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Evaluation of Time-Dependent Effects of a Leaf Extract of *Spermacoce Ocymoides* on Kidney Function

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ABSTRACT

Increase use of herbal medicines for the treatment of various diseases is suspected to cause renal toxicity. The study evaluated time-dependant effects of daily administration of leaf extract of *Spermacoce ocymoides* on renal function. The albino rats were grouped into two groups viz: control and treatment groups. The standard methods, as reported by; Butler, Evans, Vogel, Hochestrasser and Bassir, and Skeggs were employed in the *in vivo* estimation of serum kidney function. The results revealed increased significant difference, in the concentrations of serum creatinine, and urea as compared with the control untreated, at P < 0.05, on the fourteenth and eighteenth day. Chloride ion concentrations were significantly different (P <0.05) on the second, tenth and eighteenth day of administration, as compared with the control, however serum bicarbonate ion was not significant, only on fourteenth day, as compared with control. There were no significant changes in serum potassium and sodium ion concentrations. At the end of research: urea (246%) and creatinine (62%) were poorly excreted while, chloride ions (51%) was poorly regulated. Sodium and potassium ion have the least percentage fluctuations (5 and 7%). The fourteenth and eighteenth day of the daily administration of the leaf extract caused kidney impairment and by inference contains nephrotoxin.

Key words: Creatinine, Electrolyte, Kidney, Urea and *Spermacoce ocymoides.*

INTRODUCTION

From time immemorial in the history of mankind, herbs from plants have played vital roles in the lives of humans, especially for food sources and for medicinal purposes (Cseke et al., 2006; Chah et al., 2006). To a large extent, plants have been the main source of medicine for man in medieval age and advancement into Science and Technology (Schmelzer and Omino, 2003). Most of the drugs in Western medicine have herbal origin and about 25% of commonly used prescription drugs are derived from traditionally used medicinal plants (Principe, 2005; Harve, 2008). Furthermore, there are numerous plant extracts and materials which are employed commercially in the world today. According to WHO, users account for approximately 80% in 1995, 1998 and 85% in 2004 of the world's population, therefore plant materials are the primary source of health care for many people (BGCI, 1995; Kasahara and Hemini, 1998; Tan et al., 2004; Veeramuthu, 2006). In Nigeria, a WHO survey group estimated that up to 75% of the population patronizes traditional medicine (Omoseyindemi, 2003). It also recognizes traditional medicine as 'an accessible, affordable and culturally acceptable form of healthcare preferred by large numbers of people, which stands out as a way of coping with the relentless rise of chronic non-communicable diseases in the midst of soaring health-care costs and nearly universal austerity' (WHO, 2013).

In the recent time, there are growth in herbal medications (MacLennan et al., 2002) and not all plants derived medicines are harmless as purported by some herbalist and hence the need for toxicity evaluation (Lans, 2006).

Figure 1. *Spermacoce Ocymoides* (S.p).

The growth is on the seeming promise of herbal medicine to cure all diseases (Hutchinson et al., 1963), coupled with the dissatisfaction in western medicine. The need for the chronic intake of a large number of drugs with their attendant side effects in addition to their high costs which is often borne by the patients themselves is the identified reason for non-adherence to therapy amongst patients. As a result, patients often have recourse to alternative forms of therapy such as herbal medicines (Yusuff et al., 2008). These have attracted pleasing interest from wider range of disciplines on plant based medicines (Biapa et al., 2007). The leaves of *S. ocymoides* plant, represented in Figure 1 have antibacterial and antifungal activities (Oluwayemi et al., 2012). The plant is used in treatment of dysentery and diarrhea (Borokini and Omotayo, 2012; Oluwayemi et al., 2012). Again, the saps from the leaves of *S. ocymoides* are used to treat ringworm infection and eczema in Nigeria (Ebana, 1991). With the above merits of *S. ocymoides,* there are possibilities of unwarranted usage.

The research emphasized on positive use of plants-derived medicine and a dramatic rescue from unnecessary usage of an herb derived medicine. In this regard, awareness role concerning adverse herbal reactions resulting in notable kidney manifestations which are usually caused by an abuse or ignorance regarding the herb are of utmost concern. Kidney failure is on the prowl in Nigeria. More Nigerians are going down with the disease, which has been blamed mostly on irrational use of herbs among others. Chronic kidney disease (CKD) is health challenging especially in developing countries with a remarkable burden in Sub Sahara Africa (Naicker, 2009). This is largely due to the rising prevalence of risk factors, such as type 2 diabetes, hypertension, and the HIV pandemic (Eghan et al., 2009), along with indiscriminate use of herbal drugs. Before now, little was heard of kidney failure as a major kind of everyday illness, but the reverse has become the case in Nigeria. It is not an overstatement to say that Nigerian social media is conspicuously occupied with plea for financial assistance for sufferers with some ending in inglorious battle (Clement, 2016; Job, 2016). This article will provide knowledge and guide to encourage future toxicity studies on the kidney using other medicinal valuable herbs.

METHODOLOGY

Plant Materials

Matured leaves of *S. ocymoides* (Figure 1) were collected from the law School Road Bwari, Abuja FCT, in March 2013, identified as irawo-ile in Yoruba language by Hajia Rashidah A. of Ministry of Health and afterwards authenticated at Science Laboratory Technology Department of Dorben Polytechnic Abuja. The leaves were rinsed severally with clean tap water to remove dust particles and debris and thereafter allowed to completely air-dry at room temperature. The plant materials were pulverized to a uniform powder as reported by Onoruvwe and Olorumfemi (1998) and sieved with 1mm sieve. The plant extract (250 g) was soaked in distilled water (1000 ml) for two days (48 H), for thorough extraction of the plants' active components, after which it was, first filtered with cheesecloth and later with Whatman No. 1 filter paper. The concentration was determined as reported by Nwachukwu (2015).

Experimental Animals and Assay Kits

Albino rats (40), weighing about 130 to 150 g, obtained

Table 1. Time-dependent changes in concentrations of serum creatinine and urea.

Biochemical parameters	Group 1	Group 2				
	Control	2nd day	6th day	10th day	14th day	18th day
Creatinine (umol/l)	81.25 ±36.68	75.00 ±10.23	76.25 ±4.79	80.50 ±4.20	131.65 ±19.83^{*a}	131.75 ±19.84*
Urea (mmol/l)	4.70 ±1.59	3.25 ±0.50	4.00 ±0.82	5.75 ±1.50	13.50 ±2.13^{*a}	16.25 ±3.89*

Values were expressed as mean ± standard deviation of n = 8. Values bearing *p were significantly different from base line (control) at 0.05. Values bearing ^{a}p were significantly different from the immediate preceding days after administration.

Table 2. Time-dependent changes in concentrations of serum electrolyte.

Biochemical parameters	Group 1	Group 2				
	Control	2nd day	6th day	10th day	14th day	18th day
K^{+}(mmo/l)	6.08 ±0.82	5.28 ±0.92	6.15 ±0.82	6.08 ±0.92	6.23 ±0.71	6.48 ±0.69
Cl^{+}(mmol/l)	102.75 ±3.1	85.00 ±12.91^{*a}	102.00 ±4.40^{a}	86.50±9.26^{*a}	108.75±2.50^{a}	155.25 ±5.73^{*a}
Na^{+} (mmol/l)	132.25 ±12.04	125.00 ±10.23	126.25±1.50	130.50±8.19	137.75 ±27.53	138.75 ±29.87
BCO_3^{-}(mmol/l)	28.50 ±1.29	32.00 ±0.82^{*a}	24.50 ±1.29^{*a}	22.50±1.29*	28.75 ±1.50^{a}	21.73 ±2.11^{*a}

Values were expressed as mean ± standard deviation of n = 8. Values bearing *p were significantly different from base line (control) at 0.05. Values bearing ^{a}p were significantly different from the immediate preceding days after administration.

from the animal house of the Department of Science Laboratory Technology of Dorben polytechnic Abuja were employed in the research. The animals were housed in well ventilated cages (wooden bottom and wire mesh top) and kept under controlled environmental conditions of temperature (25 ± 5^{0}C), relative humidity (50 ± 5%) and 12 h light / dark cycle. The animals were maintained on palletized Growers feed (Vital Feeds, Jos, Plateau State, Nigeria) and tap water *ad libitum*. The creatinine, urea and electrolytes (Sodium, Potassium, Bicarbonate and chloride ion) assay kits were obtained from Randox Laboratories, Limited United Kingdom. Other reagents used were of analytical grade and were prepared in all glass-distilled water.

Experimental Procedure

The rats which had been maintained on growers (Vital Feeds, Jos, Plateau State, Nigeria) and water *ad libitum*, were allowed to acclimatize for fourteen days after which they were randomly grouped into two: (i) Group 1; which consisted of 8 rats, received orally, 5 ml sterile distilled water on daily basis for eighteen days. This served as the control. (ii) Group 2; which consisted of 40 rats, received orally appropriate volume corresponding to the therapeutic dose of 20 mg/kg body weight of *S. ocymoides* extract preparation on daily bases. This served as the treatment group. Eight rats in group 2 were sacrificed after 2, 6, 10, 14 and 18 days of daily administration of 20 mgkg body weight of *S. ocymoides* leaf extracts while the eight rats in the control (Group 1), were sacrificed on the eighteen after daily doses of sterile distilled water. The sera of clotted bloods were collected and used for biochemical analysis. The biochemical parameters evaluated include serum creatinine concentration as described by Butler's Jaffe's Reaction (1975), serum urea concentration as described by Evans, (1968) and serum Electrolyte concentrations (bicarbonate ion as described by Vogel, 1964 sodium and potassium ions as described by Bassir, 1971 and Chloride as described Skeggs and Hochestrasser, 1964).

Statistical Analysis

The statistical analysis was carried out by one way Analysis of variance and Turkey Duncan Multiple Range test. P values < 0.05 were considered significant.

RESULTS

The results are presented in Tables 1 and 2. The Tables (1 to 2) present the results of the effect of daily administration of *S. ocymoides* extract, in apparent healthy rats. From the results in Table 1, the serum creatinine concentration decreases non- significantly, from the second day through the tenth day, in the extract treated rats as compared to control. In the fourteenth day and eighteenth day of administration, there were sharp significant rise in the concentration at P < 0.05 with the control. The percentage increased from the control on the fourteenth and eighteenth day of administration were 62 (Table 2). These two values also showed no significant difference in-between them were approximately the same as seen in Tables 1 and 2. However fourteenth day was significantly difference from the immediate preceding day (10th day) of administration at P < 0.05 (Table 1). In the serum urea concentrations (Table 1), there were decreased concentrations from the control on the second and sixth day of administrations however from the tenth

Table 3. Percentage patterns of change in concentrations of kidney function of group 2 after the administrations of *S. ocymoides*.

Day of estimation of serum parameters	$\frac{change\ in\ concentration}{concentration\ of\ control}\ x\ 100\ \%$				
	2nd day	6th day	10th day	14th day	18th day
Creatinine (umol/l)	7.69	6.15	0.92	62.03	62.15
Urea (mmol/l)	30. 85	14.89	22.34	187.2	245.74

Table 4. Percentage patterns of change in concentrations of kidney function of group 2 after the administrations of *S. ocymoides*.

Day of estimations of serum parameter	$\frac{change\ in\ concentration}{concentration\ of\ control}\ x\ 100\ \%$				
	2nd day	6th day	10th day	14th day	18th day
K^+(mmo/l)	13.16	1.15	0	2.47	6.59
Cl^+(mmol/l)	17.27	0.74	15.52	5.84	51.09
Na^+ (mmol/l)	5.48	4.54	4.5	4.16	4.91
BCO_3^-**(**mmol**/**l)	12.28	14.04	21.05	1.75	23.75

day of administration through the eighteenth day of administration, there was definite patterned increased in the urea concentrations. Again there were sharp increased on the fourteen and eighteen days after administration and both days of administrations were significantly different ($P < 0.05$), from the control.

The percentage increased in fourteenth and eighteen day of administration from the control were much high, amounting to 187 and 245%, respectively (Table 1). The fourteenth day of administration was significantly different from the immediate preceding day (10th day) of administration at $P < 0.05$. Table 3 revealed the changes in serum electrolyte levels of rats treated with *S. ocymoides* extract. From the result, potassium ion concentration showed non-significant changes in concentrations from the control. The percentage changes in concentrations of potassium ion were not much from the control (Table 4). The highest was 13% (Table 4), on the second day of administration. In chloride ion concentration, there were decreased in concentration on the second and tenth day of administrations. In each immediate preceding day of administration, there was significant difference at $P < 0.05$. The second, tenth and eighteenth day of administration were significantly different with the control at $P < 0.05$ (Table 3). There was much percentage change in concentration (51%) on the eighteen day of administration as compared with the control in Table 4. For sodium ion concentrations, there were no significant changes in concentrations in the extract treated rats (Group 2) compared with the group control. There were decreased concentrations of sodium ion on the second day through the tenth day of administration, however on the tenth day, through the eighteenth day of administrations there were increased concentrations from the control. There were no significant changes in sodium ion concentration from the control (Table 4).

The percentage changes in sodium ion concentrations from the control were nearly the same (Table 4). Bicarbonate ion concentration increased on the second of administration only (Table 3). Bicarbonate ion concentrations decreased significantly with the control in the extract treated rats except on the second and fourteen days of administration (Table 3). There were observed significant difference at $P < 0.05$ from the control (Group 1) with the extract treated rats in group 2, except on fourteenth day of administration. There was significant difference ($P < 0.05$) with immediate preceding interval in each of the day of administration, except on tenth day of administration. There were not many changes in the percentage concentrations (Table 3) of bicarbonate ion of the extract treated group (Group 2) from the control (Group 1). The highest percentage change was 23% on eighteenth day of administration as in Table 4.

DISCUSSION

The kidney plays a crucial role in water level balancing, blood pressure regulation, electrolyte and acid base homeostasis (Yaw et al., 2014). It equally, has a major role in waste excretion, Red blood cell regulation and to some extent in hormone and vitamin production. Accordingly, some selected kidney function, parameters were exploited in understanding the effect of the extract at the dose and the period administered. Serum creatinine concentration decreased up to the ten day after administration (Table 1), this decreased is in accordance with good functioning kidney. The less

common causes are advanced liver disease and excess water intake because: liver is the primary site for protein synthesis and breakdown and excess water can dilute the concentration of all substances in the bloodstream. The decrease in concentration may be due to the initial, trying effort of the renal tissues to withstand the impact of the drug (Ngaha and Akanji, 1982). As can be seen in Table 1, on the fourteen and eighteen day after administration, there was up rose in serum creatinine concentration, reflecting a failed capacity of kidney to affectively excrete creatinine. By inference showing that the ability of the two kidneys to effectively excrete creatinine, might have been exceeded.

The percentage increased in the fourteenth and eighteenth day of administration (63% in Table 2), is an attestation to failed capacity of renal tissue in excreting creatinine on the fourteenth and eighteenth of administration. Creatinine is freely filtered by the glomeruli, but is not reabsorbed to any appreciable extent under normal circumstances (Tulassay et al., 1979). Tubular creatinine secretion may be inhibited by drugs (Schwartz et al., 1987; Kemperman et al., 2000); this may be possible in the case of definite patterned concentration as observed in Table 1. The significant build up, on the fourteen and eighteen day after administration is suggestive of a combination of tubular inhibition and kidney impairment (Angeles et al., 2004). However tubular re absorption of creatinine has been observed under certain clinical conditions, including congestive cardiac failure and uncontrolled Diabetic Mellitus (Woo and Cannon, 1991). The fact that apparent healthy rats were used may have overruled such possibility. Again raised concentration may be due to increase exercise through increasing muscle break down (Hamilton et al., 1972; Oh, 1993). But subjecting the control on the same condition annulled such possibility. By inference, it is possible that accumulation of the creatinine may be due to blockage of the process involved in creatinine secretion (Kemperman et al., 2000). And on the account that herbs can cause kidney impairment (Jha and Chugh, 2000), the researcher is of the opinion that: secretion blockage and kidney impairment in combination or in part may be responsibility for the sharp significant raise, observed on the fourteen and eighteen days after administration. For differential diagnosis, simultaneous determination of serum creatinine along with urea, is currently, on wider usage, hence this work in addition, estimated the concentration of serum urea, another marker of kidney function. Though urea is inferior to other marker such as creatinine, blood urea is grossly influenced by other factors, such as diet and nutrition (Traynor et al., 2006).

The concentration of urea decreased non-significantly on the second day after administration is an effort to resist the initial effect of the extract (Ngaha and Akanji, 1982). The significant increased observed on the fourteen and eighteen day after administration again is indicative of kidney impairment (Bishop, 2010). High serum urea concentration may be due to pre renal factors such as low water content but it is easy to draw a parallel between the two results (creatinine and urea concentration). Renal causes of elevated urea concentration as seen in Table 1 can be attributed to decreased kidney function. Urea can accumulate to a toxic level, if the kidneys are impaired (Richet, 1988). Changes in the electrolyte concentration were not significant in potassium (Table 1), which by inference depicts a non-interference of extract at the dose administered, on the levels of potassium ion. In the chloride ion concentration, the non-definite patterned changes resulting in decrease and increased in concentration along the intervals coupled with the significances in each immediate preceding day after administration may be due to the initial, trying effort to withstand the impact of the drug (Ngaha, and Akanji, 1982). However the elevated, significant in concentration of chloride ion, on the eighteen day of administration is possibly a failed effort to cushion the effects of the drug (Table 3). By extension eighteen days and beyond on daily consecutive administration of an equivalent amount as administered may adversely affect the serum chloride ion concentration.

Sodium ion concentration showed non-definite changes on the days of administration. Again this can be adduced to the initial attempt to resist the effect of the extract which resulted in the initial decreased in sodium ion concentration (already cited). The increased in fourteen and eighteen day of administrations, may be due dehydration (Ofran et al., 2004). The percentage changes in sodium ion concentrations depict non fluctuations in the concentration (Table 4). This is in view that high sodium concentration rarely occurs. In serum bicarbonate ion concentration, the significant rise on the second day of administration and the non-definite pattered changes may be connected to the disturbances in other electrolytes. Serum bicarbonate ion concentration decreased in most of the days of administration. These decreased may have been caused by damaged kidney and in prolong condition may result to acidosis, in this situation, the amount of acidic hydrogen ions in the body increases in relative proportion to bicarbonate, causing acidosis. The low decreased bicarbonate may have caused increased chloride ion concentration (Table 3). In similar way, the much decreased serum concentration of bicarbonate on the eighteen day of administration, may be the starting point in failed capacity to regulate the concentration. The percentage changes in concentrations of serum bicarbonate in relation to control were not high. Alteration of bicarbonate dissolved in plasma is a characteristic of acid-base imbalance, cannot however be inferred from bicarbonate value itself and determination of bicarbonate is rarely ordered alone.

Its value has significant in thecontext of other electrolyte determined and in screening for electrolyte imbalance.

CONCLUSION

Many traditional medicines and foods especially in the tropical regions of Africa and Asia contain renal toxic plants (Wendell et al., 2005). The kidneys are important organs with many functions and kidney failure can be fatal. According to Panda (1989), renal function tests are required to demonstrate the presence or absence of active lesion in the kidney, or to assess the normal functioning capacity of kidney. In line with this, serum urea, creatinine and electrolytes as markers of damage to renal function (Harold et al., 1980), were accessed. Elevated levels of creatinine and urea as seem in this research is an indication of kidney damage (Elizabeth, 2012). In this line of taught, this research has demonstrated that *S. ocymoides* extract (20 mg/kg body weight) caused kidney impairment in apparent healthy albino rats within fourteen days and beyond.

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