Acute and Subacute Toxicity of Aqueous Extract of *Sarcocephalus latifolius* (Sm.) Bruce Fruit in Rats

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ABSTRACT

The roots, leaves, and stems of *Sarcocephalus latifolius* (*S. latifolius*) are widely used in pharmacopeia to treat various inflammatory diseases. However, few studies have been performed on the fruits of this plant. This study set out to assess the aqueous extract of *S. latifolius* fruits' innocuity against female rats and mice. Six female mice, each weighing 23 g, were given a single dosage of 5000 mg/kg bw of the extract along with distilled water. Fourteen days were spent observing them. Thirty rats, each weighing 162 g, were given distilled water and, over 28 days, an aqueous extract of *S. latifolius* fruit at doses of 100, 250, and 500 mg/kg bw. In the acute test, no signs of toxicity or mortality were noted. In the sub-acute test, no discernible change was found in the relative weight of organs collected compared with the control group. Analysis of hematological parameters showed that the extract caused no significant variation in blood cell counts at the doses tested compared to the control. For biochemical parameters, the extract at all doses showed no significant variation from the control. Extract at 500 mg/kg bw showed no significant alteration of liver and kidney parenchyma in rats compared to controls. The fruits of *S. latifolius* are non-toxic and can be used in traditional medicine to treat patients at the doses tested.

Key Words: *Fruit, Sarcocephalus latifolius, Toxicity, Rats, Mice*

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INTRODUCTION

Medicinal plants are considered less toxic with minor adverse effects than pharmaceutical drugs. They have the potential to provide compounds with novel and complex structures capable of interacting with biological systems [1]. Twenty-eight percent (28%) of drugs used worldwide are of plant origin [2]. The World Health Organization (WHO) estimates that over 80% of the African population relies on medicinal plants to provide primary healthcare [3, 4]. *Sarcocephalus latifolius* (*S. latifolius*) has been identified as having numerous pharmacological activities [5]. It is used to treat malaria, hypertension, fever, diarrhoea, dysentery, and dental problems [6-9]. Scientific studies have shown that in Burkina Faso, the fruit is used to treat liver and kidney diseases [10, 11]. In Nigeria, fruit is used to treat haemorrhoids, while ripe and roasted fruit is used to treat measles [12]. In Congo, the fruits are consumed as a cough remedy [13]. People in developing nations employ a wide variety of plants in their traditional cuisines. When eatable, the fruits are a great source of vitamins, carbs, and minerals. This is the case of *S. latifolius* fruits, with an estimated content of 24.53 g/100 g and an energy content of 132 Kcal/100 g. The inclusion of wild plants in the diet of undernourished populations is doubly beneficial in these developing countries. This is the case of *S. latifolius* fruits, which are little used in traditional medicine and edible by local populations [14,

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15]. *S. latifolius* fruits have a high acidity and vitamin C content. Although their consumption covers daily ascorbic acid requirements (estimated at between 42 and 93 mg/day), adverse effects are revealed when they are consumed in large quantities. These include oxalate kidney stones [14]. Given these findings, a toxicity study is needed to clarify the likely effects of medium-term exposure to *S. latifolius* fruits. Therefore, this study set out to assess the aqueous extract of *S. latifolius* fruits' innocuity against female rats and mice.

MATERIALS AND METHODS

Animal

Female Wistar rats and NMRI mice from the « Laboratoire de Physiologie Animale de l'Université Joseph KI-ZERBO » were used. They weighed 160 g and 23 g respectively at the start of the experimentation. In the animal home, these animals were maintained at 22 ± 3 °C with a relative humidity of 50 ± 10% and a 12-hour light cycle. They had access to food and water.

Plant

The plant material is constituted of *S. latifolius* fruits certified under number 18028 by the « Département de Biologie et Ecologie Végétale ». In August 2021, the fruits were collected in the South-West Burkina Faso region of Gaoua. The town is 415 km from Ouagadougou.

Preparation of extract

The fruits were dried, and reduced to powder, and 400 grams of this powder were left to macerate for a whole day in 1000 milliliters of distilled water. For ten minutes, the resulting filtrate was spun in a centrifuge at 2000 rpm. After being lyophilized, the supernatant was chilled at -23 °C. After being extracted, the aqueous extract (EASL) of *S. latifolius* fruits was kept at -4 °C. 24.23% was the result of the extraction.

Experimental methods

Acute toxicity study

This study was carried out following OECD guideline 423 [16], with some modifications. Six female mice were divided into three per cage. They were fasted 4 hours before the start of the experimentation. The control group was treated with distilled water, while the test group received EASL at a single dose of 5000 mg/kg bw. Two hours after administration of the extract, the mice were re-fed. They were carefully observed for the first, four hours and during 24, 48, and 72 h after extract administration.

Subacute toxicity study

This study was performed according to the method described in OECD guideline 407 [17]. Thirty female rats weighing 160 g were used. They were divided into six groups of five rats. They were orally fed daily with water and aqueous extract of *S. latifolius* fruit as follows:

- Group I received distilled water and served as control,
- Groups II, III, and IV received *S. latifolius* fruit extract at doses of 100, 250, and 500 mg/kg bw, respectively,
- Groups V and VI served as negative and positive satellites. They received distilled water and the extract at 500 mg/kg bw, respectively.

Treatment lasted twenty-eight days. Satellite animals were observed for an additional fourteen days.

Biochemical, hematological estimation

After a 12-hour fast, the rats were given ketamine anesthesia at the end of the experiment and were then sacrificed. Blood was drawn into desiccated tubes. The serum was collected and kept at -20 °C for biochemical examination (aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (PAL), and total bilirubin (TB), as well as creatinine, urea, total cholesterol, and triglyceride) after centrifugation at 3000 rpm for 15 minutes. For these studies, Atlas diagnostic product kits were employed. A full blood count was performed using blood obtained in EDTA tubes. After blood collection, the organs such as the liver, kidneys, spleen, lungs, and heart were removed, rinsed, and weighed.

Statistical analysis

Excel 2016 software package was used for data entry. The statistical tests, graphical representations, and mean and standard error computations were all performed using Graph Pad Prism version 5.03. Tukey's test and one-way analysis of variance (ANOVA I) were utilized to compare the test and control groups. It was determined that there was a difference of statistical significance between the readings for $P < 0.05$.

RESULTS AND DISCUSSION

Acute toxicity study

No mortality and no signs of toxicity were recorded at all the entire experimental dose levels used in the acute toxicity study. The LD_{50} was estimated to be more than 5000 mg/kg b w.

Effects of S. latifolius fruit extract on body weight gain in rats

Behavioral observations such as drowsiness and excessive agitation in test and control rats showed no significant difference ($P > 0.05$). No mortality was observed in all groups. During the period of treatment, the animal body

weight gain was recorded in treated and untreated groups. There was no significant difference between the body weight gain of treated rats and the control group. Rats in satellite groups did not differ significantly in weight development (P > 0.05) **(Figure 1)**.

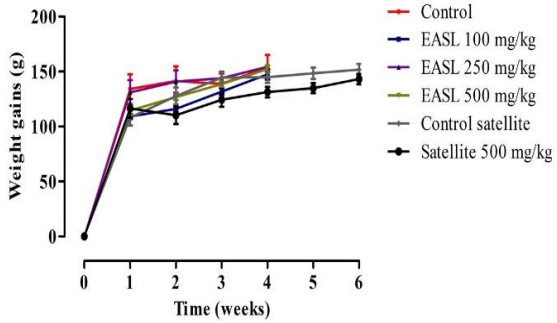

Figure 1. Effects of *S. latifolius* extract on body weight gains in rats

Effects of S. latifolius fruit extract on the relative weight of organs

Relative organ weight did not significantly change as a result of the extract at any dosage in comparison to the control. Additionally, there was no discernible variation in the relative organ weights across satellites (P > 0.05). The autopsy of the internal organs (liver, kidneys, spleen, lungs, heart) revealed no atrophy, nor hypertrophy **(Table 1)**.

Table 1. Effects of *S. latifolius* fruit extract on the relative weight of organs

Relative weights (g)	Treatments (mg/kg)					
	Control	**EASL 100**	**EASL 250**	**EASL 500**	**Negative satellite**	**Positive satellite**
Liver	2.72 ± 0.11	2.8 ± 0.1	2.67 ± 0.1	2.64 ± 0.1	2.27 ± 0.02	2.83 ± 0.06
Kidneys	0.55 ± 0.01	0.6 ± 0.01	0.59 ± 0.02	0.59 ± 0.01	0.54 ± 0.01	0.6 ± 0.01
Spleen	0.26 ± 0.03	0.24 ± 0.01	0.27 ± 0.02	0.28 ± 0.01	0.25 ± 0.03	0.32 ± 0.01
Lungs	0.92 ± 0.07	0.64 ± 0.03	0.73 ± 0.08	0.58 ± 0.14	0.67 ± 0.12	0.83 ± 0.08
Heart	0.41 ± 0.03	0.4 ± 0.01	0.39 ± 0.02	0.41 ± 0.02	0.36 ± 0.02	0.4 ± 0.01

Effects of S. latifolius fruit extract on hematological parameters

Blood constants such as white and red blood cell count, hemoglobin, lymphocytes, platelets, and hematocrits did not change significantly between control rats and those treated with EASL (P > 0.05). Blood cell counts did not differ significantly between satellites **(Table 2)**.

Table 2. Effects of *S. latifolius* fruit extract on blood cells

	Treatments (mg/kg)					
Hematological parameters	**Control**	**EASL 100**	**EASL 250**	**EASL 500**	**Negative satellite**	**Positive satellite**
WBC	5.84 ± 0.62	6.37 ± 0.13	5.91 ± 0.13	5.98 ± 0.23	5.68 ± 0.43	5.77 ± 0.42
HB	14.41 ± 0.54	14.1 ± 1.14	15.05 ± 0.25	14.41 ±0.46	13.55 ± 0.15	13.10 ±0.13
RBC	8.14 ± 0.31	8.21 ± 0.74	8.64 ± 0.07	8.03 ± 0.16	7.89 ± 0.20	7.34 ± 0.2
HCT	50.35 ± 1.94	50.26 ± 4.59	52.15 ± 0.83	49.96 ±1.46	44.69 ± 0.90	42.96 ± 0.21
LYM	75.62 ± 3.32	67.46 ± 2.97	71.02 ± 4.75	64.18 ±3.03	76.12 ± 3.86	78.13 ± 0.23
PLT	788.4 ± 108.76	898.31 ± 116.61	848.7 ± 58.10	890.88 ± 47.26	803.87 ± 55.58	598.35 ± 29.72

White blood cells, red blood cells, hemoglobin, lymphocytes, platelets, and hematocrits are all referred to as WBC, RBC, LYM, and HCT, respectively. The values are given as mean ± standard error to the mean (SEM); there are five of them. Notable distinction from the control: p is less than 0.05 (*).

Effects of S. latifolius fruit extract on biochemical parameters

The biochemical and lipid profiles of rats treated with *S. latifolius* extract and control rats are shown in **Figures 2**

and 3. These profiles showed no significant differences between test and control rats and satellite rats (P > 0.05).

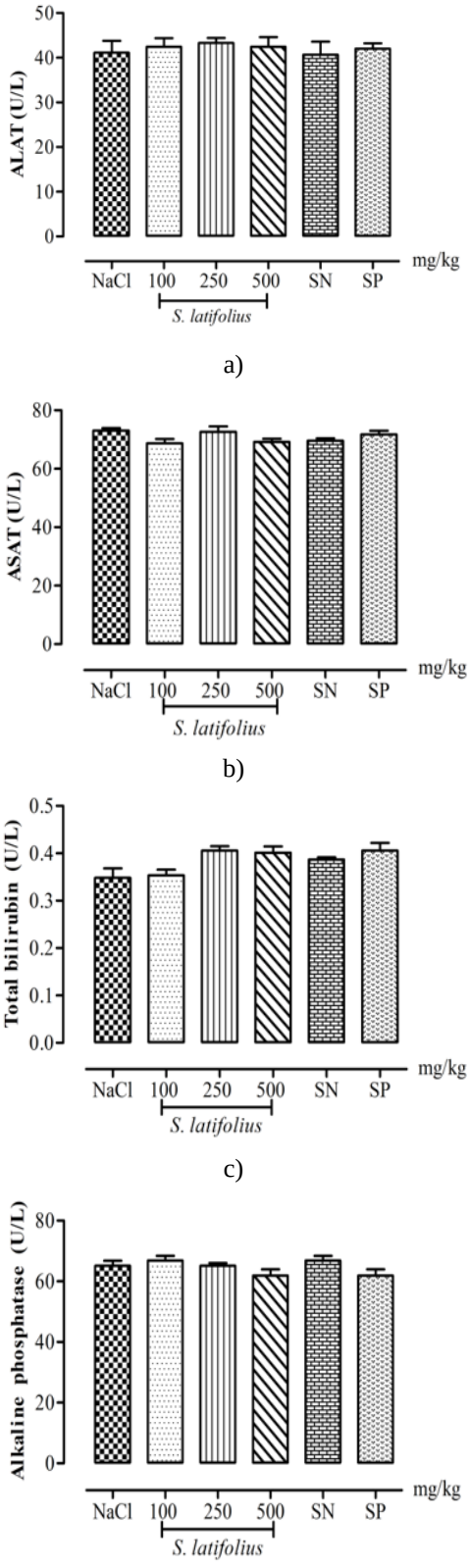

Figure 2. Effects of *S. latifolius* fruit extract on liver markers in rats

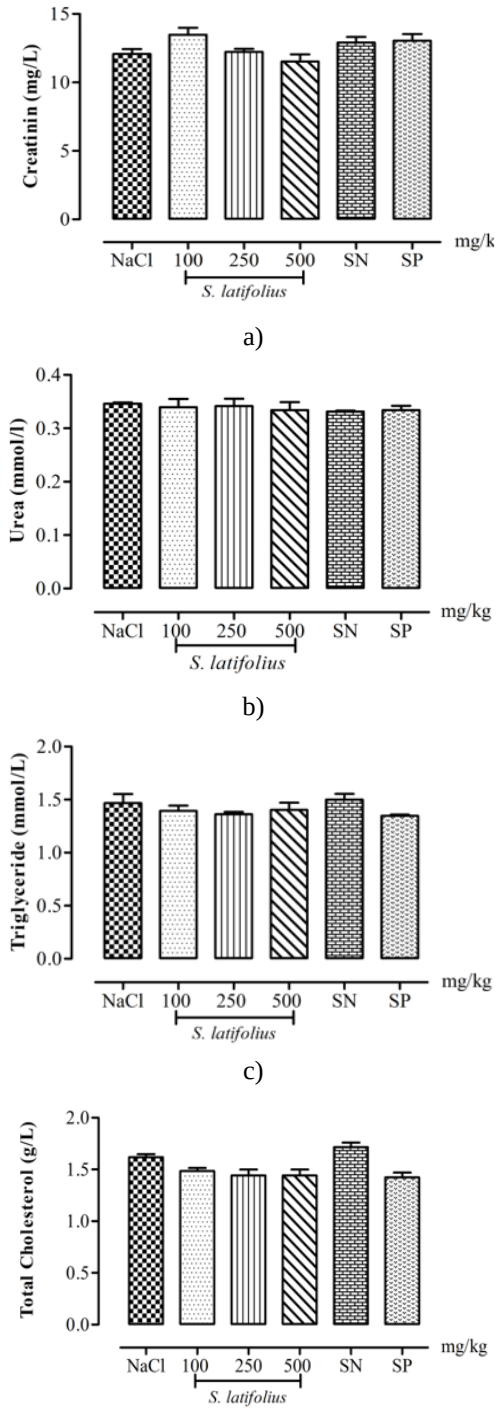

Figure 3. Effects of *S. latifolius* fruit extract on renal and lipid markers in rats

Effects of S. latifolius extract on liver and kidney structure

Histological examination of the liver and kidneys of rats treated with *S. latifolius* fruit aqueous extract showed normal architecture. However, slight edema of the hepatocytes and nephrons was observed in rats treated with extract 500 mg/kg and in control rats **(Figures 4 and 5)**.

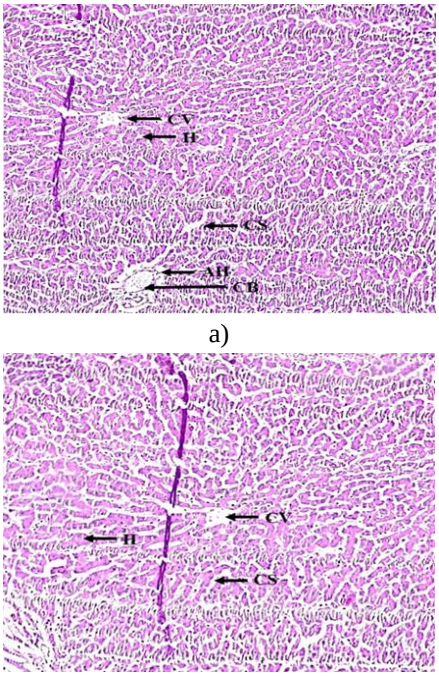

Figure 4. Effects of *S. latifolius* fruit extract on rat liver sections (H&E x 400). a) control liver, and b) liver treated with EASL 500 mg/kg. HA: hepatic artery,
CB: biliary canaliculus, CV: central vein, H: hepatocytes, CS: canaliculus.

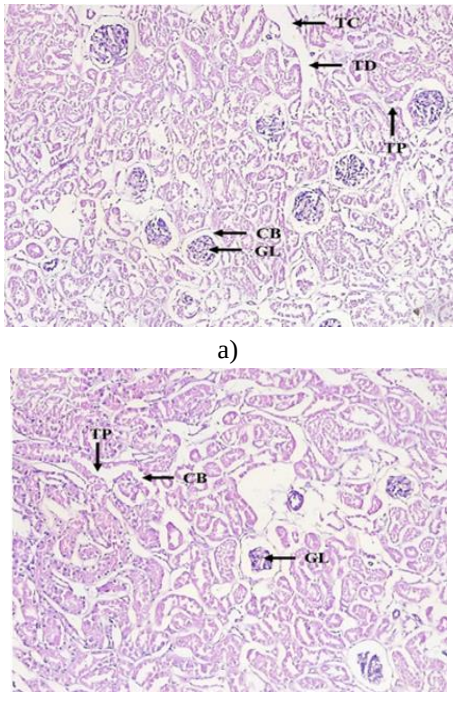

Figure 5. Effects of *S. latifolius* fruit extract on rat renal sections (H & E x 400), a) control kidney, and b) kidney treated with EASL 500 mg/kg. PT: proximal tube, DT: distal tube, CB: Bowman's capsule, GL: Glomerulus

S. latifolius fruits contain tannins, alkaloids, flavonoids, saponins, phytates, cyanogenic glycosides, phosphates, anthraquinones, coumarins, monoterpenes, fatty acid esters [12, 15, 18].

The absence of behavioral disorders of the somatic and autonomic nervous system, and mortality, indicates an LD_{50} greater than 5000 mg/kg body weight of the extract. According to the high oral LD50 (> 5000 mg/kg) observed, the extract is mostly non-toxic when used orally for ethnomedical purposes [19]. This result justifies its local use in the diet and health of populations. This result is similar to that of [20]. These authors found an LD 50 greater than 2000 mg/kg for fruit extracts of *Nauclea latifolia*.

At all doses, the extract produced a non-significant increase in body weight in treated rats compared to control rats. The phytochemical compounds of the extract may act on growth factors by activating the metabolism of primary metabolites. These compounds could induce an increase in body weight in test rats. Phenolic compounds, terpene, and alkaloids can stimulate the secretion of enzymes from the digestive tract and accessory glands. *S. latifolius* fruit is thought to stimulate food intake and digestion in rats [21, 22]. The aqueous extract of *S. latifolius* fruit contained no toxic substances, as it did not induce significant variation ($P > 0.05$) in the relative weights of the kidney, liver, spleen, heart, and lung **(Table 1)**.

In cases of liver damage, abnormal levels of liver enzymes are detected. In the body, these enzymes are crucial indicators. They assess the function of the liver. Significant alterations in the hepatocellular membrane's integrity are the reason behind fluctuations in liver enzyme levels. The non-significant variation in ALP, TB, AST, and ALT levels ($P > 0.05$) observed in test and control rats shows that the aqueous extract protects and stabilizes hepatocellular membranes. The ability of *S. latifolius* fruits to stabilize liver cell membranes is thought to be linked to the hepaprotective effect of flavonoids. Flavonoids in *S. latifolius* fruit are thought to protect liver cells from damage [20, 23, 24].

The results show a non-significant ($P > 0.05$) decrease in cholesterol and triglyceride at all extract doses. Plants containing saponins can be used in health care for their biological activities as cholesterol-lowering agents [25]. Saponins contained in the fruit have already been shown to inhibit cholesterol reabsorption and increase its excretion. They inhibit absorption directly in the small intestine, or indirectly by inhibiting the reabsorption of bile acids. The presence of saponins thus probably contributes to cholesterol reduction [26]. The non-significant variation in cholesterol levels and triglycerides in treated rats indicates that the heart was not damaged by

the administration of the extract [27]. A comparison of satellite rats showed no late or reverse effects on liver and kidney markers. The same findings were obtained for the lipid profile.

In plant toxicity studies, the variation in WBC and LYM levels indicates that the plant extract induces an immune response in treated rats [28]. Hematological analysis revealed a non-significant decrease in LYMP levels ($P > 0.05$) and a non-significant increase in WBC levels, at all doses, compared to the control ($P > 0.05$) **(Table 2)**. These results suggest that *S. latifolius* extract possesses metabolites capable of enhancing the immune system. The extract's chemical compounds are responsible for its hepatoprotective properties. The study concluded that the extract had anti-infectious properties and was capable of stimulating the immune system [25]. Aqueous extract of *S. latifolius* fruits improves the hematological potential of rats. Blood cells are produced in the red bone marrow. Hematological variations such as anemia are usually caused by bone marrow intoxication [29]. Anemia resulting from xenobiotic administration can be the result of blood cell lysis [30]. However, there was no significant variation in RBC levels ($P > 0.05$) between control and test rats. The aqueous extract of *S. latifolius* fruits would not cause lysis of red blood cells and therefore would not result in anemia. The extract's secondary metabolites could accelerate erythropoiesis, thereby preventing anemia in rats [31]. Exposure of the rats to the extract did not result in any significant change in white blood cell or lymphocyte levels, and the study concluded that the extract could boost the immune system. A comparison of satellite rats showed no late or reverse effects on blood cells.

Histopathological sections of the liver and kidneys of rats treated with *S. latifolius* fruit extract at 500 mg/kg show an overall normal cellular architecture compared to control sections. These results go in agreement with those of the biochemical parameters and confirm the practically non-toxic effect of the extract on the liver and kidneys. The presence of phytoconstituents such as flavonoids, alkaloids, and glycosides in *S. latifolius* extract may be responsible for the protection of the liver and kidneys.

CONCLUSION

The results show that the hematological, biochemical, and histological parameters studied did not differ significantly between control and test rats. The aqueous extract of *S. latifolius* fruit had practically no toxic effect on rats at the doses used. These results contribute new findings on the use of *S. latifolius* fruit in traditional medicine.

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Ethics statement: None

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