Effect Of chronic Administration of aqueous Extract Of Enantia Chlorantha On Some Renal Function Parameters In Experimental Rats.

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Abstract

Some renal function parameters were investigated in experimental rats, following chronic administration of aqueous extract of *Enantia chlorantha* stem bark.

Sixty albino rats were randomly divided into four groups of fifteen rats each. The control group A was administered 1 ml of distilled water while test groups B, C and D were administered orally daily for 28 days, 50, 100 and 200mg/kg body weight of aqueous extract of *E. chlorantha* respectively. The rats were sacrificed after 10, 20 and 28 days. There was a significant increase ($p<0.05$) in the serum Na^+ level at 100 and 200mg/kg body weight of extract but no significant changes ($p>0.05$) at 50mg/kg body weight. There was a significant reductions ($p<0.05$) in serum K^+ level at all the doses, throughout the duration of administration. There were significant increases ($p<0.05$) in urea and creatinine levels at 100 and 200mg/kg body weight of extract respectively. There were significant reductions ($p<0.05$) in the serum total protein and albumin at 100mg/kg body weight of extract, but no changes at other doses. The results of this study showed significant alterations in the parameters examined with far reaching implications on the glomerular and tubular functions of the kidneys.

Key words: Renal functions, aqueous extract, *Enantia chlorantha*, rats.

Introduction

Serum electrolytes, especially sodium and potassium ions, are usually filtered through the renal glomeruli, and majority are reabsorbed at the renal tubules, especially the proximal convoluted tubules. Alterations in their serum levels are therefore useful tools in assessing the renal functions[1]. Serum urea and creatinine are usually filtered through the renal glomeruli and are neither reabsorbed nor secreted by the renal tubular cells. Significant serum alterations are good indicators of renal glomerular damage[2]. The serum protein levels, especially albumin, are also useful in assessing the renal function status. Reductions in the serum level of albumin may indicate either glomerular damage with leakage of albumin or its reduced production by the liver cells[3].

The use of medicinal herbs to cure certain ailments are increasingly getting popular in the developing countries of Africa and Asia. *Enantia chlorantha* [family: Annonaceae] is commonly used for the treatment of fever conditions including malaria and other ailments[4,5]. Its use has been so abused that it is commonly hawked on the street by herb vendors without recourse to possible potential toxic effects.

The present study was carried out to evaluate the effect of its chronic administration on the functional integrity of the kidneys in rats.

Materials and Methods

Plant materials

The stem bark of the plant was obtained from Ifetedo, Osun State, Nigeria, in the month of May and was authenticated at the Department of Botany, Herbarium Unit, Obafemi Awolowo University, Ile-Ife, Nigeria. The voucher specimen was deposited at the herbarium with voucher number: Oliv. IFE No 13968.

Preparation of plant extract

Aqueous extract was prepared according to the method of Adesokan and Akanji[6]. Briefly, samples of the stem bark was air dried at room temperature to constant weight. It was pulverized into powdery form with an electric blender (Blender/Miller 111, model MS-223, China), from which 20 g was percolated in 100 ml of distilled water for 48 hr at room temperature with constant shaking. The filtrate water was evaporated in a regulated water bath at 70°C, and later dried to constant weight in an oven at 37°C. The residue of the extract was stored in air-tight plastic container. A known weight of the extract

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was dissolved in distilled water to give the required doses.

Experimental animals

Sixty albino rats (*Rattus novergicus*) of both sexes with average weight of 200 g ± 5 were obtained from the Animal Holding Unit of the Department of Biochemistry, University of Ilorin, Ilorin, Nigeria. They were housed in clean metabolic cages which were cleaned of waste twice daily at 12 hr intervals. They were exposed to 12 hr each of daylight and darkness daily at room temperature, and fed rat pellet (Bendel livestock feeds, Benin City) and water *ad libitum*.

Animal grouping and administration of extract

The rats were allowed to acclimatize for two weeks before commencement of the experiment. They were randomly divided into four groups of fifteen rats each. Group 1 which served as the control was orally administered 1 ml of distilled water daily through oropharyngeal tube for 28 days. Groups 2, 3, and 4 were administered 1 ml of the extract to give the required doses of 50, 100 and 200mg/kg body weight.

Preparation of serum

The neck area of the rat was cleared of fur and skin to expose the jugular veins, which were cut swiftly with sterile scalpel blade under diethyl ether anaesthesia. The blood was collected into clean dry bottles and allowed to clot for 1 hr at room temperature. It was then refrigerated at 8°C for 45 min[7].

Determination of Biochemical parameters

Serum sodium and potassium ions were measured using the flame photometer[8]. Serum protein was determined by the method of Plummer[9], and serum albumin determined using the method of Doumas[10]. The procedure of Tietz *et al*[11] was used to determine serum creatinine concentration, while the serum urea concentration was determined by the method of Kaplan[12].

Statistical analysis

The values were expressed as mean of five replicates ± standard error of mean (S.E.M) and the data analyzed using Analysis of Variance (ANOVA) and complimented with the student t-test[13].

Results

Table 1 illustrates changes in serum sodium ion (Na^+) concentration following chronic administration of aqueous extract of *Enantia chlorantha* to experimental rats. Significant increases ($p<0.05$) was observed at the doses of 100 and 200mg/kg body weight, while at 50mg/kg body weight, there was no significant change ($p>0.05$) when compared to the control. However, there were significant reductions ($p<0.05$) in the serum potassium ion (K^+) concentrations in all the treatment groups, throughout the duration of administration (Table 2).

Table 3 showed changes in serum urea concentration. There was a significant increase ($p<0.05$) in the serum urea level only at 100mg/kg body weight, but no significant change ($p>0.05$) at 50 and 200mg/kg body weight, when compared

Table 1: Effect of chronic administration (28 days) of aqueous extract of *E. chlorantha* on serum Na^+ conc. in rats. (mmol/L).

Treatments	Day 10	Day 20	Day 28
Control ($D.H_20$)	136.50±1.03	136.95±1.06	137.20±1.07
Extract 50mg/kg	137.65±1.14	138.10±1.19	138.40±1.21
Extract 100mg/kg	138.85±1.48	140.44±1.58*	140.80±1.66*
Extract 200mg/kg	142.40±1.58*	142.82±1.52*	143.80±1.46*

n=5±SEM, * statistically significant ($p<0.05$) compared to control; $D.H_20$ = distilled water.

Table 2: Effect of chronic administration (28 days) of aqueous extract of *E. chlorantha* on serum K^+ conc. in rats. (mmol/L).

Treatment	Day 10	Day 20	Day 28
Control ($D.H_20$)	5.25±0.12	5.29±0.10	5.36±o.08
Extract 50mg/kg	4.45±0.13*	4.38±0.11*	4.52±0.13*
Extract 100mg/kg	4.46±0.14*	4.58±0.12*	4.76±0.13*
Extract 200mg/kg	4.55±0.22*	4.42±0.24*	4.38±0.20*

n=5±SEM, * statistically significant ($p<0.05$) compared to control; $D.H_20$ = distilled water.

Table 3: Effect of chronic administration (28 days) of aqueous extract of *E. chlorantha* on serum urea conc. in rats (mmol/L)

Treatment	Day 10	Day 20	Day 28
Control ($D.H_20$)	7.75±0.38	7.81±0.42	7.84±0.40
Extract 50mg/kg	7.95±0.55	8.20±0.60	8.06±0.64
Extract 100mg/kg	9.99±0.36*	10.45±0.33*	10.56±0.35*
Extract 200mg/kg	8.25±0.26	8.65±0,30	8.52±0.32

n=5±SEM, * statistically significant ($p<0.05$) compared to control; $D.H_20$=distilled water.

Table 4: Effect of chronic administration (28 days) of aqueous extract of *E. chlorantha* on serum creatinine level in rats (mmol/L).

Treatment	Day 10	Day 20	Day 28
Control ($D.H_20$)	70.85±2.20	71.45±2.32	71.80±2.64
Extract 50mg/kg	71.20±2.35	70.95±2.45	71.60±2.52
Extract 100mg/kg	70.35±5.12	70.65±5.20	70.20±6.40
Extract 200mg/kg	84.95±4.22*	85.22±4.12*	85.40±4.35*

n=5±SEM, * statistically significant ($p<0.05$) compared to control; $D.H_20$ = distilled water.

to the control.

The serum creatinine level showed significant increase ($p<0.05$) only at the highest dose of 200mg/kg body weight of the extract but not significantly different ($p>0.05$) from the control at the lower doses (Table 4).

Administration of the extract at 100mg/kg body weight led to significant reductions ($p<0.05$) in the serum total protein and albumin throughout the experimental period but no significant changes ($p>0.05$) at other doses, when compared to the control (Tables 5 & 6).

Table 5: Effect of chronic administration (28 days) of aqueous extract of *E. chlorantha* on serum total protein conc. in rats (g/L).

Treatment	Day 10	Day 20	Day 28
Control ($D.H_20$)	61.50±2.35	60.50±2.35	60.00±2.43
Extract 50mg/kg	58.80±2.40	56.95±2.55	57.40±2.35
Extract 100mg/kg	50.55±3.50*	51.50±3.65*	51.80±3.85*
Extract 200mg/kg	60.95±2.12	61.50±2.20	61.60±2.06

n=5±SEM, * statistically significant ($p<0,05$) compared to control; $D.H_20$ = distilled water.

Table 6: Effect of chronic administration (28 days) of aqueous extract of *E. chlorantha* on serum albumin conc. in rats (g/l).

Treatment	Day 10	Day 20	Day 28
Control ($D.H_20$)	34.85±0.12	35.10±1.10	35.00±0.00
Extract 50mg/kg	34.20±1.42	33.85±1.35	33.40±1.47
Extract 100mg/kg	32.80±1.20	31.20±1.35*	31.80±1.50*
Extract 200mg/kg	33.95±0.85	37.15±1.10	38.20±0.97

n=5±SEM, * statistically significant ($p<0.05$) compared to control; $D.H_20$ = distilled water.

Discussion

Biochemical indices such as the serum electrolytes, urea, creatinine, total protein and albumin are useful in assessing the renal function status. Sodium and potassium ions are normally filtered through the renal glomeruli and completely reabsorbed by the renal tubular cells[14].

Elevation in sodium ion concentration in the serum may be due to impaired filtration from renal glomerular damage or increased aldosterone secretion from the adrenal cortex through rennin-angiotensin-aldosterone axis[14,15]. Impaired renal glomerular damage will result in elevation of both sodium and potassium ion concentrations. The results of this study showed elevation in sodium ion and reduction in potassium ion concentrations. This observation could only be ascribed to induction of aldosterone secretion by the administered extract. Aldosterone causes sodium retention and reduction in serum potassium ions from increased urinary excretion in exchange for sodium ions[14].

Blood urea nitrogen is derived in the liver from proteins/amino acids from diet or tissue sources and is normally filtered by the renal glomeruli and excreted in the urine[14]. In renal glomerular damage, the serum urea accumulates (resulting in uraemia) because the rate of serum urea production exceeds the rate of clearance[15]. Other causes of uraemia include high protein diet, increased tissue catabolism due to starvation and sepsis, hypovolaemia and shock, steroid treatment and absorption of amino acids and peptides from upper gastrointestinal bleeding[16]. Serum urea elevation observed in this study may be due to renal glomerular damage from the administered extract.

Creatinine, on the other hand, is mostly derived from endogenous sources by tissue creatine breakdown. The plasma creatinine concentration in normal individuals are usually affected by a number of factors such as muscle mass, and high tissue catabolism[14,16]. It is entirely filtered by the renal glomeruli and neither secreted nor reabsorbed by the renal tubular cells. Therefore, serum creatinine concentration is often considered a more sensitive renal function predictor than urea[14]. In the present study, elevated serum creatinine showed that high dose of the extract would induce renal glomerular filtration.

Serum total protein and albumin are derived from synthesis in the liver and tissue breakdown. Reduction in the serum levels might be due to either impaired synthesis by the liver or leakage from the kidneys due to renal damage[14]. This result showed significant reduction at 100mg/kg body weight of the extract and normal value at the highest dose of 200mg/kg body weight. This implied a reversible effect either on the liver that synthesizes protein on one hand, or transient leakage through the glomerular basement membrane[3,14].

The result of the present study has shown that chronic administration of high doses of extract of *Enantia chlorantha* is capable of producing significant alterations in renal function parameters with far reaching implications on its functions. The active ingredients implicated in this impairment and the mode of action needs to be further investigated.

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