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Acute Toxicity of *Solanum macrocarpon* Linn (Solanaceae) on Wistar Rats: Study about Leaves and Fruits

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Abstract *S. macrocarpon* is a highly consumed vegetable in Benin with values recognized by herbal medicine. The objective of this study was to assess its acute toxicity on Wistar rats. Fruits and leaves were shade dried, powdered, boiled and filtered. The powders obtained from leaves and fruits were orally administered to randomly selected animals divided into five groups treated with saline, 300 mg/kg and 2000 mg/kg of powders. The anomals were observed along 14 days focusing attention on different behavior manifestations. Body weight, hematological (Complete Blood Count) and biochemical analyses (urea, creatinine and transaminases) were conducted. About *S. macrocarpon*'s leaves, the dose of 300 mg/kg resulted in the death of no rat. No mortality was recorded at the dose of 2000 mg/kg. It was the same for the fruit powder. Powders of leaves and fruits of *S. macrocarpon* then have an LD_{50} greater than or equal to 5000 mg/kg. There was a significant increase in the weight of rats after administration of powders of *S. macrocarpon*. Powder of *S. macrocarpon* has not resulted in a weight loss of Wistar rats but weight gain is not due to the administration of a single dose of powders. No statistical difference was observed when comparing averages of different groups ($p > 0.05$) for both transaminases ALT and AST. Powders of *S. macrocarpon* induced a significant decrease in blood urea in groups II, III and IV. From the two parts used (leaves and fruits), only fruit had this effect regardless of dose. The hematological parameters were not significantly different between the groups. Biochemical and hematological assays showed that neither leaves nor fruit of this vegetable have toxicity on the rats. These results proved that fruits and leaves of *S. macrocarpon* can be safely consumed.

Keywords *S. macrocarpon*, Medicinal Plants, Food Security, Toxicity

1. Introduction

S. macrocarpon is a plant of the same family as tomatoes, peppers: eggplant family called Solanaceae[1]. The botanical genus includes herbaceous plants or shrubs leaves usually alternate, sometimes opposite. The inflorescence is a cyme, usually single seed. The flowers are hermaphrodite, with star-shaped corolla with five petals often reflected (back to back). The protruding stamens form a cone around the gynoecium. The ovary is superior. The fruits are berries[1]. Also called *S. macrocarpum*, it is used as a vegetable in many countries in West Africa[2-3]. *S. macrocarpon* is also used for its therapeutic properties. Despite this dual purpose, little scientific data on the knowledge of the plant species exist.

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Although studies have been conducted on the aqueous extract of *S. macrocarpon*[2], no data on the toxicity of powders of leaves and fruits are available in Benin. Since there is in the world almost 1500 species belonging to the genus Solanum[4], preliminary studies have shown that the Benin variety of *S. macrocarpon* has a similar nutritional value to *Moringa oleifera*, a vegetable heavily used in the nutritional recovery of children and people with compromised immunity[5-6] in Benin. Unfortunately, the presence of certain chemical compounds such as alkaloids, especially in fruits, fears its promotion as a dietary supplement. That is why an earlier study was to evaluate the cytotoxicity at short and medium term of powders of leaves and fruits of *S. macrocarpon*[7]. The results suggested that the leaves and fruit vegetable showed no risk and that its consumption could be promoted. However, it is important to make more extensive toxicity studies on Wistar rats (model physiologically similar to humans) to investigate the effect of *S. macrocarpon* on hematological parameters, liver and kidney to further reassure the scientific world. This study is

then to complete cytotoxicity tests performed on larvae shrimp (*Artemia salina*) and will confirm or not the harmlessness of the empirical use of *S. macrocarpon* as food and medicine.

2. Material and Methods

2.1. Material

The mature leaves and fruits of *S. macrocarpon* were the plant material used in this study. It were purchased in July 2012 on the site of Houeyiho located at 6° 21' 20" North latitude and 2° 21' 35" East longitude in Benin. It is the biggest site of Benin and the soil is enough fertile[8].

Wistar albino rats were bred in the Laboratoire de Recherche en Biologie Appliquée (LARBA), University of Abomey-Calavi (Benin) at constant temperature of 22 ± 1°C with a cycle of 12 hours at light and 12 hours of darkness. They were fed with granulated provender and water *ad libitum*.

2.2. Methods

The leaves were thoroughly washed with distilled water (with a few drops of bleach) and then dried at laboratory temperature of 16°C in LARBA for 17 days while fruits were also washed and finely cut into small pieces before being dried for 09 days. Leaves and dried fruits were ground for ten minutes using a Moulinex Sayona. The powders were then sieved using sieves of 0.2 mm and stored in sterile containers until needed.

2.2.1. Toxicity Tests

The tests were performed according to OECD Guideline for testing of chemicals through the method 423 (OECD, 2001). The principle of this test is that, with only a sequential process, using a minimum number of animals per step, information on the acute toxicity of the substance are obtained and is sufficient for the purposes of classification. A fixed dose of the substance is orally administered to a group of animals.

The absence or presence of mortality related to the substance in a group will determine the next step, ie:

– Stopping test

– Administration of the same dose to three additional animals,

– Administration of the dose immediately above or below to three additional animals.

At the beginning of the test, the rats aged of 12 weeks and weighing between 140 and 170 grams were randomly selected, marked to permit individual identification, and kept in their cages for acclimatization to the laboratory conditions for five days before the experiment. Powders of leaves and fruits were dissolved in physiological saline and administered to rats at doses of 1 ml / 100 g of body weight. It were given in a single dose using a feeding tube. The rats were fasted overnight but with access to water. Each step required three animals. The initial level of 300 mg/kg was chosen. Since it is a vegetable which was used, from four doses proposed by the Directive 423, it is the one for which it might expect to observe mortality among some of the treated animals. Thus, the rats were divided into different lots. The control lot received no treatment while lots I and II were respectively given 300 mg/kg and 2000 mg/kg of powdered leaves. Lots III and IV were respectively given 300 mg/kg and 2000 mg/kg of fruit powders.

The animals were observed individually at least once during the first 30 minutes, periodically during the first 24 hours after treatment. Particular attention was observed for 14 days after administration of the substance. All observations were recorded systematically, individual records being maintained for each animal. Attention has focused in particular on the observation of the various manifestations of tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma.

The following parameters were investigated:

– Body Weight

Individual weight of each rat was determined shortly before administration of the powders. At the end of the test, the animals were weighed and then sacrificed.

– Pathology

Blood samples were performed on all rats for Complete Blood Count and biochemical (urea, creatinine, transaminases) parameters in LARBA. The retro-orbital sampling was adopted. The Complete Blood Count was to determine the number of red blood cells (NGR), the number of white blood cells (WBC), hemoglobin (Hb), hematocrit (Hte), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin Concentration (MCHC), Mean Corpuscular Concentration in hemoglobin (MCHC) and platelet count. These tests were performed using a Sysmex KX-N21 according to the methodology of **Sodipo *et al.*[**2]. Urea, creatinine and transaminases were assayed by the kinetic method in accordance with the methodology of **Sodipo *et al.*[**2].

2.2.2. Statistical Analysis

Means and standard deviations were compared with a significance level of 5%. Using the nonparametric Mann-Whitney test, the average of the control lot were compared to those of Lots I, II, III and IV and those of lots I, II on the one hand and III, IV on the other hand were compared. XL Stat 2011 software was used for statistical tests while Microsoft Excel 2013 has permitted the creation of graphs.

3. Results and Discussion

3.1. Determination of LD_{50}

About *S. macrocarpon*'s leaves, the dose of 300 mg/kg resulted in the death of no rat. No mortality was recorded at the dose of 2000 mg/kg. It was the same for the fruit powder.

Powders of leaves and fruits of *S. macrocarpon* then have an LD_{50} greater than or equal to 5000 mg/kg[9]. Nevertheless, a certain lethargy was noted in treated rats. Plants with LD_{50} above 1000 mg/kg by oral route are safe or of low toxicity[10]. These results confirm previous work done on the same substances[7]. Lethargy observed in rats could be due to stress caused by handling.

3.2. Effect Powders of *S. macrocarpon* on Weight Gain in Wistar Rats

There was a significant increase in the weight of rats after administration of powders of *S. macrocarpon*. Powder of *S. macrocarpon* has not resulted in a weight loss of Wistar rats (Figure 1). However, the variation is similar between lots; so weight gain is not due to the administration of a single dose of powders. As the purpose of this study was just to evaluate the *in vivo* toxicity of powders, it would be interesting to explore the role of these powders on weight gain in malnourished children or people exactly as other authors did it on *Moringa oleifera*[5].

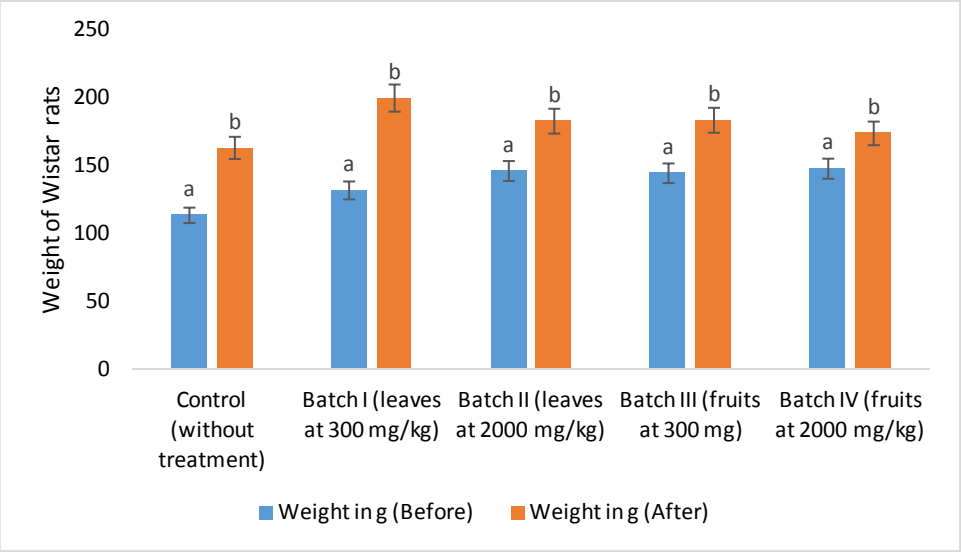
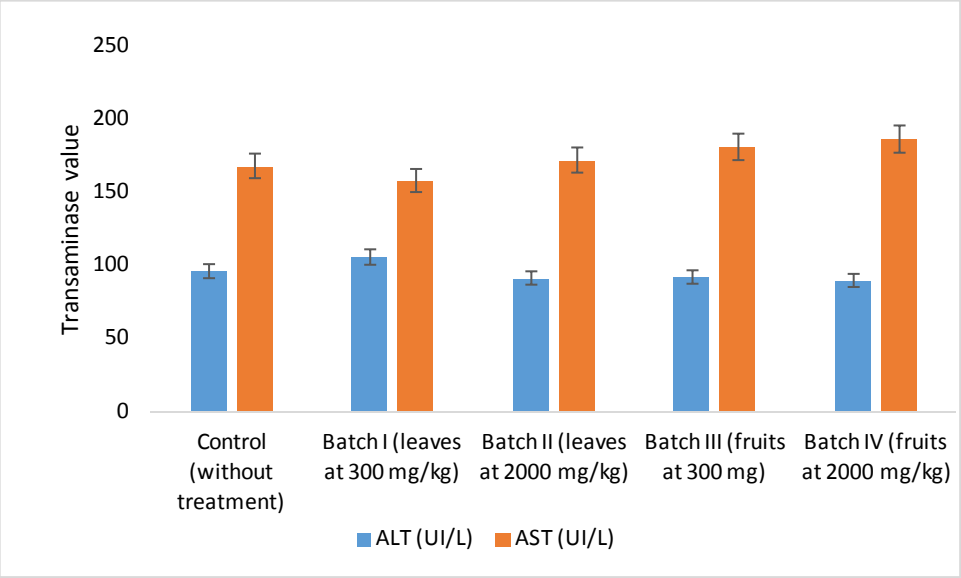


Figure 1. Weight's variation on Wistar rats

3.3. Exploration of Liver Damage

No statistical difference was observed when comparing averages of different groups ($p > 0.05$) for both transaminases ALT and AST (Figure 2).



Lot I and Lot II: $p > 0.05$; Control and Lot I: $p > 0.05$; Control and Lot II: $p > 0.05$; Lots III and IV: $p > 0.05$; Control and Lot III: $p > 0.05$; Control and Lot IV: $p > 0.05$.

Figure 2. Variation of transaminases on Wistar rats

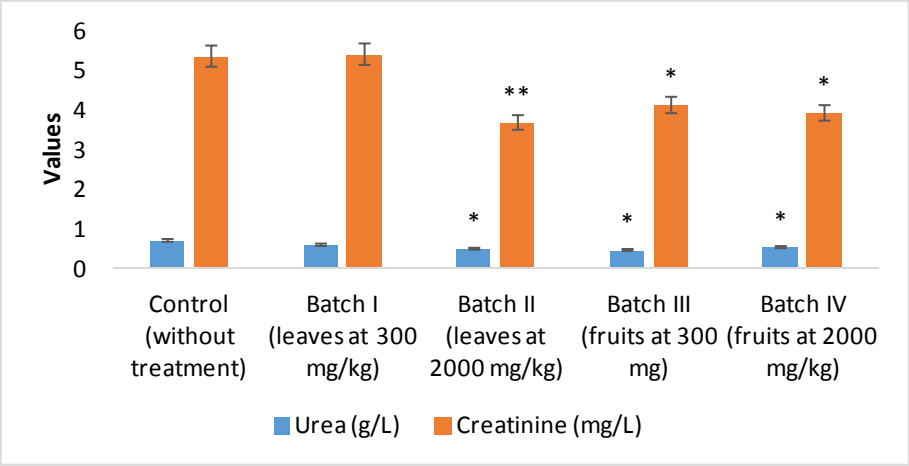
Normal values of ALT differ from those defined by Kamdem *et al*.[11] which was 74.7 ± 3.8 IU/L but are not far from those established by Vaissaire[12]. Indeed, this author proposed 130 IU/L as the average value of ALT in rats aged from three months, while the values in this study ranged around 100 IU/L. These differences between studies are due to the age of the rats, their diet and physiology[12]. As there was no difference between the control group and the test lots, powders of *S. macrocarpon* had no toxic effects on the liver of rats. Normal values of AST obtained are consistent with those proposed by Kamdem *et al*.[11] (178 ± 20.99 IU/L). These results are different from 42.9 ± 10.1 IU/L established by Kaneko[13] and 200 ± 26 IU / L established by Vaissaire[12]. The age factor could also be implicated in these cases.

3.4. Exploration of Renal Parameters

Powders of *S. macrocarpon* induced a significant decrease in blood urea in Lots II, III and IV. From the two parts used (leaves and fruits), only fruit had this effect regardless of dose (Figure 3). The fruits of *S. macrocarpon* therefore have a better effect on renal function[4],[2] than leaves that regulates urea until a dose of 2000 mg/kg. This situation was further tested in the assay of creatinine. Only leaves powder at 2000 mg/kg induced decrease in creatinine, especially when compared to the lot receiving leaves powder at 300 mg/kg.

3.5. Exploration of Hematological Parameters

White blood cells and platelets were significantly elevated (Table 1). From these two parameters, a possible witness trombocytose coupled with leukocytosis can be explained by the use of nasogastric tube metal. Indeed, rats of test group were overfed while the control group had free access to water. The material used to feed rats of test groups may have abused the esophageal wall of these animals, causing acute inflammatory syndrome. As the other parameters have been no significant difference, this explanation is reinforced.



*: Significant difference between treated Lot and Lot Control for the parameter considered ($p < 0.05$)
**: Significant difference between treated Lot and Control Lot on one hand and between the considered lot and the lot I on other hand ($p < 0.05$)

Figure 3. Variation of urea and creatinine on Wistar rats

Table 1. Hematological parameters in Wistar rats feed with *S. macrocarpon* powders

	WBC (G/L)	RBC (T/L)	HGB (g/dl)	HCT (%)	MCV (fl)	MCH (pg)	MCHC (%)	Platelets (G/L)
Control (without treatment)	4.90 ± 0.26	6.74 ± 0.65	12.06 ± 0.77	40.26 ± 2.13	59.90 ± 2.70	17.93 ± 0.52	29.96 ± 0.63	507 ± 77.94
Lot I (leaves at 300 mg/kg)	6.06 ± 0.15*	6.20 ± 0.27	12.10 ± 0.69	40.63 ± 1.24	65.70 ± 4.65	19.50 ± 0.52	29.83 ± 2.27	513.66 ± 31.8*
Lot II (leaves at 2000 mg/kg)	7.03 ± 2.02*	7.02 ± 1.10	12.53 ± 0.25	42.83 ± 1.06	66.73 ± 0.56	19.56 ± 0.25	29.26 ± 0.41	865 ± 26.7*
Lot III (fruits at 300 mg)	6.80 ± 2.51*	6.36 ± 0.34	12.50 ± 0.40	41.96 ± 1.79	66.06 ± 4.82	19.66 ± 0.47	29.80 ± 1.55	895 ± 19.2*
Lot IV (fruits at 2000 mg/kg)	7.43 ± 2.49*	7.16 ± 0.33	13.60 ± 0.50	47.23 ± 2.37	65.96 ± 0.72	19 ± 0.36	28.80 ± 0.79	952 ± 12.2*

*: Significant difference between the treated Lot and Control Lot for the parameter considered ($p < 0.05$)

4. Conclusions

The present study revealed that leaves and fruits of *S. macrocarpon* has no toxicity on biological parameters. S. macrocarpon is safe for consumption, showing no liver or renal acute toxicity. Thus its medical properties should be explored and assessed.

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