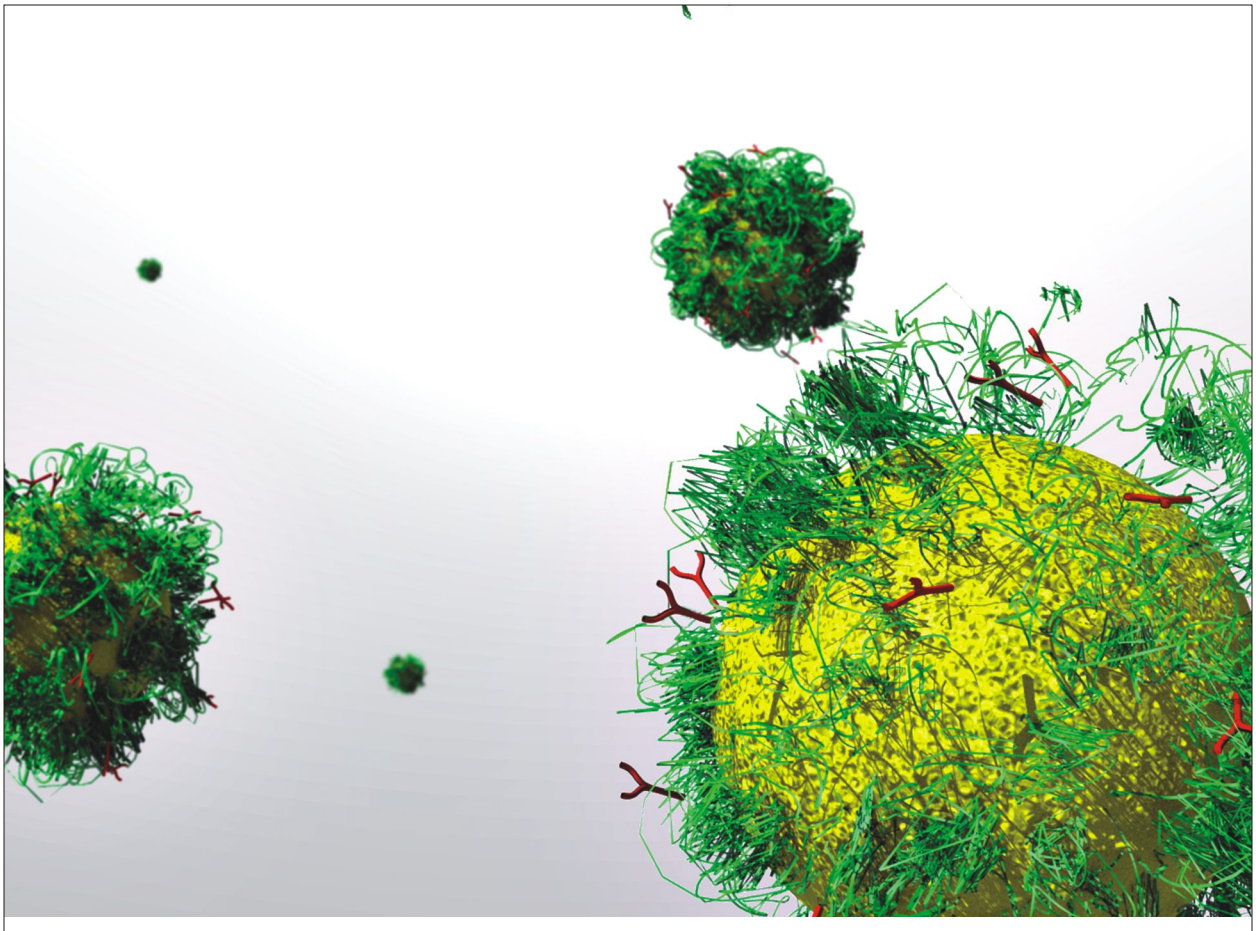

American Journal of
Drug Discovery and Development

ISSN 2150-427X

Academic
Journals Inc.

www.academicjournals.com

American Journal of Drug Discovery and Development 3 (3): 194-199, 2013
ISSN 2150-427x / DOI: 10.3923/ajdd.2013.194.199

Effects of Ethanol Extract of *Sida acuta* Leaves on Some Organ Function Parameters and Physiologically Important Electrolytes in Normal Wistar Albino Rats

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ABSTRACT

Ethanol extract of *Sida acuta* leaves was administered to wistar albino rats to monitor the effects of the plant components on some organ function parameters including creatinine, urea and bilirubin, as well as some physiologically important electrolytes. Thirty six animals, divided into six groups of six animals each and labeled A, B, C, D, E and F were used. Doses of the extract 100, 200, 300, 400 and 500 mg kg^{-1} b.wt., were administered daily for two weeks to groups A, B, C, D and E, respectively. The animals in group F (control) were sustained on normal diet and water during the studies. Creatinine was assayed by the Jaffe reaction whereas urea was analyzed using diacetyl monoxime reaction. Bilirubin measurement was carried out by diazotized sulphanilic acid reaction. Chloride was analyzed by use of Randox reagent kit while sodium and potassium were done by means of flame photometer. Decreases ($p>0.05$) in mean concentrations (mg dL^{-1}) of both urea and creatinine were recorded for all the test groups, comparative to the control. Serum bilirubin concentrations (mg dL^{-1}) were relatively nonsignificantly affected by the extract. Studies on electrolytes showed significant decreases in serum Na^+ concentration (mmol L^{-1}) for doses 300 mg kg^{-1} b.wt. and above. Similarly, K^+ and HCO_3^- concentrations (mmol L^{-1}) were reduced significantly whereas Cl^- concentrations (mmol L^{-1}) were significantly increased for all the experimental groups, comparative to the control. However, notwithstanding that *Sida acuta* extract may not impair liver and kidney functions, possible effects on fluid and electrolyte balance should be seriously monitored.

Key words: *Sida acuta*, serum, electrolyte, organ function

INTRODUCTION

Sida acuta (broom weed) is a shrub that grows commonly in different parts of Nigeria. It is perennial in nature, surviving different seasons. It appears to be a stubborn species with a high capacity to thrive in harsh environmental conditions. It is a shrub with multiple stems and often seen growing along road sides and in bushes. In some parts of Nigeria it is commonly treated as a harsh weed with no form of economic benefit. This opinion coincides with the views of Murphy *et al.* (1996) who emphatically viewed teaweed or ironweed as a "weed" that has great capacity to adversely affect agricultural yield and should therefore not be allowed to grow within agricultural areas.

However, beyond agricultural perceptions, *Sida acuta* has found both recognition and use in healthcare dispensation in many parts of the world. Information we gathered from local sources in Nigeria shows that traditional practitioners of herbal medicine have been applying *Sida acuta* for the treatment of different illnesses such as malaria, fever, headache, infectious diseases and rheumatism, among others. Various reports from around the world have justified the usefulness and effectiveness of the weed in healthcare delivery. The wide spread of *Sida acuta*, especially within the tropical areas and its relevance in traditional management and/or treatment of various ailments have been stated by some workers (Karou *et al*., 2006). The Usefulness of *Sida acuta* for the therapeutic management of disturbing conditions such as asthma, renal inflammation, colds, fever, headache, ulcers and worm infections in regions around Central America has been reported (Caceres *et al*., 1987). The potentials of *Sida acuta* for the treatment of snake bite have been reported. For example, some research reports had claimed that the ethanol extract of the Sida plant was pharmacologically effective against the venom of certain snake species (Otero *et al*., 2000a, b).

Chemically, several alkaloids and steroidal compounds have been isolated from *Sida acuta*, as variously reported (Cao and Qi, 1993; Jang *et al*., 2003). Cryptolepine alkaloid was identified as the major alkaloid of the plant responsible for its antimalarial properties (Banzouzi *et al*., 2004; Dicko *et al*., 2003). Reports of the antimicrobial activity of alkaloids in *Sida acuta* against different microorganisms are also available (Karou *et al*., 2006).

It has become evident that *Sida acuta* Burm. f. has wide medicinal values and its components potentially stand as lead for development of new medicines. This study therefore sought to determine the effects of the ethanol extract of the plant leaves on certain organ function indices and some physiologically important electrolytes in non-pathologic (normal) experimental albino rats. Thus, the findings from the present investigations will help define, at least in part, the margin of safety in the traditional use of *Sida acuta* for healthcare delivery.

MATERIALS AND METHODS

Collection and processing of plant specimen: *Sida acuta* was identified by P.O. Ugwuozor, a taxonomist in the Department of Botany, Nnamdi Azikiwe University, Awka, in the South East of Nigeria. A large quantity of fresh leaves of *Sida acuta* were harvested and dried under shade at room temperature within the laboratory of Department of Biochemistry, Madonna University, Elele, in Rivers State of Nigeria. The leaves were then pulverized using electric blender, Eurosonic (ES 6613).

Preparation of extract: Exactly 1 kg of the pulverized leaf sample was weighed and soaked in ethanol (80%) for 24 h. The mixture was carefully filtered using whatman filter paper and the filtrate was concentrated by evaporation in a rotary evaporator RE 52-2 (Searchtech Instruments). The concentrate (extract) was kept in the refrigerator and was used for administration to the experimental animals.

Experimental animals: Wistar albino rats were obtained from a Veterinary Stock in Ibadan, Nigeria. The animals were housed in cages kept in an adequate animal house environment at the Madonna University, Elele, Nigeria. The animals were allowed to acclimatize for seven days before the commencement of administration. They were adequately fed with normal rat chow purchased from Bendel Feeds and Flour Mills Limited, Ewu, Nigeria.

Administration of extract: A total of thirty-six male albino rats were divided into six groups of six animals per group. The groups were numbered A to F and animals in each group were marked for proper identification. Groups A-E, all experimental groups, were administered graded doses of the extract, 100, 200, 300, 400 and 500, mg kg^{-1} b.wt., respectively. They were orally administered daily for two weeks. Members of group F were kept as control and were maintained on normal feeding and water.

Preparation of serum sample: About 24 h, after the last administration the animals were sacrificed, group by group, by cardiac puncture and the blood transferred into already labeled centrifuge tubes and allowed to stand for 30 min at room temperature. They were then centrifuged at 4000 rpm for five minutes in an 80-1 electric centrifuge (B-Bram Scientific and Instrument Co., England). The resulting sera were used for the analysis of creatinine, urea, bilirubin, sodium, potassium, chloride and bicarbonate concentrations.

Analysis of biochemical parameters: Creatinine and urea were assayed by methods involving protein precipitation. The measurement of creatinine was carried out by the Jaffe reaction method (Fabiny and Erthinghausen, 1971). The determination of urea was carried out by the diacetyl monoxime method as described by Vijayalakshmi *et al* (2000). Absorbances for both indices were read from a spectrumlab 22 spectrophotometer at 520 nm. Bilirubin was assayed by the method involving diazotized sulphanilic acid reaction (Srivastav *et al*., 1999) with absorbance read at 540 nm.

Sodium and potassium were determined by use of flame photometer (IL 943). Bicarbonate concentration was assayed by simple titration method (Scribner and Caillouette, 1954). Biorex reagent kits (UK), BXCO281A was used to analyze chloride concentration according to specifications of the manufacturer.

Statistical analyses: Data generated in the course of this study were statistically analyzed using student t-test (2-tailed) and analysis of variance (ANOVA) at 0.05 level of significance. The Statistical Package for Social Sciences (SPSS) for windows was used for the analysis.

RESULTS

Analysis of serum samples from wistar albino rats treated with varying doses of ethanol extract of *Sida acuta* leaves showed that urea levels of the test animals were nonsignificantly decreased, comparative to the control (Table 1). Creatinine levels were nonsignificantly reduced except for 300 and 400 mg kg^{-1} b.wt. schedules which showed significant increases ($p<0.05$) (Table 1).

Table 1: Serum concentrations (mg dL^{-1}) of urea, creatinine and bilirubin (Data represented as Mean±SD)

Group/dose mg kg^{-1} b.wt.	Urea (mg dL^{-1})	Creatinine (mg dL^{-1})	Total bilirubin (mg dL^{-1})	Direct bilirubin (mg dL^{-1})	Unconjugated bilirubin (mg dL^{-1})
A 100	24.92±1.71	1.38±0.28	0.68±0.45	0.18±0.10	0.51±0.39
B 200	24.92±3.74	1.37±0.29	0.69±0.50	0.20±0.09	0.49±0.41
C 300	23.42±2.81	2.45±0.24*	1.00±0.37	0.20±0.07	0.81±0.34
D 400	24.45±5.14	1.88±0.23*	0.89±0.52	0.24±0.11	0.69±0.50
E 500	24.68±4.44	1.63±0.22	1.14±0.57	0.26±0.09	1.09±0.24*
F (control)	27.74±1.58	1.67±0.36	0.74±0.45	0.17±0.10	0.57±0.39

*Significantly different from the control ($p<0.05$). NB: SD (standard deviation); mg kg^{-1} b.wt. (milligram per kilogram body weight); mg dL^{-1} (milligram per deciliter)

Table 2: Serum concentrations (mmol L^{-1}) of various electrolytes (data represented as Mean±SD)

Group/dose (mg kg^{-1} b.wt.)	Na^+ (mmol L^{-1})	K^+ (mmol L^{-1})	Cl^- (mmol L^{-1})	HCO_3^- (mmol L^{-1})
A 100	134.20±3.19	3.92±0.27*	102.80±1.92*	24.40±1.82
B 200	135.17±2.32	4.15±0.18*	102.67±2.16*	25.00±2.53
C 300	131.33±1.75*	4.22±0.40*	102.50±3.33*	22.17±1.47*
D 400	132.33±2.58*	4.15±0.19*	102.67±1.97*	24.50±1.87
E 500	133.67±3.61	3.33±0.33*	102.67±2.16*	24.33±2.73
F (control)	136.20±2.77	5.00±0.16	94.80±2.39	28.20±2.59

*Significantly different from the control ($p < 0.05$). NB: SD (standard deviation), mg kg^{-1} b.wt. (milligram per kilogram body weight); mmol L^{-1} (millimol per liter)

Bilirubin levels were apparently unaffected by the extract, showing only slight fluctuations when compared with the control. Only at a dose of 500 mg kg^{-1} b.wt. was a significant increase recorded comparative to the control (Table 1).

The effects of the extract on various electrolytes are shown on Table 2. Sodium decreased nonsignificantly ($p>0.05$) except with 300 and 400 mg doses which showed significant reductions ($p<0.05$). Comparative with the control, both potassium and chloride concentrations were significantly affected; potassium levels were significantly reduced ($p<0.05$) while chloride levels were significantly increased ($p<0.05$).

DISCUSSION

Sida acuta extract showed only slight reductions in blood urea concentrations. Creatinine levels were also slightly reduced except in a few cases that are insufficient to elicit any fears of toxicity. There are reports that confirm the capacity of some plant extracts to cause major fluctuations in both urea and creatinine levels (Lienou *et al*., 2007; Ghasi *et al*., 2011). An increase in blood creatinine level would indicate kidney dysfunction since creatinine is cleared rapidly from the blood and excreted. Any medication that interferes with the normal actions of the kidney can lead to elevations in blood creatinine levels. Thus the relatively non-significant influence of *Sida acuta* extracts on these markers of kidney function is a proof of its non-toxic effect on this organ. Several plant extracts also can remarkably affect serum status of bilirubin (Takate *et al*., 2010; Kolawole and Kolawole, 2010; Tsala *et al*., 2010). Thus, *Sida acuta* would have no adverse effects on the liver linked to alteration in bilirubin functions. Reduction in sodium ion levels is an indication of the antihypertensive potentials of *Sida acuta*. However, significant decreases in potassium levels may be a source of worry since hypokalaemia is believed to predispose to clinical conditions such as muscular weakness, cardiac arrhythmias and hypotonia. Bicarbonate is reduced nearly almost insignificantly. Reduction in bicarbonate may lead to a drop in blood pH. This situation occurs when losses through urine and/or gastrointestinal tract exceeds the rate at which it can be replenished by normal homeostatic mechanisms. This situation can arise with intake of certain drugs and thus may be aggravated by *Sida acuta* extracts if taken in very large concentrations. Components of *Sida acuta* may work synergistically to depress bicarbonate and elevate chloride which was significantly elevated. Chloride is known to function actively in keeping a normal balance of fluids in the body. Administration of certain drugs may lead to elevated blood chloride (hyperchloraemia), associated with hypokalaemia. *Sida acuta* extract may be so implicated, from the outcome of balance of these electrolytes following its administration.

The use of crude plant extracts for treatment of diseases dates back in history. This is because plants constitute important sources of biologically active compounds. Certainly, several modern

drugs in use today were developed from plants. Obviously, too, certain health challenges have presently defied orthodox medications and interestingly a good number are responsive to traditional herbal preparations, sources of which are in most cases concealed as patents. The dependence on herbal medication has continued to increase. What is more disturbing is that emphases are often placed on efficacy of the herbal extract or products with little and in numerous cases no attention directed to any possible harmful effects. Most traditional practitioners of herbal medicine lack any formal education and identify their herbal plants based only on evidence of their efficacy over certain health challenges, in most cases as inherited from some predecessors. Herbal substances and products are often administered as water extracts and tinctures (using local gins) and in many cases as blends of mixture of different plants believed to work in synergy. Unfortunately, many of these herbal blends are not scientifically resolved. We continue to process identifiable species of commonly used medicinal plants and assessing their margin of safety by monitoring the effects of administration of such extracts on essential biochemical markers.

Sida acuta has been shown extensively to possess rich medicinal properties. It is as important to exploit the rich pharmacological potentials of these natural resources that have decorated our environment which also bears numerous inundations of diseases, some of which have no defined remedies. Nevertheless, caution is necessary in the use and applications of crude plant extracts since many are also sources of certain toxic compounds. Consequently, despite the ability of *Sida acuta*, as for many other plants' crude extracts to effectively cure ailments, the best approach consists in extracting the active principles and incorporating them into formulations of refined medications.

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