

EFFECTS OF REPEATED ADMINISTRATION OF *CHROMOLAENA ODORATA* ON SELECTED KIDNEY FUNCTIONS PARAMETERS OF WISTAR RATS

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ABSTRACT

The uneducated indiscriminate increase in herbal usage in complementary and alternative medicines, for the treatment of various diseases may in part contribute to rapid increase in kidney disease around the globe, equally economic and cultural factors associated with these practices are also contributing factor. The present study was conducted to evaluate the effects of crude aqueous extracts of *Chromolaena odorata* on kidney function parameters. In the study, the rats received repeated dose of 20mg/kg body weight, daily. The kidney function parameters were estimated four days after administration. The results shows that in urea and creatinine, concentration there was definite patterned increase, up to 9 day after administration, and upsurge on 13th day after administration and each result is significantly different from the 13th day after administration ($P < 0.05^a$).

Creatinine concentration was significantly different from the control (day 0) at $P < 0.05$, in the entire estimate. Sodium and Chloride ion concentrations decrease from the control and increase on the 13th day after administration. Potassium ion concentration increases from control. Sodium ion concentration was significantly different from the normal at $P < 0.05$. Potassium and Chloride ion were significantly different ($P < 0.05$), from the control on (9th and 13th) and (5th and 9th) day after administration respectively. Albumin was not significant from normal. From the result, it is glaring that there was some degree of kidney impairment but insufficient to include nephrotic syndrome as the albumin level showed no significant changes.

KEYWORDS: Kidney Health, *Chromolaena odorata*, Electrolytes, urea, Creatinine, Albumin.

1. INTRODUCTION

The knowledge of the medicinal value of plant is largely based on folklore in Nigeria. The nutrient composition of some plant enhances their use and increases their consumption which in turn improves the nutrient profile of a good proportion of the populace.^[1] In the globe, the use of medicinal plants is increasing worldwide, in view of the tremendous expansion of traditional medicine and a growing interest in herbal treatments. Most available herbal products have no clear statement of content or medically related information on the package labels, and have not been validated or certified by any recognized body in Nigeria. They are in fact sold mostly in public vehicles in the midst of persuasions, because targeted consumers have health challenges, will fall prey to them. I am obliged to say that no forms of preaching will change the pharmacology of drug. Although Nigerian Med watch said everybody should be pharmacovigilant, there is urgent need for scientific rigorous testing and evaluation by concerned researchers. WHO, has advised for scientific testing of the efficacy of herbal plant to authenticate the claims made on them. This concerns consumers and medical practitioners who may unknowingly counter-prescribe these herbal products. Not all of the plants reported to be useful are harmless. These considerations underlie the study of ethno-medicinal plants.^[2] In recent years, an increasing number of people have been using complementary and alternative medicines.^[3] Adverts on herbs are now frequently hard over the media station in Nigeria. The herbal therapies appear most promising, thus encouraging the necessary toxicity studies to be performed on these therapies. The literature search conducted on herbs, regarding renal toxicity shows in-vivo evidence of toxicity in animals. Herbs will also be defined as “potentially beneficial” to the kidneys if there is strong in vivo evidence of renal protection from toxic substances or drugs.

Interestingly herbs have recorded so much relevance in treatments of humans and animals, innumerable health challenges, the use of herbal therapy has increased dramatically in the past 10 years and may lead to renal injury or various toxics.^[4] In view of this tremendous expansion of traditional medicine, there is a growing interest in herbal treatments. Plants are used in medicine to maintain and augment health - physically, mentally and spiritually - as well as to treat specific conditions and ailments. The exponential increase in herbal treatment may parallel the unwarranted increase in the number of people experience kidney problem.

This assertion may reach impasse but more herbal testing of the effect on kidney may pave the way.

The kidneys are protected through adequate consumption of water. Kidneys are aided through avoiding excess protein intake, except in special circumstances such as pregnancy and childhood. Research have found that eating meals rich in ginger (*Ziniber offiinale*), onions (*Allium cepa*) and garlic (*Allium sative*) could be the novel preventive and therapeutic diet or drug against the menace.^[5] It is observed that regular eating of meals prepared with lime grapefruit and vitamin B rich ingredient protect the kidneys damage from the hypertension, alcohol, cancer drugs and poisons. A recent publication in Journal of renal nutrition concludes - alcohol induced nephrotoxicity, was attenuated by ginger extracts treatment thus ginger can be used as a regular nutrient.^[5]

In addition, diet rich in anti-oxidants can reduce the undesirable effects of some herbs, by use of more fruits and vegetables in the diet.^[6] Dietary factors affect heavy metal uptake. For example, an adequate level of dietary iron reduces uptake of cadmium and lead.^[7] Foods high in fiber also limit the uptake of heavy metals. Many heavy metals take part in creation of free radicals in the cellular environment.

Some herbal medicine may exert renal toxicity through their inherent properties. If found to have some degree of toxicity, the risks can be weighed against the benefits and decisions can be made regarding their continued usage, also a meticulous research to reduce to barest minimal, the effects on kidney should be encouraged. Importantly, the inherent properties of the herb are not the only source of herb-associated renal disorders, as herb-drug interactions, mistakes in dosage and identification, and contaminants within the mixture are all issues of concern. This article presents information about the toxicity of medicinal herbs on kidney functions, focusing on *Chromolaena odorata* used for various treatments.

1.1 Significance of the Study

Kidney failure is on the prowl in Nigeria. More Nigerians are going down with the disease, which has been blamed mostly on complications from diabetes and hypertension possibly menace,^[5] as a result of irrational treatment with herbs. Nowadays, it is noteworthy that traditional medicine is gaining popularity in developing countries (Konate 2011), and Nigeria is not an exception to this rapid surge. The increase in popularity and the scarcity of scientific studies on their safety and efficacy have raised concern regarding toxicity and advance effect

of this remedy.^[8] Accordingly Bent and Ko,^[9] noted that products of plants contain bioactive principles with the potentials to cause adverse effects. This article will provide knowledge and guidance to encourage future toxicity studies on the kidney using other medicinal valuable herbs.

1.2 Justification of the Study

These days, it has virtually become the tradition while watching prime time TV shows to have programmes interrupted for a few minutes, not for product advertisement but for funds solicitation. Nigerians are now familiar with gaunt figures lying critically sick on the bed and plugged to dialysis machine begging for donations from government and kind-hearted members of the public. The solicited funds usually run into millions of naira to cover the temporary dialysis in Nigeria and subsequent organ transplantation overseas.^[10]

The causes of kidney disease are multifactorial, ranging from hypertension to diabetes and herbal medications. When it comes to size, the kidneys are small.^[10] However, I opine that the kidney may be small but they perform many vital functions, they help maintain the overall health, including filtering waste and excess fluid from the blood. These organs equally maintain the balance of salt and minerals in the blood and also help regulate blood pressure. The online portal, webmd.com, warns that when the kidneys are damaged, waste products and fluid can build up in the body, causing swelling of the ankles, nausea, vomiting, weakness, poor sleep, shortness of breath, fatigue, confusion, difficulty concentrating, loss of appetite, abdominal pain, abnormal low urine levels and low blood flow to the kidneys. These are all a serious and potentially fatal condition. Serious kidney disease may lead to complete kidney failure and the need for dialysis treatments or a kidney transplant 'Once kidney transplant, medications follows for life, I aver.

Though effective treatments are available for many kidney diseases, kidney disease can often be prevented. This work will contribute towards prevention of kidney disease in cases that are not from genetic or congenital causes. The pains from kidney disease are usually intense. Following the cost of treatment, it is justifiable to review a known herb that has medicinal value, on its effects on kidneys.

2. MATERIALS AND METHODS

2.1 Animals and Assay Kits

A total of thirty white albino rats (*Rattus novergicus*) weighing between 120-140g were obtained from the laboratory Animal Unit of the Department of Science laboratory Technology of Dorben Polytechnic Abuja FCT.

The Creatinine, Urea, Electrolytes (Sodium Potassium, chloride ion) and albumin assay kits were obtained from Randox Laboratories, Ltd., United Kingdom. Other reagents used were of analytical grade and were prepared in all glass-distilled water.

2.2 Plant Material

The plant *Chromolaena odorata* materials used in this study were collected along Garam Bwari Road, one Kilometre away from the Polytechnic site, in February 2012. It was identified and authenticated in the Department of science laboratory technology.

2.3 Extraction of Plant Materials

Fresh leaves of *Chromolaena odorata* were air-dried at room temperature for twenty two days, in controlled environmental conditions. The dried leaves were pulverised to a uniform powder and sieved through 1mm sieve. The powdered plant materials was soaked in cold distilled water (25% w/v) for a period of 48 hour, after which it was filtered using a piece of clean, sterile, white Muslin cloth to remove debris. 6ml of the filtrate was evaporated in a drying cabinet, and used in calculating equivalent amount present in milligram.

2.4 Animal Groupings and Drug Administration

The rats which had been maintained on growers (Grand Cereals LTD Nigeria PLC) and water ad libitum, were allowed to acclimatize for seven days after which they were randomly grouped into two: (i) Group A- which consisted of 5 rats, received orally 1ml sterile distilled water on daily basis. This served as the control. (ii) Group B- which consisted of 20 rats received orally appropriate volume corresponding to the therapeutic dose of 20mg/kg body weight of *Chromolaena odorata* preparation on daily basis and this was administered to the rats. This served as the test group. Five rats each in group B were sacrificed 24hours after 1st, 5th, 9th and 13th days daily doses of *Chromolaena odorata* while the five rats in the control group were sacrificed 24hours after the 13 daily doses of sterile distilled water.

2.5 Serum Preparation

The rats were anaesthetized using cotton wool soaked in chloroform vapour. When they became unconscious, they were quickly brought out of the jar. The neck area was cleared of fur and skin to expose the jugular veins. These veins were then cut sharply with sterile scalpel blade and the rats were held head downwards and allowed to bleed into clean dry corked test tubes, allowed to clot and left for 10mins at room temperature for serum formation.^[11] The serum was collected using Pasteur pipette after centrifugation at 3000rpm for 5minutes, kept frozen and used for the selected liver function analyses within 14hours of collection.

2.6 Statistical Analysis

Data were expressed as mean \pm Standard deviation. The results were analyzed using One way ANOVA. Post hoc test was also conducted to determine level of significance between the treated and control groups using Turkey HSD Comparisons Test. Statistical significance was considered at $P < 0.05$.

3. RESULTS AND DISCUSSION

3.1 Results

The result of creatinine, and urea showed a steady decrease up to 9th day after administration and superfluous increase on the 13th day after administration (Table 1). There were significant different from the days after treatment, compared to the control at $P < 0.05^*$ in each of the estimation period in creatinine while urea concentration was only significantly different ($P < 0.05^*$), on the 13th day following administration (Table 1). In both creatinine and urea, each day after administration was significantly different ($P < 0.05^a$), from the 13th day after administration (Table 1). Albumin level showed a non gradation increase with highest value observed on the 1st day after administration (Table 1). There were no significant changes in albumin concentration in any of the days after administration (Table 1). In electrolyte concentration, sodium and chloride ion concentration decreased up to the 9th day after administration (Table 2). The 13th day after administration showed increased in all the electrolyte parameters measured (Table 2). Sodium ion concentration showed significant difference ($P < 0.05^*$), in all the days after administration, compared to the control, also the days after administration were significantly difference ($P < 0.05^a$), to the 13th after administration (Table 2). Chloride ion concentration was non-significant ($P > 0.05$), on the 13th day after administration (Table 2). In potassium ion concentration, there was increased concentration, from the control on the 9th and 13th day after administration and also days,

5th and 9th day after administrations were significantly different ($P < 0.05^a$) from the 13th day after administration (Table 2). The 1st, 5th, and 9th days after administration were significantly different ($P < 0.05^a$) from the 13th day after administration in Sodium and Chloride ion concentration. Potassium ion concentration was significantly different ($P < 0.05^a$) from the 13th day after administration.

Table 1: Effects of the extract on concentration of Some Selected serum Kidney Function parameters and Albumin during the period of administration

Days after administration	0	1	5	9	13
Urea (mmol/l)	5.22±0.74 ^a	5.14±0.57 ^a	3.2±0.31 ^a	3.64±0.19 ^a	24.44±4.05*
Creatinine (umol/l)	85±4.80 ^a	84±7.64 ^{*a}	50.6±4.27 ^{*a}	53±4.89 ^{*a}	126.5±16.88*
Albumin (g/dl)	41.00±4.47	45.4±5.18	43.8±7.69	44.6±7.73	44.40±3.28

Values are mean ± standard deviation of n = 5. * = Significantly different from the control ($P < 0.05$), ^a = significantly different from the 13th day after administration ($P < 0.05^a$), using one way analysis of variance.

Table 2: Effect of extract administration on the concentration of electrolyte level in serum

Days after administration	0	1	5	9	13
Na (mmol/l)	124.00±5.79	106.80±1.9 ^{*a}	104.00±5.29 ^{*a}	104.60±4.33 ^{*a}	139.20±13.14*
K (mmol/l)	3.70±0.49 ^a	6.08±0.44 ^a	5.34±0.24 ^a	4.64±0.20*	4.36±0.40*
Cl (mmol/l)	101.60±5.18	66.00±5.15 ^{*a}	20.80±5.40 ^{*a}	32.80±3.83 ^{*a}	105.40±3.58

Values are mean ± standard deviation of n = 5. * = Significantly different from the control ($P < 0.05$), ^a = significantly different from the 13th day after administration ($P < 0.05^a$), using one way analysis of variance.

3.2 DISCUSSION

Kidney plays several vital roles in maintaining health. One of the most important functions is to filter waste materials from the blood and expel them from the body as urine; otherwise waste products will accumulate in the body to reach toxic level. The present study reveals the effect of repeated administration of *Chromolaena odorata* (20mg/kg body weight) on some selected kidney function parameters of rats. Serum Urea along side with creatinine were estimated (Table 1). Serum urea, creatinine among others are markers of damage to renal function.^[12] The blood urea is primarily used along with the creatinine test, to evaluate kidney. The creatinine and urea concentration decreased from control (0 day), through 9th day after administration but increased significantly on the 13th day after administration. The increased creatinine and urea levels on the 13th day after administration may be due to the

cumulative effect of the crude aqueous extract on kidney cells. It may be possible that the kidney before this time, adjusted in its effort to function well but probably, progressive retention of the extract caused the raised in creatinine and urea levels. These raised levels may be an indication of impaired kidney function.^[13]

The research again revealed the possible effects of the aqueous extract of *Chromolaena odorata* on concentration of some selected electrolyte function parameters, so as to further evaluate the kidney (Table 2). The kidneys maintain electrolytes concentrations by filtering electrolyte to the blood, and excreting excess if any, into the urine. In the same vein, the kidneys regulate fluid absorption, excretion and maintain a narrow range of electrolyte fluctuation. Thus imbalance of electrolyte may denote kidney failure.^[14] The concentrations of sodium and chloride ion showed a similar trend with that of urea and creatinine (Table 1 and 2). Sodium ion concentration decreased from control up the 9th day administration but showed increased on 13th day of administration (Table 2). The observed much decreased and increased in electrolyte ions (Sodium and Potassium) concentration from the control up to 9th day and on the 13th day after administration, respectively may be indicative of kidney impairment among others.^[14] The Potassium ion concentration level increased from the 0 day (control) though, not in a definite pattern. It is also due to phenomena of kidney impairment, it is possible that the initial administration may be the needed amount to trigger the increase in potassium ion concentration.

Albumin in conventional practices is used exclusively in assaying for liver synthetic function. Albumin is a protein specifically made by the liver. However it was assayed here, to be used in understanding the nature of kidney diseases. Nephrotic syndrome, a non specific kidney disorder and characterised by increased permeability of the capillary walls of the glomerulus leading to the passage in urine of protein, instead of being retained in the blood, will result with time a decrease in blood albumin concentration (hypoalbuminemia) and hence the albumin concentration may rule out nephrotic syndromes.^[15] In nephrotic syndrome, there is altered capacity of kidney to filter the substances transported in the blood. Again affected kidneys by nephrotic syndrome have small pores in the podocytes, large enough to permit proteinuria and subsequently hypoalbuminemia. This is because some albumin has gone from the blood to the urine. Healthy kidneys do not allow a significant amount of proteins to pass through their filters, but filters damaged by kidney disease may let proteins such as albumin leak from, into the urine and decrease blood concentration of

albumin. Low albumin levels can reflect diseases in which the kidneys cannot prevent albumin from leaking from the blood into the urine and being lost and the fact that there is no significant patterned increase from control (Table 1), shows that the impairment on 13th day after administration as observed in other measured parameters, was not through the enlargement of the pose as it did not permit the excretion of albumin into the urine since the blood concentration of albumin did not reduce. Moreover, several studies demonstrated that serum albumin concentrations are associated with general health status.^[15]

Kidney disease often has no nearly symptoms as such albumin estimation is advised even in evaluating the effect of extract on kidney as it may give added advantage to the state or status of kidney.

4. CONCLUSION

The selected kidney function parameters is well established predictive kidney state and the fact that kidney failure and disease may not present clear signs before the deteriorating condition also following the pains, agony and cause of treatment, the work serves as signal remark on users of this highly rated medicinal plant (*Chromolaena odorata*) of wide therapeutic window, to see the duality of the plant and take the great advantageous potential of it. The prolonged usage at the proportionate dose administered in the animals to human may within the period cause adverse effect. The concentration usage of this plant extract in herbal therapy is furthest below the concentration administered. From the result in the study, it is glaring that there was some degree of kidney impairment but insufficient to include nephrotic syndrome as the albumin level showed no significant changes.

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