for 21 days. After 21 days of extract administration, 5 rats from each group were sacrificed. Same was done after 42 days. The lethal dose (LD_{50}) of the extract was found to be safe up to 5000 mg/kg body weight. After 21 and 42 days, administration of the extract at both doses (100 and 200 mg/kg body weight) significantly ($P < 0.05$) increased the concentration of Na^+ in the serum of the animals. Treatment with the ethanolic seed extract at both doses (low and high) did not significantly ($P > 0.05$) affect the concentration of serum Cl^- after 21 and 42 days respectively. After 21 days, the extract at both doses significantly ($P < 0.05$) increased the concentration of serum K^+ when compared with the control. After 42 days, the extract at low dose (100 mg/kg body weight) significantly ($P < 0.05$) increased the concentration of K^+ in the serum of the animals, however, the extract at high dose (200 mg/kg body weight) does not significantly ($P > 0.05$) affect serum K^+ level. While the low dose of extract did not affect serum HCO_3^- concentration after 21 and 42 days respectively, it significantly ($P < 0.05$) decreased serum HCO_3^- level after 21 days but increased after 42 days. After 21 days, administration of the extract at both doses significantly ($P < 0.05$) decreased creatinine concentration in the serum of the animals while its concentration was significantly ($P < 0.05$) increased by both doses of the extract after 42 days. After 21 days, treatment with the extract at 100 mg/kg body weight significantly ($P < 0.05$) increased serum urea concentration while the high dose did not alter serum urea concentration when compared with the control. However, after 42 days, extract administration at both doses did not significantly ($P > 0.05$) affect the concentration of urea in the serum of the animals when compared with the control. The non-significant effect displayed by the extract at some doses suggest an improvement and a protective activity on the renal function hence the recommendation of *Garcinia kola* for a reduced or declining renal function. However, the alterations in biomolecules are indication of impaired renal function suggesting that the extract may not be completely 'safe' as oral remedy at the doses investigated in this study.

Keywords: *Garcinia kola*, Renal function, Protective activity, Biomolecules, Alterations

INTRODUCTION

The use of plants for medicinal purposes is the oldest form of health care known to mankind (Auta *et al*., 2012). Many of these plants as explained by Gill (1992) and Iwu (1993) contain substances that can be used for therapeutic purposes. The World Health Organization (WHO) (2004) estimated that about 80% of the population in developing countries relies on traditional medicine for their health care purposes (Murray, 1995). Furthermore, the use of plants as medicine to cure or prevent illness and to lubricate the wheels of social interaction at the interpersonal and group level is a behaviour that predates civilization, and in today's civilization, it is found in every society irrespective of its level of development and sophistication (Odugbemi, 2006). The use of medicinal plants constitutes an important part of traditional medicine which is a part of African heritage. Though modern /orthodox medicine has improved the lot of many people worldwide, it is noteworthy that in many cultures, modern medicine complements traditional practices as is obtainable in industrialized societies e.g. China and India (Odugbemi, 2006). In Nigeria, majority of citizens still uses medicinal plants and visit traditional medicine practitioners for their health care need (Odugbemi, 2006).

Medicinal plant is therefore defined as various plants used in herbalism and thought by some to have medicinal properties (Ogunlesi *et al*., 2008). Medicinal plants contain numerous biologically active compounds such as carbohydrates, proteins, enzymes, fats and oils, minerals, vitamins, alkaloids, quinones, terpenoids, flavonoids, carotenoids, sterols, simple phenolic glycosides, tannins, saponins, polyphenols, to mention a few which have medicinal activities (Olowokudejo *et al*., 2008). Despite the wide acceptance and consumption of herbal concoction from these medicinal plants, there is little evidence to scientifically verify the shortcomings of their usage or knowing the possible adverse effect they pose on tissues (kidneys) of animal model. One of such medicinal plants is *Garcinia kola*.

Garcinia kola, a dicotyledonous plant belonging to the *Clusiaceae* or Guttiferae family is commonly found in the subtropical and tropical forests of some countries of West and Central Africa such as Benin, Cameroon, Democratic Republic of Congo, Ivory Coast, Ghana, Liberia, Nigeria, Senegal and Sierra Leone, Asia and Europe (Plowden, 1972; Adesuyi *et al*., 2012). It is a medium-sized tree growing up to 12 m tall and 1.5 m wide and usually found in the rain forest of Nigeria (Iwu, 1993). The seed is popularly known as bitter kola or male kola in English. In Nigeria, the seed is commonly called "*Namiji goro*" in Hausa, "*Akilu*" in Igbo, "*Orogbo*" in Yoruba and "*Efiari*" by the Efiks (Esomonu *et al*., 2005). It is a brown nut-like seed, used in traditional medicine (Braide and Vitrotio, 1989). The seeds when chewed have a bitter astringent taste. The seed extract and dry powdered seed of *G. kola* plants have been made into various forms including tablets, cream and toothpaste (Iwu, 1985). It is used in traditional medicine for various therapeutic purposes based on the pharmacological effects of the active components (flavonoid) in the seed and other parts of the plant (Braide and Vitrotio, 1989).

On renal function, previous studies by Adedara *et al* (2014) reported *Garcinia kola* seed to ameliorate renal damage while Adaramoye (2009) studied the comparative effects of Vitamin E and a biflavonoid from *Garcinia kola* on carbon tetrachloride-induced renal oxidative damage in mice. Furthermore, Ajayi *et al* (2012) worked on the protective effects of kolaviron on the renal functions of female Wistar rats treated with Clomiphene citrate while Okoko and Awhin (2007) saw that *Garcinia kola* could reduce cisplatin-induced kidney dysfunction in rats. Despite these studies, there is still paucity of information on duration-dependent renal function study at 100 and 200 mg/kg body weight of the plant, which is unique to the present work. Therefore, this study was designed to evaluate the possible safety or toxicity risk of *Garcinia kola* seed ethanolic extract on renal function indices in male Wistar rats.

MATERIALS AND METHODS

Materials:

Plant Materials and Authentication:

Garcinia kola seeds which were purchased from Karu Market, in the Federal Capital Territory, Abuja and were authenticated at Forestry Research Institute of Nigeria (FRIN), Ibadan, Nigeria with voucher specimen number (F.H.I. 10847).

Experimental Animals:

Male Wistar rats (*Rattus norvegicus*) weighing 150.42±3.98 g were obtained from the Animal House of Federal College of Animal Husbandry, Kuru, Jos, Plateau State, Nigeria.

Other Reagents:

All other chemicals and reagents used which were of analytical grade were products of Sigma Aldrich Ltd., Buchs, Canada and are prepared in volumetric flask using glass wares with distilled water except otherwise stated.

Methods:

Preparation of *Garcinia kola* Seed Ethanolic Extract:

Dried seeds of *Garcinia kola* were peeled to remove the testa. This was cut into smaller sizes and thereafter pulverized in a blender (PHILIPS, Model HR-1724, Brazil) to obtain smooth powder. A known weight (200 g) of the powder was extracted in 1000 ml of ethanol for 72 hours at room temperature. The extract was filtered with Whatman No. 1 filter paper (Maidstone, UK) and the resulting filtrate concentrated in a Rotary Evaporator (MODEL: RE-52A, SHANGHAI YA RONG BIOCHEMISTRY INSTRUMENT FACTORY, China). The mixture was further transferred into water bath (Model: NL-420S, NEWLIFE® MEDICAL INSTRUMENT, England) where it was further evaporated to give the required brownish-black residue. This was then reconstituted in distilled water to give the required doses (100 and 200 mg/kg body weight) used throughout the experimental period.

Acute Toxicity Study (LD_{50}):

The method described by Lorke (1983) was adopted to determine lethal dose (LD_{50}). The experiment was carried out in two stages:

Stage I: Nine rats were completely randomized into 3 groups (A-C) of 3 rats each. The animals in group A received *Garcinia kola* seed ethanolic extract at a dose of 10 mg/kg body weight. Group B received 100 mg/kg body weight. Group C received 1000 mg/kg body weight. The animals were observed/monitored for 24 hours. The number of deaths in each group was noted.

Stage II: This stage was carried out based on the results of the first stage. Three groups (A-C) of one rat each were used. The animal in Group A received 1000 mg/kg body weight of the extract. The animal in Groups B and C received 3000 and 5000 mg/kg body weight of the extract respectively. The animals were monitored for another 24 hours during which the number of deaths or abnormal reaction/behaviour was noted.

Animal Grouping and Extract Administration:

A total of thirty (30) male Wistar rats, housed in clean aluminum cages contained in well ventilated standard housing conditions (temperature: 28-31°C; photoperiod: 12 hours; humidity: 50-55%) was used for the study. The animals were allowed free access to rat pellets (Premier Feed Mill Co. Ltd., Ibadan, Nigeria) and tap water *ad libitum*. The cages were also cleaned on daily basis. The animals were acclimatized for two weeks before the commencement of the experiment. The thirty (30) male Wistar rats weighing 150.42 ± 3.98 g were completely randomized into three groups (I, II and III) comprising ten animals each. Animals in group I (control) received 0.5 ml of distilled water while those in groups II and III were administered 100 and 200 mg/kg body weight of the extract respectively once daily for 21 days using polystyrene. After 21 days of extract administration, 5 rats from each group were sacrificed. Same number was sacrificed after 42 days. Extract administration was done daily using polystyrene. The experiment was conducted in compliance with the National Institute of Health Guidelines for Care and Use of Laboratory Animals (Pub No.85-23 revised 1985). All animals were examined and approved by the Bingham University's Animal Ethical Committee according to the ethical standards laid down in the 1964 Declaration of Helsinki.

Preparation of Serum:

The rats were anaethesized in a glass jar containing cotton wool soaked in diethyl ether. The unconscious rats were quickly removed and the neck area cleared of fur. The jugular vein which was slightly displaced (to avoid contamination of the blood with interstitial fluid) was cut with a sterile scapel blade and an aliquot of the blood was collected into a sample bottle. The blood was then left undisturbed for 10 minutes at room temperature to clot. The blood was thereafter centrifuged at 2000 g for 15 minutes using Uniscope Laboratory Centrifuge (Model 800D, New Life Medical Instrument, England). The sera were later aspirated with Pasteur pipette into dry, sample bottles and used within 12 hours of preparation for the determination of renal function parameters.

Determination of Renal Function Indices:

The concentration of serum urea and creatinine was determined by adopting the procedure described by Veniamin and Vakirtzi (1970) and Bartels and Bohmer (1972). Serum concentrations of Na^+, K^+, Cl^- and HCO_3^- were determined by the method of Tietz (1995), Tietz (1990), Skeggs and Hochstrasser (1964) and Tietz *et al* (1994) respectively.

Statistical Analysis:

Results were expressed as the mean ± SEM of ten determinations. Means were analyzed using Duncan's Multiple Range Test and complemented with Student's t-test. The differences were considered statistically significant at $p<0.05$. All these analyses were done using SPSS 16.0 Software (Statistical Package for Social Sciences, Inc., Chicago, IL, USA).

RESULTS

Findings from acute toxicity study revealed that all the graded doses of *Garcinia kola* seed ethanolic extract administered to the animals showed no signs of toxicity and no deaths were recorded. Therefore, the LD_{50} of *Garcinia kola* seed ethanolic extract was found to be safe up to 5000 mg/kg body weight.

After treatment for 21 days, the *Garcinia kola* seed ethanolic extract at 200 mg/kg body weight significantly ($P < 0.05$) increased the serum sodium ion concentration from 140 ± 3.10 mmol/L (control) to 145.2 ± 2.16 mmol/L (high dose) and there was also an increase to 147.6 ± 2.96 mmol/L in the low dose group (100 mg/kg body weight) as shown in Table 1.

After treatment for 42 days, the *Garcinia kola* seed ethanolic extract significantly ($P < 0.05$) increased the serum sodium ion concentration from 138.8 ± 2.50 mmol/L (control) to 149.2 ± 2.92 mmol/L (high dose) and there was also a significant ($P > 0.05$) increase to 162.4 ± 7.40 mmol/L in the low dose group (100 mg/kg body weight) as shown in Table 1.

After treatment for 21 days, both doses of the *Garcinia kola* seed ethanolic extract significantly ($P < 0.05$) increased the serum potassium ion concentration from 3.22 ± 0.10 mmol/L (control) to 3.96 ± 0.31 mmol/L (high dose) and there was also an increase to 3.68 ± 0.21 mmol/Lin the low dose group as shown in Table 2.

After treatment for 42 days, the *Garcinia kola* seed ethanolic extract seed at 200 mg/kg body weight did not significantly ($P > 0.05$) alter the serum potassium ion concentration from 4.6 ± 0.11 mmol/L (control) to 4.16 ± 0.23 mmol/L (high dose) and there was a significant ($P > 0.05$) increase to 6.78±0.21mmol/L in the low dose group (100 mg/kg body weight) as shown in Table 2.

After treatment for 21 days, the *Garcinia kola* seed ethanolic extract at 200 mg/kg body weight did not significantly ($P > 0.05$) alter the serum chloride ion concentration as the values: 94.6 ± 6.86 mmol/L (control) and 99.8 ± 7.78 mmol/L (high dose) were comparable and there was also a non-significant effect giving the value 93.2 ± 5.10 mmol/L in the low dose group (100 mg/kg body weight) as shown in Table 3.

After treatment for 42 days, the *Garcinia kola* seed ethanolic extract at 200 mg/kg body weight did not significantly ($P > 0.05$) alter serum chloride ion concentration when compared with the control maintaining values from 93.42 ± 1.15 mmol/L (control) to 91.56±2.62 mmol/L (high dose) and there was also no significant difference in serum chloride ion concentration giving 94.28 ± 1.01 mmol/L in the low dose group (100 mg/kg body weight) as shown in Table 3.

After treatment for 21 days, the *Garcinia kola* seed ethanolic extract at 200 mg/kg body weight significantly ($P > 0.05$) decreased the serum bicarbonate concentration from 25.6±1.61mmol/L (control) to 23 ± 0.85 mmol/L (high dose) and there was no significant ($P > 0.05$) difference giving 26.2 ± 1.31 mmol/L in the low dose group (100 mg/kg body weight) as shown in Table 4.

After treatment for 42 days, the *Garcinia kola* seed ethanolic extract at 200 mg/kg body weight significantly ($P > 0.05$) increased the serum bicarbonate concentration from 21.8 ± 2.32 mmol/L (control) to 25.2 ± 1.68 mmol/L (high dose) but there was no significant ($P > 0.05$) difference in HCO_3^- which gave 23.2 ± 1.11 mmol/L in the low dose group (200 mg/kg body weight) as shown in Table 4.

After treatment for 21 days, the *Garcinia kola* seed ethanolic extract at 200 mg/kg body weight did not significantly ($P > 0.05$) affect the concentration serum urea giving a relative value of 2.34 ± 0.21 mmol/L (control) to 3.5 ± 0.09 mmol/L (high dose) whereas there was significant ($P < 0.05$) increase to 2.9±0.26 mmol/L in the low dose group (100 mg/kg body weight) as shown in Table 5.

After treatment for 42 days, the *Garcinia kola* seed ethanolic extract at 200 mg/kg body weight did not significantly ($P > 0.05$) alter serum urea concentration with values ranging from 6.12 ± 0.41 mmol/L (control) to 6.58 ± 0.25 mmol/L (high dose). Similarly, there was non-significant effect with a value of 6.36 ± 0.46 mmol/L at the low dose group (100 mg/kg body weight) as shown in Table 5.

After treatment for 21 days, the *Garcinia kola* seed ethanolic extract at 200 mg/kg body weight significantly ($P < 0.05$) decreased serum creatinine concentration from 70.97 ± 4.54 mmol/L (control) to 48.83 ± 2.03 mmol/L (high dose). Similarly, there was a significant ($P < 0.05$) decrease in serum creatinine concentration to 45.63 ± 2.94 mmol/L at the low dose group (100 mg/kg body weight) as shown in Table 6.

After treatment for 42 days, *Garcinia kola* seed ethanolic extract at 200 mg/kg body weight significantly ($P < 0.05$) increased serum creatinine concentration from 54.32 ± 7.60 mmol/L (control) to 59.58 ± 2.93 mmol/L (high dose) and there was also an increase to 70.41 ± 3.93 mmol/L in the low dose group (100 mg/kg body weight) as shown in Table 6.

TABLE 1: EFFECT OF TREATMENT WITH *GARCINIA KOLA* SEED ETHANOLIC EXTRACT ON SERUM SODIUM ION (Na^+) CONCENTRATION

DAYS/TREATMENT	CONTROL	HIGH DOSE (200mg/kg) (mmol/L)	LOW DOSE (100mg/kg) (mmol/L)
21 DAYS	140±3.10	145.2±2.16 *	147.6±2.96*
42 DAYS	138.8±2.50	149.2±2.92*	162.4±7.40*

All values are expressed as mean ± SEM of 10 determinations, ($P < 0.05$).

*****shows that the serum Na^+ concentration of the treated groups is significantly increased in comparison with the untreated control group at $P < 0.05$

TABLE 2: EFFECT OF TREATMENT WITH *GARCINIA KOLA* SEED ETHANOLIC EXTRACT ON SERUM POTASSIUM ION (K^+) CONCENTRATION

DAYS/TREATMENT	CONTROL	HIGH DOSE 200mg/kg (mmol/L)	LOW DOSE 100mg/kg (mmol/L)
21 DAYS	3.22±0.10	3.96±0.31	3.68±0.21
42 DAYS	4.6±0.11	4.16±0.23	6.78±0.21*

All values are expressed as mean ± SEM of 10 determinations, ($P < 0.05$).

*****shows that the serum K^+ concentration of the treated groups is significantly increased in comparison with the untreated control group at $P < 0.05$

TABLE 3: EFFECT OF TREATMENT WITH *GARCINIA KOLA* SEED ETHANOLIC EXTRACT ON SERUM CHLORIDE ION (Cl^-) CONCENTRATION

DAYS/TREATMENT	CONTROL	HIGH DOSE 200mg/kg (mmol/L)	LOW DOSE 100mg/kg (mmol/L)
21 DAYS	94.6±6.86	99.8±7.78	93.2±5.10
42 DAYS	93.42±1.15	91.56±2.62	94.28±1.01

All values are expressed as mean ± SEM of 10 determinations, ($P < 0.05$).

*****shows that the serum Cl^- concentration of the treated groups is significantly increased in comparison with the untreated control group at $P < 0.05$

TABLE 4: EFFECT OF TREATMENT WITH *GARCINIA KOLA* SEED ETHANOLIC EXTRACT ON SERUM BICARBONATE (HCO_3^-) CONCENTRATION

DAYS/TREATMENT	CONTROL	HIGH DOSE (200mg/kg) (mmol/L)	LOW DOSE (100mg/kg) (mmo/L)
21 DAYS	25.6±1.61	23±0.85*	26.2±1.31
42 DAYS	21.8±2.32	25.2±1.68*	23.2±1.11

All values are expressed as mean ± SEM of 10 determinations, ($P < 0.05$).

*****shows that the serum HCO_3^- concentration of the treated groups is significantly different in comparison with the untreated control group at $P < 0.05$

TABLE 5: EFFECT OF TREATMENT WITH *GARCINIA KOLA* SEED ETHANOLIC EXTRACT ON SERUM UREA CONCENTRATION

DAYS/TREATMENT	CONTROL	HIGH DOSE- 200mg/kg (mmol/L)	LOW DOSE 100mg/kg (mmol/L)
21 DAYS	2.34±0.21	3.5±0.09*	2.9±0.26
42 DAYS	6.12±0.41	6.58±0.25	6.36±0.46

All values are expressed as mean ± SEM of ten determinations, $P < 0.05$.

*****shows that the serum urea concentration of the treated groups is significantly increased in comparison with the untreated control group at $P < 0.05$

TABLE 6: EFFECT OF TREATMENT WITH *GARCINIA KOLA* SEED ETHANOLIC EXTRACT ON SERUM CREATININE CONCENTRATION

DAYS/TREATMENT	CONTROL	HIGH DOSE-200mg/kg (mmol/L)	LOW DOSE-100mg/kg (mmol/L)
21 DAYS	70.97±4.54	48.83±2.03*	45.63±2.94*
42 DAYS	54.32±7.60	59.58±2.93*	70.41±3.93*

All values are expressed as mean ± SEM of ten determinations, $P < 0.05$.

*****shows that the serum creatinine concentration of the treated groups is significantly different in comparison with the untreated control group at $P < 0.05$

DISCUSSION

Renal function is an indication of the state of the kidney and its role in removing wastes like creatinine and urea, controlling the body's fluid balance, and regulating the balance of electrolytes. Examples of electrolytes include calcium ion, magnesium ion, potassium ion, phosphate ion, sodium ion, chloride ion, bicarbonate ion e.t.c (Walter, 2004). For the kidneys to carry out their normal functions they have to be in good condition both functionally and structurally (Thomas, 2005). Several research works have been done showing the help plants (its leaves, fruits, bark, seeds etc.) render in improving the functions of the kidneys and other body organs and systems. In the last few years, there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects (Grover *et al*., 2002). Herbal products cause few adverse effects but have beneficial pharmacological and therapeutic uses in a number of illnesses, including HIV where they have been examined for their capacity to reduce symptoms and improve quality of life (Weber *et al*., 1999). This might not be unconnected with the medicinal importance of *Garcinia kola* seed.

Renal mechanism is the third line of defence in acid-base balance. Long term acid-base control is exerted by renal mechanism. Kidney participates in the regulation of acid-base balance primarily by maintaining the bicarbonate ion concentration (alkali reserve in the plasma) and by formation and excretion of ammonia as the case may be (Naik, 2007). The LD_{50} of *Garcinia kola* seed ethanolic extract was found to be safe up to 5000 mg/kg body weight as previously reported by Atsukwei *et al*., (2015).

Serum creatinine is commonly measured as an index of glomerular function. The most common uses of creatinine clearance and serum creatinine include assessment of glomerulus/kidney function in patients with acute renal failure and in monitoring patients with acute renal failure or chronic renal failure. It is also used in monitoring patients on nephrotoxic drugs. Because of the relationship between serum creatinine and creatinine clearance is inverse and geometric as opposed to linear, significant declines in creatinine clearance may occur before the serum creatinine rises above normal range (Bolarin and Bolarin, 2005). Therefore, the decrease in serum creatinine concentration by both doses after 21 days of administration may be adduced to increased creatinine clearance while the reverse may be attributed to increased serum creatinine concentration at both doses observed after 42 days of treatment.

Urea, the primary end product of nitrogen and amino acid metabolism, is produced by the liver in larger amounts than is eliminated in the urine (Walser and Bodenlos, 1959). Indeed, in normal conditions, between 20–30% of the urea synthesized is hydrolyzed by the action of bacterial urease in the gastrointestinal tract (Walser and Bodenlos, 1959), leading to the production of ammonia that can be used as a nitrogen source for microbial protein synthesis or can be reabsorbed and made available for subsequent catabolic or anabolic purposes in the body (Long *et al*, 1987). Because this process provides substantial amounts of ammonia nitrogen available for amino acid biosynthesis (Sarraseca *et al*, 1998), urea hydrolysis may be a key step for the salvage of urea nitrogen, and it may play a central role in nitrogen homeostasis (Langran *et al*, 1992). Therefore, the significant increase in serum urea concentration at 100 mg/kg body weight after 21 days of treatment could be a result of impaired renal function due to an increased protein catabolism to amino acids and then ammonia which is then channeled for increased urea synthesis by the urea cycle. However, the non-significant effects of the extract at both doses after 42 days of treatment suggest maintenance in functioning capacity of the kidney's glomerulus.

Inorganic electrolytes occur in large quantities in both extracellular and intracellular fluids. Due to their ability to dissociate readily into their constituent ions or radicals, they comprise the single most important factor in the

transfer and movement of water and electrolytes between three divisions of the extracellular and intracellular compartment (Zilva *et al*., 1991).

Sodium ion (Na^+) is the major cation of extracellular fluids (Naik, 2007). The rate of Na^+ excretion is related to the glomerular filtration rate (GFR). When the GFR falls, less Na^+ is excreted and vice versa (Horton *et al*., 1993; Naik, 2007). Therefore, the significant increase in serum Na^+ concentration at both doses after 21 and 42 days may be adduced to increased excretion of Na^+ resulting from rise in glomerular filtration rate (GFR).

Potassium ion (K^+) is the major intracellular cation, and maintains intracellular osmotic pressure. Although an intracellular cation, potassium could move out of the cell by acidosis, lack of insulin and severe cell damage/death (Vasudevan *et al*., 2011). Potassium ions play an important role in the way in which nerve impulses are propagated along the nerve cells and transmitted to receptor cells. Nearly all the potassium filtered at the glomerulus is reabsorbed in the proximal tubule. Less than 10% reaches the distal tubule, where the main regulation of potassium excretion occurs. Thus, during sodium reabsorption, there is an obligatory loss of potassium (Naik, 2007). Therefore, the significant increase in serum K^+ concentration at both doses of the extract after 21 days of treatment may be attributed to decreased Na^+ reabsorption to the distal tubule of the kidney. However, the no significant effect of the extract at 200 mg/kg body weight on serum K^+ level after 42 days suggest that the functioning capacity of the nephron was not compromised.

Chloride is the major anion in the extracellular fluid space. Being part of sodium chloride, chloride is essential for water balance, regulation of osmotic pressure and acid-base balance. Since Na^+ and Cl^- act almost parallel, abnormalities of sodium metabolism are generally accompanied by abnormalities in chloride metabolism (Naik, 2007). Sequel to this, in most cases, the causes of hypochloremia and hyperchloremia are the same as hyponatremia and hypernatremia. The major clinical exceptions to the usual parallel changes in serum sodium and chloride concentrations occur during metabolic acidosis and alkalosis. With metabolic acidosis, hyperchloremia may not be associated with hypernatremia; with metabolic alkalosis hypochloremia may not be associated with hyponatremia (Naik, 2007). Therefore, the non-significant effect in serum Cl^- concentration by both doses of the extract after 21 and 42 days suggest no abnormalities in chloride metabolism.

Bicarbonate (HCO_3^-) is alkaline, and a vital component of the pH buffering system of the human body (maintaining acid-base homeostasis) (Bray, 1999). Greater percentage of CO_2 in the body is converted into carbonic acid (H_2CO_3), which can quickly turn into bicarbonate. The base constituent, bicarbonate (HCO_3^-) is regulated by the kidney (metabolic component) while the acid part, carbonic acid (H_2CO_3) is under respiratory regulation (respiratory component) (Vasudevan *et al*., 2011). Serum bicarbonate is therefore a measure of the base that remains after all acids, stronger than carbonic acid, have been neutralized. It represents the reserve of alkali available for the neutralization of such strong acids and it has been termed the alkali reserve. The rise in blood HCO_3^- is compensated by increased renal excretion of HCO_3^-. Therefore, the decrease in serum HCO_3^- concentration after 21 days of treatment may be an indication of reduced renal excretion of HCO_3^- while the non-significant effect of the extract at 100 mg/kg body weight after treatment for both 21 and 42 days suggest normalcy in tubular reabsorption of filtered bicarbonate. Overall, the increase and decrease observed in biomolecules are alterations and would impair proper renal function.

CONCLUSION

The non-significant effect displayed by the extract at some doses suggest an improvement and a protective activity on the renal function hence the recommendation of *Garcinia kola* for a reduced or declining renal function. However, the alterations in biomolecules are indication of impaired renal function suggesting that the extract may not be completely 'safe' as oral remedy at the doses investigated in this study.

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