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PHARMACOLOGICAL BASIS FOR THE CONTINUAL USE OF THE ROOT OF *SENNA SIAMEA* IN TRADITIONAL MEDICINE

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ABSTRACT

The sub-acute toxicity of the aqueous extract of the root of *Senna siamea* was studied in rats. Oral administration of *S. siame* for 28 days produced neither mortality nor changes in behavior or any physiological activities. Results obtained showed that the extract insignificantly ($p>0.05$) affected the mean body and organ weight of wistar rats. Hematological parameters (PCV, Hb, WBC. and RBC) and biochemical parameters, (Serum creatinine, serum urea, sodium, potassium ions, alkaline phosphatase (ALP), alanine aminotransaminase (ALAT), aspartate aminotransaminase (ASAT)) were not affected by the extract. Histological studies of vital organs did not show any statistical significant difference between the same organs. These results may explain the continual use of *S. siamea* in folk medicine.

KEYWORDS

Senna siamea, hematological, biochemical parameter, body and organs weight, acute toxicity study

INTRODUCTION

Senna siamea (Lam.) Irwin & Barneby (Family: caesalpiniaceous) root decoction is used for the management of diabetes and different disease conditions in Nigeria. It is called Bikini raskata in Hausa, Odan in Yoruba, *Bois perdix* in French, Flamboyan Amarillo in spanish. It has different English names; these include Cassod tree, Pleasant wood, Thai cassia or Thailand shower. It is also known as *Cassia siamea* [Linn]. Mixture of *Senna siamea* fruit and *Ficus thonnigii* leaves is used to prevent convulsion in children, and for the treatment of typhoid fever in both children and adult. Its stem has laxative properties and is used in the management of several ailments including genito-urinary tract infection, herpes and rhinitis[1,2]. Extract from the plant has been reported to have anxiolytic properties, increase exploratory and locomotor behavior[3]. It is also used as a mild laxative, and in the management of insomnia[4]. The timber from *S. siamea* is used for the production of timber pole, fuel wood, furniture, turney, and

cabinetwork. *S. siamea* tree is planted to provide shade and also widely used as ornamentals[1,2].

S. siamea root is rich in alkaloids, saponin, phylobatannins flavonoids, tannin, steroid, carbohydrate, glycoside and anthraquinone. Its leaves have been reported to be toxic. Toxicity of the leaves depends on how it is processed during extraction. If properly processed, the toxic principle (tannin, oxalate, barakol and phytate) will be reduced to negligible concentration[5,6]. *S. siamea*, fresh young flowers and/or young leaves have been used as vegetables in Thailand. They can be prepared as food by boiling in water at a ratio of 1:3 for 1 hour, 2-3 times to reduce the bitterness[6], and reduce (or eliminate) toxic constituents. In this study, the sub-acute toxicity of the root of S. siamea was evaluated.

MATERIALS AND METHOD

Collection and Identification of Plant Materials

The fresh root of the *Senna siamea* was collected from the University of Jos premises, Jos, Plateau State, Nigeria in June 2006. The plant was identified and authenticated by Dr. I.A Abdulkareem of School of Forestry, and Prof. Huesaini of Botany Department, University of Jos, Jos, Plateau State, Nigeria.

Experimental Animals

Female, non-pregnant healthy Wistar rats (weighing about 200 g) bred in the animal house of Department of Pharmacology, Faculty of Pharmaceutical Sciences, University of Jos, were used for this study. They were fed with feeds (Vital feeds, Nigeria) and tap water *ad libitum*. The experiment was approved by the ethical committee on the use of experimental animals of the University of Jos.

REAGENTS USED

Reagent used include: Creatinine test kit (Dialab Austria), AST test kit (Dialab Austria), ALT test kit (Dialab Austria), Protein test kit (Dialab Austria), and Urea test kit (Dialab Austria).

Preparation of Extract

Fresh root of the *Senna siamea* was air dried at room temperature (25^{o}C) in the laboratory. Dried roots were reduced to coarse powder with the aid of mortar and pestle. Three hundred (300) grams of the powdered plant parts was stirred in 500ml of distilled water and allowed to stay for 48 hours. The mixture was then filtered and the resultant decoction freeze dried. The powder was kept in the desiccator till use.

Administration of the Extract

Female rats were randomly distributed into five groups of five animals per group. Group 1 served as control and received distilled water while Groups 2, 3 and 4 received the aqueous extract of the root of *S. siamea* (0.5, 1.0 and 1.5 g/kg respectively). Animals received their doses once a day (at 10:00 am daily) orally, via polythene cannula for 28 days. The rats were observed daily for clinical/pharmacological signs of toxicity, throughout the period of study.

Haematological Parameters

Blood samples were collected from rat's tail after 28 days of treatment into heparinized blood sample bottles. Packed cell volume (PCV) of each sample was determined using a Hawksley micro-haematocrit centrifuge[7]. The bleeding and clotting time were determined using the methods described by McGowen et al. 1955[7]. Erythrocytes (RBC) and total leucocytes (WBC) were counted using the improved Neubauer haemocytometer as describe by Otimenyin et al, 2009[8].

Biochemical analysis

At the end of 28 days treatment periods, 4 ml of blood was collected from the heart of each rat. The blood was allowed to clot, and then centrifuged at 1500g for 10min. The resultant serum was used for assay of alkaline phosphatase (ALP), alanine aminotransaminase (ALAT), aspartate aminotransaminase (ASAT), creatinine, urea, and serum protein concentration using kit methods. Sodium and potassium were assayed using atomic absorption spectrophotometric method.

Histological examination of vital organs

Livers, heart, stomach, lung, testis and spleen from treated animals were fixed in 10 percent neutral buffered-formalin prior to routine processing in paraffin embedded blocks. Sections (4 µm thick) were cut and stained using hematoxylin-eosin stain and photomicro graphed[8].

Statistical Analysis

Data were analyzed using ANOVA and student t- test[9].

RESULT

Effect of *S. siamea* on rat's body and organ weight

The results obtained from this study suggests that the extract of the root of *S. siamea* did not produce significant (P>0.05) effect on rat`s body weight. It was observed that rats significantly (P<0.05) increased in weight when body weight of animals on day 1 was compared to that of day 28, but there was no difference in weight of the rats in control group and those in the treated group. The increase in body weight observed may have resulted from normal growth of the animals. This shows that the extract did not have effect on the feeding habit or growth of rats

Table 1

Evaluation of body and organ weight (grams) after 28 days treatment with the extract of S. siamea

Treatment	Initial body weight	Final body weight	Heart	Spleen	Kidney	lungs	Liver	stomach
Control	200.31±10.24	210.28±8.51	1.50±0.40	0.99±0.05	3.12±0.43	2.21±0.23	8.01±1.20	2.41 ± 0.18
500	195.94±8.38	200.27±10.73	1.35±0.35	1.13±0.23	2. 97±0.29	2.56±0.52	7.91±1.42	2.55 ± 0.10
1000	210.25±14.37	215.51±14.16	1.47±0.52	1.01±0.28	3.03±0.15	2.41±0.83	9.07±0.80	2.59 ± 0.15
1500	200±05±20.73	215.62±17.31	1.63±0.39	1.11±0.14	2.99±0.59	2.63±0.30	7.83±0.98	2.73 ± 0.21

Data are expressed as mean±S.E.M., n = 5 in each group.
P>0.05, when values were compared with control.

Effect of S. siamea on haematological parameters

It was observed that oral administration of the extract of the root of *S. siamea* did not significantly (p>0.05) alter the levels/ values of WBC, PCV and Hb.

TABLE 2

Effect of aqueous extract of S. siamea on heamatological parameters in rat

Treatment	Hb (g/100ml	PCV (%)	RBC (millions/ per mm^3)	WBC (per mm^3)
CONTROL	18.6 ± 0.29	57.8 ± 2.4	7.1 ± 1.3	18,150 ± 205
S. siamea 500mg/kg	19.3 ± 0.5	56.3 ± 2.2	6.6 ± 14	17,300 ± 197
1000mg/kg	17.2 ± 0.4	55.9 ± 2.9	4.7 ± 0.2	17,938 ± 221
1500mg/kg	16.4 ± 0.4	56.9 ± 1.4	5.0± 0.18	18,313 ± 211

n= 5 p>0.05, when compared with the control

Effect of aqueous extract of *S. siamea* on biochemical parameters.
The serum urea, serum protein, serum creatinine, sodium and potassium ions values were not statistical significantly different from their control values.

TABLE 3

Effect of aqueous extract of S. siamea on plasma protein, serum urea, creatine, sodium and potassium after 28 days treatment.

Treatment	Serum Protein (g/l)	Serum Urea (mmol/l)	Serum creatinine	Na (mmol/l)	K (mmol/l)
CONTROL	78.70 ± 7.60	7.80± 0.19	79.50 ± 3.18	165.30 ± 2.40	8.07 ±0.19
S siamea 500 mg/kg	68.40 ±3.50	7.29 ±0.19	77.70 ±2.60	158.50 ± 2.80	8.33 ± 0.17
1000 mg/kg	69.00 ± 5.90	7.40 ± 0.16	77.23 ± 4.50	160.80 ±2.50	7.66 ± 0.50
1500 mg/kg	75.50 ± 6.90	7.42 ± 0.24	78.72 ± 3.70	157.50 ±5.20	6.95 ± 0.19

n= 5 p>0.05, when compared with the control

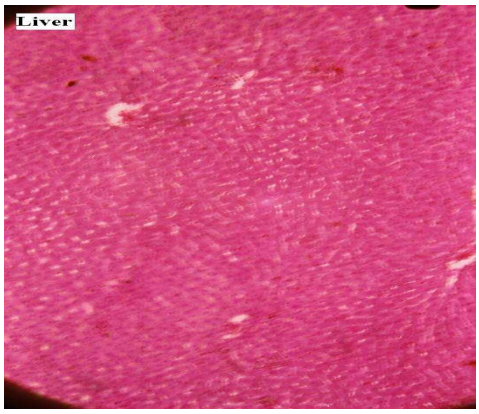
Effect on Liver enzymes

Alkaline phosphatase (ALP), alanine aminotransaminase (ALAT), aspartate aminotransaminase (ASAT) values showed no significant difference between control and treated animals.

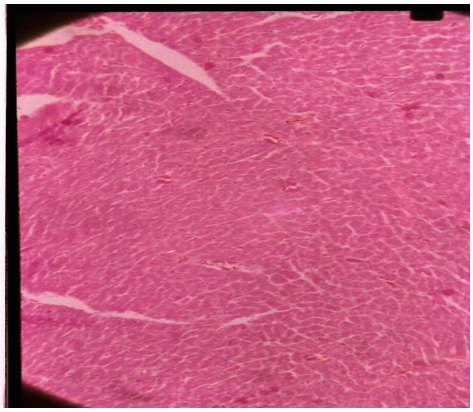
TABLE 4
Effects of the aqueous extract of Senna siamea on liver ezymes

Treatment	AST (U/l)	ALT (U/l)	ALP (U/l)
CONTROL	155.00 ± 5.54	54.50 ± 2.86	141.33 ± 6.95
Senna s. 500mg/kg	160.33 ± 9.73	55.67 ± 2.11	143.67 ± 7.38
1000mg/kg	158.42 ± 8.79	56.67 ± 3.01	153.77 ± 7.68
1500mg/kg	153.83 ± 6.27	59.17 ± 3.46	154.33 ± 9.76

Figure 1; Effect of *S.siamea* on the liver

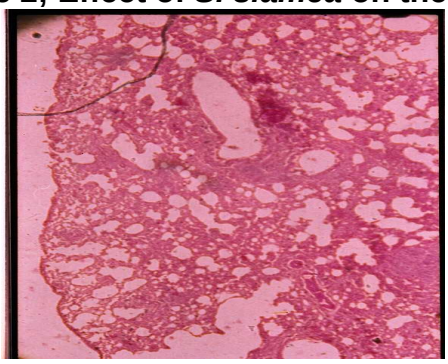


Control (distilled water) liver showing normal cells (3.52)

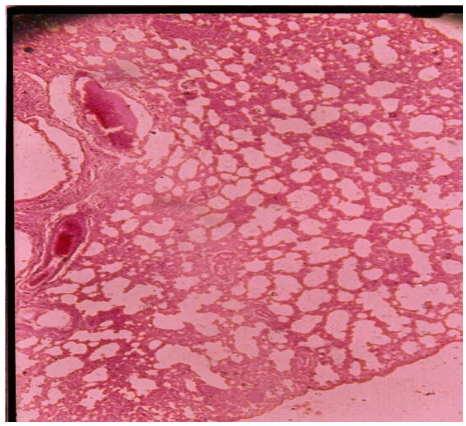


Test (*S. siamea* 1000 mg /Kg) liver showing normal cells (3.52)

Figure 2; Effect of *S. siamea* on the lungs

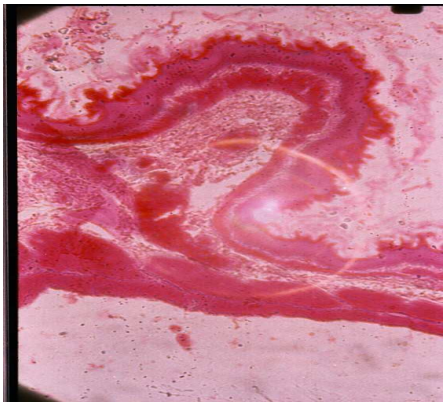


Control (distilled water) lung showing normal cells (3.52)

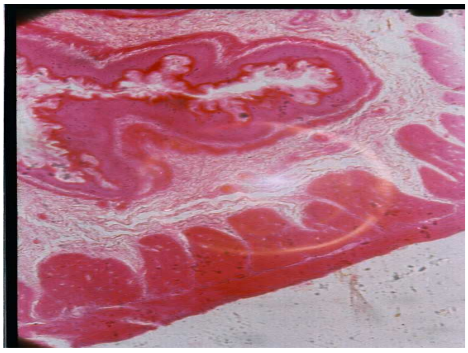


Treated (*S. siamea* 1000 mg /Kg) lung showing normal cells (3.52)

Figure 3; Effect of *S. siamea* on the stomach

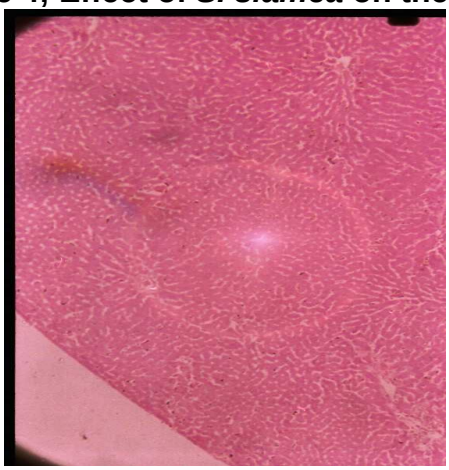


Control (distilled water) Stomach showing normal cells (3.52)

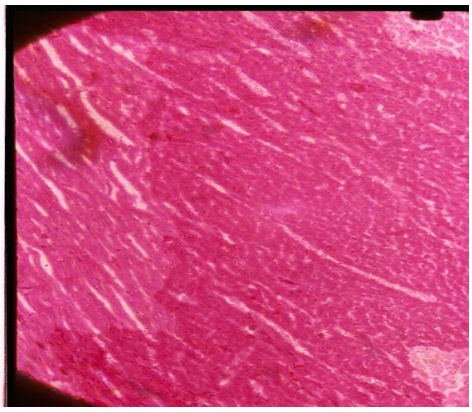


Treated (*S. siamea* 1000 mg /Kg) Stomach showing normal cells (3.51)

Figure 4; Effect of *S. siamea* on the heart

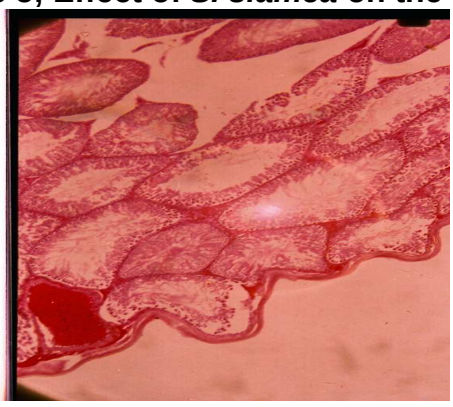


Control (distilled water) heart showing normal cells (3.52)

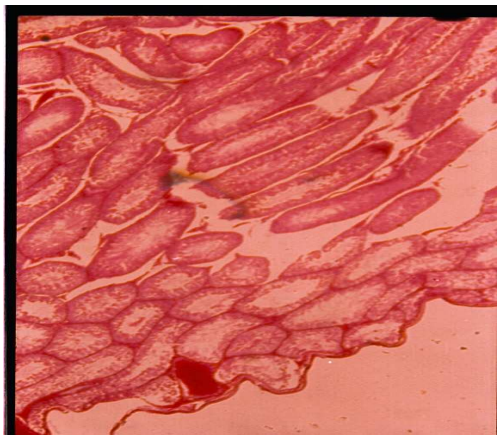


Treated (*S. siamea* 1000 mg /Kg) heart showing normal cells (3.51)

Figure 5; Effect of *S. siamea* on the testis

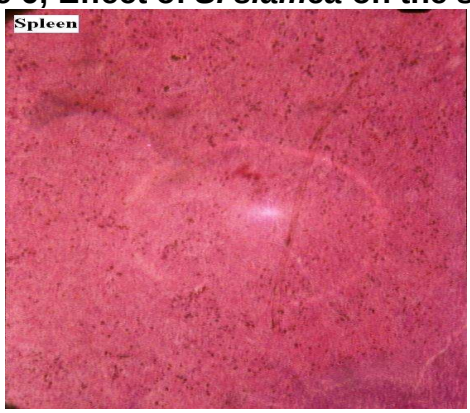


Control (distilled water) Testis showing normal cells (3.51)

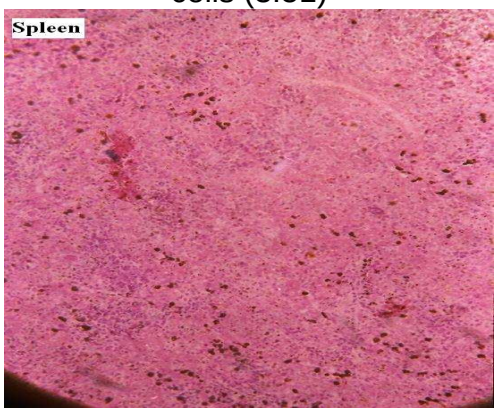


Treated (*S. siamea* 1000 mg /Kg) Testis showing normal cells (3.51)

Figure 6; Effect of *S. siamea* on the spleen



Control (*Distil water*) Spleen showing normal cells (3.51)



Treated (*S. siamea* 1000 mg /Kg) Spleen showing normal cells (3.51)

DISCUSSION

Folk medicine uses plant extracts without taking into account the toxicity of the plants material. Traditional herbal practitioners believe that over the years, toxic plants have been screen out of folk medicine. Toxic plants, when observed in folk medicine are immediately withdrawn from the practice. This belief has on many occasions been scientifically proven wrong. The toxic effects of herbal preparations on specific organs in animals and humans have been of medical concern[10,11], as this is not taken into consideration by traditional healers. Organ toxicity is of concern because most herbal medicines are often used in their crude form, which contains several constituents. Plant like *Anacardium occidentale* has been used for years in folk medicine with the belief that it has no toxic effects. Scientific investigation however, revealed that it is toxic[12,13], as it gradually destroy internal organs. A number of medicinal plants have also been shown to be safe for human consumption, an example is *Momordica balsamina*[8]. It is therefore necessary for each plant to be scientifically screened for safety before it is registered for use by drug regulatory authorities.

S. siamea is used as a medicinal plant in the tropical rainforest of South America and Western Africa. In some countries, Leaves are used for the management of different disease conditions. The leaves of *S. siamea have* been reported to be toxic. The toxic effect of the leaves of *S. siamea* was linked to the presence of tannin, oxalate, phytate[14] and barakol[6]. Tanit[6] also reported that these toxic constituents can be eliminated by proper processing the leaves. *S. siamea* has antimicrobial properties and is used mainly for the management of diarrhea and infectious diseases[15,16,17],. The anti-bacterial activity of *S, siamea* was reported to be exhibited by its flavonoids contents[16,17]. *S. siamea* has been reported to have mild tranquilizing effect, reduce anxiety, promotes better sleep, improves general well-being and is rich in vitamin C and A[3].

In Nigeria, the root of *S. siamea* is used for the management of diabetes. The results from this studies showed that *S. siamea* root extract is relatively safe compared to its leaves. Barakol, a major constituent of *S. siamea* leaves has been reported to be responsible for the toxic effect of the leaves[6].

S. siamea leaves was withdrawn from the market in 2003 due to hepatotoxicity [18]. Chivapat[19] *et al* reported that barakol caused dose dependent degeneration and necrosis of hepatocytes in Wistar. What was not clear though was why *S. siamea* leaves toxicity has not been reported for hundreds of years and why it has not been withdrawal from herbal medicine pharmacopeia. Tanit (2006)[6] reported that the method of preparation may affect barakol content in the final preparation, and may explain lack of toxicity of *S.siamea*.

The result from this study revealed that the extract of the root of *S. siamea* did not have statistical significant effect on Livers, heart, stomach, lung, testis and spleen (Figure 1, 2, 3, 4, 5 and 6). The effect of the extract on body weight of rat (treated with oral dose daily for four weeks) revealed that the extract of *S. siamea* root had no significant ($P > 0.05$) effect on the body weight (Table 1). The increases in body weight observed were due to normal growth resulting from nutritious feeding. This increase cuts across the groups, and there was no significant difference when treated groups were compared with the control group at different stages of this experiment. The Rats that received that extract had dose dependent changes in the WBC, Packed Cell Volume and Heamoglobin values (Table 2). Biochemical studies revealed that this plant extract has no toxic effects on kidney (Table 3) and liver cells (Figure 1, Table 4). Serum urea, serum protein, serum creatinine, sodium and potassium ions (biochemical parameters for evaluating kidney integrity) in the treated rats (Table 3) and the control showed no significant difference ($p>0.05$). This shows that the kidney integrity was not compromised by the extract during the treatment periods. Blood levels of liver enzymes (ALP, ALAT and ASAT) were also not significantly ($P> 0.05$) affected by the extract, revealing that the extract has no damaging effect on the liver (figure 1, table 4). Increase in serum liver enzymes (ALP, ALAT and ASAT) are commonly used in diagnoses of liver damage by chemical agents. The reason why the leaves of *S. siamea* are hepatotoxic and the root of *S. siamea* is not hepatotoxic cannot

be explained from this study. It is likely that the concentration of barakol in the root is lower than its concentration in the leaves. It is also possible that the duration of administration may have been too short to reveal the plants toxicity. Further studies need to be carried out to determine which of the listed reasons above explains S. siamea reported toxicity

The result obtained from this work explains the reason for the continuous use of the root of *S. siamea* in the management of diabetes in Africa. Indicating that it is safe for consumption, this may explain the continual use of its root extract in Nigerian folk medicine.

CONCLUSION

The crude aqueous extract of the root of *S. siamea* showed no significant effect on hematological, histological and biochemical parameters evaluated. The finding suggests that the root extract of *S. siamea*, is relatively not toxic on blood, hepatic and renal cells at oral dose of 500 mg/kg, 1000 mg/kg and 1500 mg/kg for the period of administration.

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