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Acute and subacute toxicity of *Solanum aethiopicum* Linn Gilo (Solanaceae) aqueous leaves extract in Wistar rats

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Abstract
The aims of this study was to evaluate the acute and sub-acute toxicity of *Solanum aethiopicum* Linn Gilo aqueous leaves extract in *Wistar* rats. Female rats received a single dose (2000, 3000, 4000 and 5000 mg/kg/ bw) of the extract for acute toxicity. Both, male and female rats received 300,500 and 800 mg/kg/ bw during 21 days for sub-acute toxicity measurements. Blood sample was collected for the determination of some haematological, biochemical and oxidative stress parameters. Besides, the histological sections of the liver, heart, lungs and kidneys were analyzed. Results showed that the lethal dose of the extract greater than 5000mg/kg. the extract did not alter the haematological parameters. It maintained blood sugar and proteinuria within normal limits and had good antioxidant activity. The histopathological analysis revealed normal architecture of lung, kidney, heart and liver. *Solanum aethiopicum* LINN GILO aqueous leaves extract at doses of 300,500,800mg/kg/bw has therefore shown any sign of toxicity.

Keywords: *Solanum aethiopicum*, toxicity, haematological and biochemical assays

Introduction
More than 80% of African populations resort to medicine and traditional pharmacopoeia to deal with health problems [1]. Among the 500.000 plant species recorded on earth, only half are listed by botanists. The World Health Organization (WHO) has identified 22.000 plant species used in traditional medicine of which, 3.000 have been the subject of scientific evaluations so far [2]. From all these medicinal plants listed, 15% have been studied phytochemically and 6% for their biological activities [2]. Ethnobotanical study is undoubtedly an interest for the discovery of new plants, which are important source of drugs via their precious active ingredients. Medicinal plants are used in rural African communities as basic medicine, prepared by herbalists without training nor knowledge on their safety and efficacy. As a result, a good evaluation of the popular activities of these medicinal plants makes it possible to ensure their level of safety and effectiveness [3]. However, the pharmacological efficacy of a substance is not sufficient to justify its use in therapy [4]. A toxicant is a substance capable of disrupting immediately or at long term, temporarily or durably, the normal functioning of a living organism, and can also lead to death [5]. It is therefore necessary to define the risk /benefit ratio in the therapeutic indication of each substance. Toxic effects can be detected by macroscopic pathological examination during post-mortem or histopathological examination after a complete toxicity study. Besides, some toxic effects can also be detected using clinical and chemical analysis of body fluids [5]. Plant consumption and herbal medicine must provide a certain guarantee and carefulness. The safety of a substance can be assessed either by studying its acute toxicity after administration of a single dose or, by studying its chronic toxicity after its repeated administration. *S. aethiopicum* commonly known as *Garden* egg is a seasonal plant of nightshade family also called "Eggplant"or "Missahal" in *Banen* and "*Edinda zom*" in Bulu which are two local languages in Cameroon. Leaves of *S. aethiopicum* contain dietary fiber, calcium, iron, zinc, vitamins and phytonutrients [6]. They are usually used to make soups. Also, in traditional medicine, *S. aethiopicum* leaved are used to treat asthma, constipation, stomach aches and allergies [7]. A few studies have shown the anti-inflammatory, lipid-lowering, hypotensive, antimicrobial and anticancer properties of fruits extracts of *S. aethiopicum* [8-10]. However, to our knowledge, no studies has been done on the toxicity of the aqueous extract of this vegetable.

Material and Methods

Material

Biological material

Solanum aethiopicum LINN GILO

Fresh leaves of *S. aethiopicum* used in this work were harvested during the raining season (June - July 2021) at Bonepoupa village, Nkam Divison, Littoral Region of Cameroon (4°4'6" Nord latitude and 10°1'60" East longitude). They were identified under the number 43008 / HNC at the Cameroon National Herbarium in Yaounde by comparison to Westphal sample number 9046.

Rattus norvegicus

This animal model was chosen because they are docile, easy to handle and are physiologically similar to humans. Female rats were used for acute toxicity since they are more sensitive than males. For sub-acute toxicity, both male and female rats were included for a better appreciation of the effect of the plant extract on both sexes [11].

Preparation of aqueous extract

The crude aqueous extract was prepared by decoction in which 500 g of leaves powder were added to 2 liters of distilled water. The mixture was boiled for 20 minutes then cooled and filtered. The filtrate obtained was then dried in an oven at 37 °C for 2 days. The extract was later stored in amber glass pill jars at 4 °C [12].

Acute toxicity

The acute toxicity test was performed using the protocol described by OECD No. 424 [13]. Fifteen female Wistar albino rats age 1.5 months and weighing 80-110g were used in experiments. During the study, single oral doses of 2000, 3000, 4000 and 5000 mg/k/bw of the aqueous extract were given to rats. Food and water were provided *ad libitum* during the experiments. During this period, signs of toxicity including change in coat, motility, tremors, grooming, breathing, sensitivity to noise, appearance of faeces, mobility as well as the number of deaths were documented.

Sub-acute toxicity

Experimental protocol

Sub-acute toxicity was measured using the OECD protocol [13]. Forty Wistar albino rats (male and female), aged 1.5 months, weighing 90-115g were used for this study. They were divided into 8 groups of 5 rats which received the extracts at the following oral doses: 300, 500 and 800 mg / kg/ bw for 28 days. During this period, a behavioral study was carried out. Food and fluid intake as well as body weight were assessed. On the 29th day, the rats were sacrificed. Their heart, liver, lung, kidneys and spleen were removed, rinsed with physiological water and then weighed in order to determine their relative weight and prepare organ homogenates. Blood was collected from the arterial trachea and introduced in dried or EDTA tubes, then centrifuged at 3000 rpm for 15 min. Whole blood and sera obtained were used for assessment of a few hematological and biochemical parameters respectively.

Determination of some biochemical parameters and stress markers

The following biochemical parameters were assessed: total cholesterol (CT), Hight density lipoproteins cholesterol (HDL), low density lipoproteins cholesterol (LDL), triglycerides (TG), blood sugar, proteinemia, ASAT, ALT, uremia, serum creatinine, total and direct bilirubin, alkaline phosphatase and γGT. They were assayed by enzymatic and colorimetric methods using the CHOD-PAP Autospan Liquid Gold, Spain; PEG-CHOD-PAP Autospan Liquid Gold, Spain and GPO-PAP SGM Italia, Italy kits as described by Nader *et al.* [14], Kaplan and Pesce [15] protocols. Protein and creatinine were measured in the urine. The activity of catalase (CAT) and superoxide dismutase (SOD) were determined using spectrophotometric methods described by Sinha [16] and Misra *et al.* [17] respectively. The thiol groups (GSH) and thiobarbituric acid reactive substances (TBARS) were determined by spectrophotometric methods as described by Ellman [18] and Wilbur *et al.* [19] respectively.

Determination of hematological parameters

Red blood cells (RBC), hemoglobin (Hb), hematocrit (Hte), leukocytes (LEU), mean corpuscular volume (MCV), mean corpuscular hemoglobin content (TCMH), mean corpuscular hemoglobin concentration (CCMH), platelets (PLA), lymphocytes (LYM), MID and GRAM were determined using an automated hematological reader (QBC Autoread plus, United Kingdom).

Histopathological analyzes

Rats' liver, heart, kidneys and lungs were removed, rinsed with physiological water and stored in 10% formalin. The different sample tissues were then dehydrated in ethanol solutions enclosed in paraffin and cut in 5 µm sections using a microtome. The cuts were stained with hematoxylin-eosin and examined in microscope. The microscopic characteristics of the treated same were compared with those of the control group [20].

Statistical analyzes

Results were analyzed using SPSS 16 software (SPSS, Inc., Chicago, USA). Quantitative values were presented as mean ± standard deviation using graphs and tables. The mean values were compared using one factor analysis of variance (ANOVA). Newman-Keuls post hoc test was used for multiple pair comparisons.

Ethic of experimentations

The experimental procedure adopted in this study was in accordance with the United States National Health Guidelines for Care and Use of Laboratory Animals in Biomedical Research [21].

Results and Discussion

Acute toxicity

No death was recorded amongst rats following oral administration of aqueous leaves extract of *S. aethiopicum* at doses 2000, 3000, 4000 and 5000 mg/Kg of body weight. This result shows that those doses are non-toxic for rats and that the lethal dose should be greater than 5000mg/Kg/bw. According to Gosselin *et al.* [22] classification, this extract could be classified as non-toxic one.

Sub-acute toxicity

Effect of oral administration of *S. aethiopicum* LINN GILO leaves extract on food intake

The results of the food intake are shown in Table 1

Table 1: Changes of food intake of the rats during the experiment.

Weeks	W_1	W_2	W_3	W_4
Aq 300 female	114.28±8^a	118.85±6.12^b	104.85±6.12^b	103.28±5.61^b
Aq 500 female	113.85±7.562^a	118.42±5.06^b	104.42±5.28^b	103.57±3.77^b
Aq 800 female	112.71 ±6.78^a	92.71±5.6^a	92.71±5.2^a	98.57±3.7^a
FC	113.0±5.02^a	114.14±7.01^b	111.14±3.97^b	115.0±5.0^c
Aq 300 male	129.85±8.99^b	126.14±6.03^a	124.85±2.03^b	123.14±5.72^a
Aq 500 male	112.85 ±6.49^a	125.85±7.47^a	114.71±3.78^a	120.28±7.34^a
Aq 800 male	113.28±6.34^a	124.85±5.4^a	113.0±3.21^a	107.57±7.30^b
MC	130.71±6.28^b	131.28±6.60^b	122.14±5.58^b	116.42±9.88^a

Aq 300mg / kg: aqueous extract at a dose of 300mg / kg; Aq 500mg / kg: aqueous extract at a dose of 500mg / kg; Aq 800mg / kg: aqueous extract at a dose of 800mg / kg; MC and FC: Male and female rats given distilled water. W: week. Values are means ± standard deviation, n = 5. Value in the same column with different letter in superscript are statistically different (p<0. 05)

Table 1 shows that food intake decreased significantly (P<0.05) in females whatever be the dose and in males treated with 800 mg/kg of bw compared to control females and males respectively. Similar results were reported by Celestine *et al.* [23] who showed that in rats, the administration of *S. aethipicum* aqueous leaves extracts at 200 and 400 mg/kg reduced food intake, probably due to the presence of dietary fiber [24].

Effect of oral administration of *S. aethiopicum* leaves extract on body weight

Table 2 shows growth percentage of rats receiving the different treatments.

Table 2: Growth rate as a function of dose

Weeks	W_1	W_2	W_3	W_4
Aq 300 female	25.94±1.78^b	16.9±2.21^b	12.17±2.06^b	8.24±0.36^c
Aq 500 female	19.39±2.02^{ab}	6.16±1.61^a	2.83±0.99^a	3.09±1.59^{ab}
Aq 800 female	13.74±1.72^a	7.59±1.44^a	2.45±1.16^a	1.88±0.98^a
FC	12.86±2.13^a	7.09±2.00^a	3.71±1.15^a	3.76±0.85^b
Aq 300 male	12.63±1.16^a	13.76±0.86^a	8.69±1.53^b	8.67±1.01^b
Aq 500 male	17.00±1.00^a	15.01±1.80^a	6.70±2.06^a	5.81±1.26^{ab}
Aq 800 male	14.03±0.98^a	12.44±1.14^a	5.24±1.30^a	4.37±1.27^a
MC	31.20±1,07^b	12.16±1,19^a	8.56±1,08^b	5.64±1,50^a

Aq 300mg / kg: aqueous extract at a dose of 300mg / kg; Aq 500mg / kg: aqueous extract at a dose of 500mg / kg; Aq 800mg / kg: aqueous extract at a dose of 800mg / kg; MC and FC: Male and female rats given distilled water. W: week. Values are means ± standard deviation, n = 5. Value in the same column with different letter in superscript are statistically different (p<0. 05)

Table 2 shows that growth rate decreased significantly (p<0.05) in females and males treated with 800 mg / kg/bw compared to the other groups and at the fourth week respectively. Celestine *et al.* [23] reported similar results in rats treated with aqueous leaves extract of *S. aethiopicum* at 200 and 400 mg/kg bw. Weight control may be due to the combine action of dietary fiber and polyphenols as mentioned by Ayodele [25].

Effect of oral administration of leave extract of *Solanum aethiopicum* on the relative organs weight.

Table 3 shows the relative weight of the targetted organs of rats treated with the extracts

Table 3: Relative weight of organs

Groups	Liver	Kidneys	Heart	Lungs	Spleen
Aq 300 female	2.86±0.17^a	0.62±0.05^a	0.36±0.01^a	0.75±0.09^a	0.38±0.10^a
Aq 500 female	2.68±0.17^a	0.62±0.04^a	0.35±0.02^a	0.74±0.10^a	0.38±0.10^a
Aq 800 female	2.78±0.22^a	0.62±0.06^a	0.36±0.04^a	0.75±0.11^a	0.39±0.10^a
FC	2.68±0.12^a	0.58±0.04^a	0.34±0.01^a	0.63±0.15^a	0.38±0.10^a
Aq 300 male	2.89±0.64^a	0.56±0.09^a	0.34±0.03^a	0.72±0.18	0.30±0.06^a
Aq 500 male	2.80±0.14^a	0.55±0.05^a	0.34±0.01^a	0.62±0.13^a	0.29±0.03^a
Aq 800 male	2.68±0.19^a	0.52±0.06^a	0.32±0.03^a	0.58±0.10^a	0.28±0.04^a
MC	2.66±0.26^a	0.52±0.04^a	0.32±0.00^a	0.63±0.10^a	0.28±0.03^a

Aq 300mg / kg: aqueous extract at a dose of 300mg / kg; Aq 500mg / kg: aqueous extract at a dose of 500mg / kg; Aq 800mg / kg: aqueous extract at a dose of 800mg / kg; MC and FC: Male and female rats given distilled water. W: week. Values are means ± standard deviation, n = 5. Value in the same column with different letter in superscript are statistically different (p<0. 05)

Relative organ weight does not vary significantly (P>0.05) between the different groups regardless of sex. Similar results were reported by Bonfanti *et al.* [26] in rats treated with *S. guaraniticum* leaves extract. Aqueous extracts of *S. aethiopicum* leave don't induce organomegaly. Relative weight is used to monitor an organ growth compared to the entire organism [27].

Effect of oral administration of *S. aethiopicum* leaves extract on some biochemical parameters.

The lipid profile, blood glucose, proteinemia and some hepato-renal markers are shown in table 4. In males treated with 500 and 800 mg / kg of body weight, total cholesterol, triglycerides and LDL cholesterol decrease significantly (P<0.05) compared to the control group. The same doses in females increase or decrease HDL and LDL cholesterol

compared to the control group respectively. This result confirms the lipid-lowering propriety of aqueous leaves of *S. aethiopicum*. Celestine *et al.* [23] showed that, the administration of *S. aethioipicum* aqueous leaves extract to rats at doses of 200 and 400 mg / kg reduced blood lipid levels. According to Etoundi *et al.* [28], flavonoids, alkaloids, saponins and steroids can lower serum lipid. This could be explain by the fact that, saponins inhibit acetyl-CoA carboxylase which is involved in fatty acid synthesis. In addition, flavonoids stimulate the activity of lecithin cholesterol acyltransferase (LCAT) and 7α-hydrolase, involved in the synthesis of bile acids [29]. Moreover, blood glucose decreased significantly in females treated with the different concentration and in male's receiving 800 mg/kg when compared to the control group. Thus, aqueous leaves extract of *S. aethioipicum* has hypoglycemic property. Similar results were reported by Opeyemi *et al.* [30] in rats treated with methanolic extract from the fruits of the same vegetable. Hypoglycemic effect of the extract may be due to macrophages action and the stimulation of GLUT4 translocation by flavonoids [31].

A decreased activity of transaminases, PAL and γGT was also recorded regardless of gender. Bonfanti *et al.* [26] equally showed a decrease in transaminase activity in rats treated with S. *guaraniticum* leaves extract. Transaminases are synthesized and are released in blood in case of cell damage or trauma. In fact, ALT, PAL and γGT are more linked to liver damage while ASAT is less specific. Decrease in the activity of those enzymes could be explained by a possible hepato-protective effect [32]. Bilirubin is a yellow pigment resulting from the breakdown of hemoglobin. An increase amount of bilirubin in blood or tissue predisposes to yellow fever. A decrease in bilirubin level following the extract administration suggested an action against liver damage and severe hepatitis [33]. Urea, creatinine and protein levels were reduced in rats receiving *S. aethiopicum* aqueous leaves extract, showing a reno-protective action. Increased levels of urea and creatinine are currently observed in kidney failure [34].

Effect of oral administration of *S. aethiopicum* leaves extract on some hematological parameters.

Significant (p<0.05) changes occurred in red blood cells count, hemoglobin, lymphocytes and MID of rats treated with the extract compared to control. These results were not confirmed by those of Mbegbu *et al.* [35]. Hemoglobin is important in the transfer of respiratory gases in the body and in maintaining the acid/base balance [36]. High red blood cell values predict polycythemia. Thus, the aqueous extract of *S. aethiopicum* leaves doesn't induce anemia or polycythemia. Important amount of secondary metabolites, minerals and vitamins found in the extracts could explain this result. On the other hand, minerals and vitamins favor hematopoiesis and erythropoiesis in the bone marrow [37]. Iron is an important part of hemoglobin, myoglobin, and cytochrome. As a cofactor, zinc plays an essential role in hemoglobin synthesis, protects the integrity of erythrocytes and reduces oxidative stress [38]. Substances that affect red blood cells count and associated parameters have effects on bone marrow, kidneys and hemoglobin metabolism [39]. Therefore, treatment with the leaves aqueous extract of *S. aethiopicum* could not have adverse effects on bone marrow, kidneys and hemoglobin. White blood cells are involved in host defense system against bacteria, fungi, viruses and other exogenous substances. An increase number of white blood cells is generally linked to a defense mechanism by the immune system [40]. Our results showed a significant (p<0.05) increase in lymphocytes of rats treated with the extract when compared to the controls. Mbegbu *et al.* [35] showed that the administration of methanoic extracts from the fruits of *S. macrocarpon* to rats at doses of 400, 800 and 1600 mg/kg increased the number of white blood cells. An increased number of lymphocytes is observed in the activation of the defense system, inflammatory or necrosis process [41]. This result show that, the aqueous extract of *S. aethiopicum* leaves has a stimulating effect on the immune system.

Table 4: Changes in some biochemical parameters

Biochimical parameters	Female				Male			
	AQ300	AQ500	AQ800	CN	AQ300	AQ500	AQ800	CN
TC (mg/dL)	133.96±25.27^{a}	120.74±22.95^{a}	109.18±23.33^{a}	154.87±22.18^{a}	177.59±10.77^{bc}	155.69±10.07^{b}	113.55±11.06^{a}	185.19±10.16^{c}
TG (mg/dL)	75.76±4.41^{a}	73.25±2.75^{a}	70.24±4.31^{a}	73.22±4.09^{a}	90.15±6.07^{a}	93.42±7.32^{a}	87.59±5.00^{a}	100.86±5.11^{b}
HDL (mg/dL)	72.53±5.73^{ab}	74.23±6.48^{b}	85.50±9.47^{b}	70.62±6.19^{a}	72.16±8.04^{a}	76.07±6.51^{a}	67.81±6.06^{a}	72.02±8.66^{a}
LDL (mg/dL)	61.42±4.89^{a}	47.54±4.17^{c}	33.03±4.46^{b}	69.61±3.91^{a}	105.43±9.50^{c}	79.61±10.14^{b}	22.79±10.04^{a}	112.02±8.67^{c}
Glucose (mg/dL)	82.94±4.64^{a}	79.74±6.22^{a}	74.23±4.16^{a}	112.57±4.68^{b}	94.61±6.97^{ab}	89.77±7.18^{ab}	75.77±6.63^{a}	100.57±6.82^{b}
PT (g/dL)	8.40±0.87^{a}	7.55±1.02^{a}	7.59±0.64^{a}	7.59±1.10^{a}	8.14±0.87^{a}	8.10±1.03^{a}	7.74±0.47^{a}	7.85±2.09^{a}
ASAT (UI/L)	8.72±0.91^{b}	6.69±0.82^{a}	7.97±0.53^{b}	11.85±0.66^{c}	7.83±0.52^{ab}	9.09±1.34^{b}	8.59±0.66^{b}	7.12±0.58^{a}
ALAT (UI/L)	6.25±1.26^{a}	5.20±1.51^{a}	6.54±1.52^{a}	14.60±1.27^{b}	14.02±5.93^{a}	14.69±6.02^{a}	14.88±6.70^{a}	15.35±7.21^{a}
PAL (UI/L)	12.21±1.85^{a}	12.10±2.31^{a}	12.18±1.31^{a}	12.26±2.54^{a}	10.55±1.30^{a}	10.38±0.82^{a}	10.66±1.01^{a}	10.63±0.95^{a}
γGT (UI/L)	4.54±0.74^{a}	3.76±1.22^{a}	4.05±1.35^{a}	4.92±1.27^{a}	7.11±1.31^{a}	6.75±2.37^{a}	5.98±2.19^{a}	7.23±2.44^{a}
TB (g/dL)	1.48±0.52^{a}	1.39±0.55^{a}	1.23±0.27^{a}	1.49±0.64^{a}	1.26±0.33^{a}	1.03±0.38^{a}	1.15±0.30^{a}	1.47±0.11^{a}
DB (g/dL)	0.78±0.67^{a}	0.52±0.50^{a}	0.61±0.37^{a}	0.84±0.56^{a}	0.85±0.59^{a}	0.74±0.37^{a}	0.78±0.19^{a}	0.78±0.54^{a}
Creatinine (mg/dL)	0.68±0.10^{a}	0.83±0.10^{a}	0.83±0.09^{a}	0.87±0.20^{a}	0.84±0.10^{a}	0.73±0.10^{a}	0.76±0.07^{a}	0.86±0.11^{a}
Urea (mg/dL)	15.15±0.99^{a}	15.47±0.72^{a}	15.15±0.89^{a}	16.02±0.95^{a}	14.38±1.91^{a}	15.99±3.21^{a}	15.50±2.56^{a}	17.63±3.00^{a}
Proteinuria (mg/dL)	10.44±0.84^{a}	10.94±1.64^{a}	10.20±0.82^{a}	13.89±1.18^{b}	15.76±0.76^{a}	16.67±0.70^{ab}	16.11±0.54^{ab}	17.08±0.57^{b}
Creatininuria (mg/dl)	0.85±0.45^{a}	0.97±0.20^{a}	0.77±0.29^{a}	1.01±0.39^{a}	0.95±0.06^{a}	1.12±0.16^{a}	0.98±0.09^{a}	0.97±0.13^{a}

Aq 300mg / kg: aqueous extract at a dose of 300mg / kg; Aq 500mg / kg: aqueous extract at a dose of 500mg / kg; Aq 800mg / kg: aqueous extract at a dose of 800mg / kg; CN: Male and female rats given distilled water. S: week. TC: total cholesterol; TG: triglycerides; HDL: high density lipoprotein; LDL: low density lipoprotein. ASAT: aspartate aminotransferase; ALAT: alanine aminotransferase; PAL: alkaline phosphatase; γGT: Gamma glutamyl transferase; TB: total bilirubin; DB: direct bilirubin; PT: total proteins; Values are means ± standard deviation, n = 5. The values in the same line with the different letter at superscript are significant (p<0.05).

The oral administration of aqueous leave extracts of *S. aethiopicum* to male and female rats didn't induce any significant change in red blood cell indices (CCMH, TCMH, VGM and MCV). Similar results were obtained by Sodipo *et*

al. [42] in rats treated with the aqueous extract of *Solanum macrocarpon* leaves. This result shows that incorporation of hemoglobin into the red blood cells has not modify their morphology nor their osmotic fragility. The increased MCV is probably related to macrocytic anemia [37].

Effect of oral administration of *S. aethiopicum* leaves extract on some markers of serum and tissue oxidative stress.

Oxidative stress decreased significantly (P<0.05) in rats treated with the aqueous extract of *S. aethiopicum* leaves at doses of 300, 500 and 800 mg/kg in both male and female at serum and tissue levels compared to the control group. Treatment with the different doses increases the activity of catalase and superoxide dismutase as well as amount of thiol groups in serum and tissue, showing the antioxidant properties of the extract. Bonfanti *et al.* [26] reported different results in rats treated with *S. guaraniticum* leaves exact at a doses of 1250, 2500 and 5000 mg/kg. The difference could be due to difference in dose or depends on the specie [43]. The hepato-reno-cardioprotective properties could be explained by the occurrence of secondary metabolites such as polyphenols and flavonoids. Bonfanti *et al.* [44] showed that supplementation by antioxidant significantly decreases serum malondialdehyde levels and restore antioxidant mechanisms to their normal level in the liver and other organs. Polyphenols and especially flavonoids inhibit and trap lipid peroxidation and free radicals respectively [45].

Table 5: Variations of some haematological parameters

Parameters	RBC (mm^3)	Hb (g/dl)	Ht (%)	LEU (mm^3)	VGM (μm^3)	TCMH (Pg)	CCMH (g/dl)	PLAQ (mm^3)	LYM (µl)	MID (µl)	GRAM (µl)
Aq 300fem	3.62±1.70^{ab}	15.0±1.63^{ab}	51.91±4.41^{a}	4.375±1.79^{a}	89.25±3.40^{a}	32.25±2.06^{a}	33.5±1.0^{a}	333.75±52.54^{a}	0.5±0.08^{ab}	0.42±0.18^{ab}	4.5±2.05^{a}
Aq 500 fem	4.53±1.29^{ab}	15.75±1.25^{ab}	48.36±4.83^{a}	4.75±0.95^{a}	88.75±8.65^{a}	30.0±0.81^{a}	32.25±1.25^{a}	392.25±50.83^{a}	0.47±0.17^{ab}	0.45±0.17^{ab}	4.7±2.38^{a}
Aq 800 fem	5.53±1.29^{b}	16.75±1.25^{b}	51.23±4.95^{a}	6.0±1.41^{a}	93.75±7.67^{a}	32.0±0.816^{a}	34.25±0.95^{a}	401.0±52.70^{a}	0.65±0.23^{b}	0.6±0.18^{b}	5.22±2.32^{a}
FC	2.53±1.73^{a}	14.0±1.15^{a}	49.86±4.50^{a}	4.25±2.21^{a}	88.75±2.98^{a}	30.25±2.06^{a}	33.75±1.5^{a}	322.0±46.44^{a}	0.3±0.08^{a}	0.3±0.14^{a}	3.45±1.89^{a}
Aq 300 male	4.53±0.57^{a}	4.5±1.91^{a}	15.25±0.5^{ab}	52.27±0.18^{a}	89.0±5.47^{a}	29.75±2.21^{a}	34.0±1.41^{a}	306.0±26.05^{a}	0.55±0.17^{a}	0.42±0.12^{a}	4.25±1.36^{a}
Aq 500 male	4.53±0.57^{a}	4.75±2.21^{a}	15.75±0.95^{ab}	51.86±2.51^{a}	90.25±7.88^{a}	29.75±2.21^{a}	33.75±3.5^{a}	310.5±34.37^{a}	0.55±0.20^{a}	0.47±0.23^{a}	3.45±1.25^{a}
Aq 800 male	4.78±0.5^{a}	5.25±1.5^{a}	16.12±0.85^{b}	52.36±2.82^{a}	91.75±6.18^{a}	30.5±1.29^{a}	34.75±3.40^{a}	313.75±29.83^{a}	0.6±0.14^{a}	0.52±0.20^{a}	3.95±0.95^{a}
MC	4.53±0.5^{a}	4.25±1.92^{a}	14.5±1.11^{a}	52.11±0.43^{a}	89.0±4.74^{a}	29.75±1.92^{a}	33.25±1.29^{a}	303.5±30.06^{a}	0.55±0.15^{a}	0.37±0.14^{a}	4.2±1.22^{a}

Aq 300 fem / kg: aqueous extract at a dose of 300mg/kg for female; Aq 800mg / kg: aqueous extract at a dose of 800mg/ kg for female; FC and MC: female and male rats given distilled water. RBC: red blood cells. Hb: hemoglobin; Ht: hematocrit; LEU: leukocytes; VGM: mean globular volume; TCMH: mean corpuscular hemoglobin content; CCMH: mean corpuscular hemoglobin concentration; PLA: platelets; LYM: lymphocytes; MID: GRAM: Values are means ± standard deviation, n = 5. Values in the same column with different letter at superscript are significant (p<0.05) different.

Table 6: Changes in oxidative stress parameters in organs

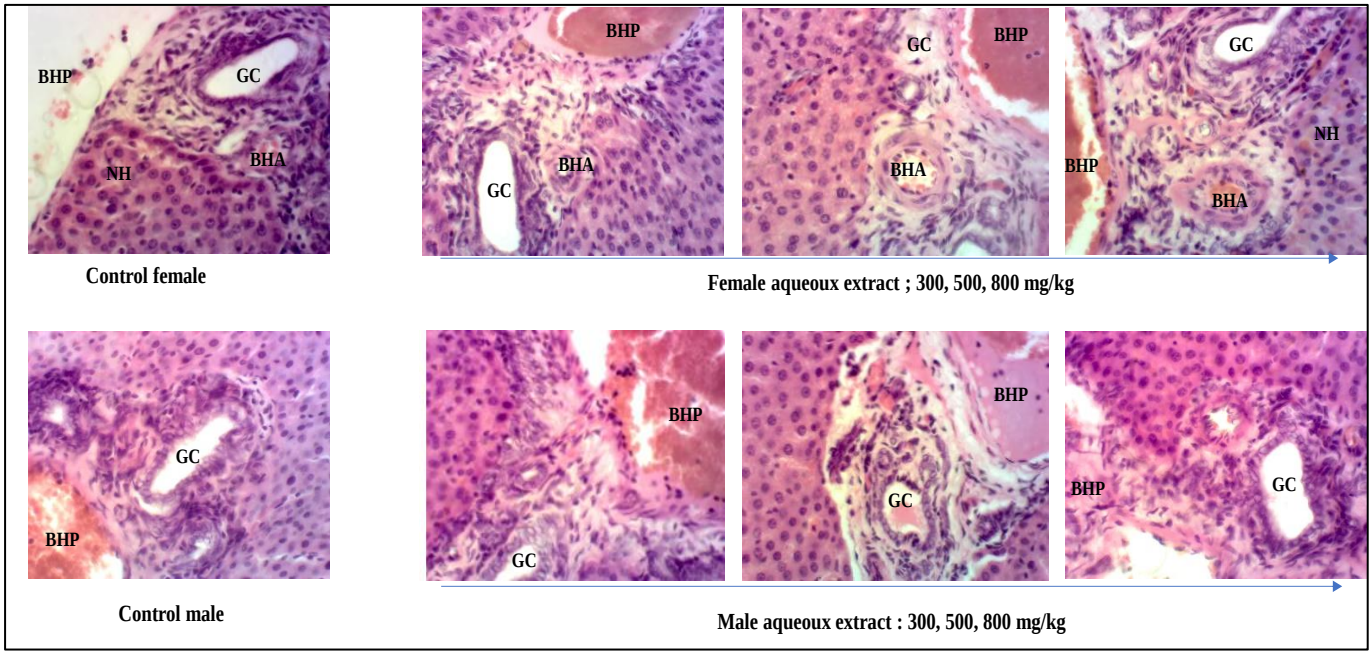
		Female				Male			
	Parameters	**AQ300**	**AQ500**	**AQ800**	**CN**	**AQ300**	**AQ500**	**AQ800**	**CN**
Serum	TBARS (nM MDA/mg protein)	0.41±0.36^{b}	0.22±0.15^{a}	0.10±0.25^{a}	0.88±0.22^{c}	0.11±0.04^{a}	0.07±0.01^{a}	0.07±0.02^{a}	1.44±0.16^{b}
	CAT (nM of H_2O_2/min/mg protein)	47.47±4.69^{a}	93.70±4.95^{b}	97.38±6.29^{b}	42.03±4.26^{a}	41.33±4.12^{ab}	82.73±3.62^{ab}	86.98±1.01^{b}	39.01±4.20^{a}
	SOD (Unit/mg protein)	201.85±7.01^{ab}	231.61±5.29^{b}	237.94±6.01^{b}	188.31±5.35^{a}	202.95±4.19^{a}	205.52±5.09^{a}	223.41±4.17^{a}	182.57±7.29^{a}
	GSH (µM/mg protein)	1.36±0.19^{a}	1.91±0.26^{b}	2.30±0.22^{b}	1.19±0.21^{a}	2.88±1.38^{a}	3.48±1.84^{a}	4.66±1.79^{a}	2.96±1.09^{a}
Liver	TBARS (nM MDA/mg protein)	1.95±0.85^{a}	2.27±0.62^{a}	1.95±0.85^{a}	3.23±1.04^{a}	5.56±2.60^{a}	5.45±1.6^{a}	5.26±1.45^{a}	6.11±0.84^{a}
	CAT (nM of H_2O_2/min/mg protein)	251.19±4.25^{a}	309.91±3.26^{a}	325.27±5.04^{a}	242.11±2.70^{a}	338.64±4.31^{a}	487.07±2.58^{a}	488.10±3.64^{a}	330.25±3.24^{a}
	SOD (Unité/mg protein)	1546.68±2.67^{a}	1676.7±3.42^{a}	1691.72±1.16^{a}	1356.9±3.24^{a}	1678.97±2.96^{b}	1798.55±2.57^{bc}	1847.61±1.06^{c}	1329.29±3.42^{a}
	GSH (µM/mg protein)	2.26±2.27^{b}	2.88±1.92^{bc}	5.18±1.62^{c}	1.15±1.38^{a}	3.27±1.49^{a}	3.62±1.16^{a}	3.91±2.02^{a}	2.70±1.51^{a}
Heart	TBARS (nM MDA/mg protein)	9.76±2.18^{a}	8.85±1.24^{a}	5.93±3.02^{a}	11.61±2.23^{a}	3.48±0.55^{ab}	4.00±1.49^{bc}	2.30±0.78^{a}	5.16±0.83^{c}
	CAT (nM of H_2O_2/min/mg protein)	2223.78±9.59^{a}	3107.17±9.13^{b}	3274.68±7.66^{b}	1991.28±8.04^{a}	2556.87±7.32^{a}	2239.91±7.07^{a}	2474.93±8.32^{a}	2294.9±6.70^{a}
	SOD	3490.26±8.83^{a}	3693.39±8.13^{a}	3896.35±7.50^{b}	2891.04±7.56^{a}	3159.56±7.48^{a}	2477.37±9.64^{a}	2653.58±8.70^{a}	2179.23±7.83^{a}

	(Unité/mg protein)	b	b						
	GSH (µM/mg protein)	43.70±5.30^{ab}	60.49±5.06^{bc}	75.10±5.35^{c}	33.73±4.79^{a}	55.60±9.33^{b}	41.84±10.60^{ab}	55.46±10.29^{b}	33.00±10.46^{a}
Kidneys	TBARS (nM MDA/mg protein)	3.46±0.77^{ab}	3.38±0.89^{ab}	2.53±0.95^{a}	4.33±0.29^{b}	4.95±0.53^{a}	4.74±0.57^{a}	4.18±0.90^{a}	4.84±0.43^{a}
	CAT (nM of H_2O_2/min/mg protein)	1266.68±14.01 b	1657.8±13.77^{a}	1938.61±17.86 a	1379.77±15.52 b	1277.21±22.97 b	3016.86±19.06 a	3282.49±22.21 a	1335.32±18.25 b
	SOD (Unité/mg protein)	1772.99±12.23 b	1861.54±16.60 b	1949.81±15.80 b	1041.42±13.82 a	1177.48±14.61 a	1173.51±17.07 a	1295.23±16.51 a	895.17±14.68^{b}
	GSH (µM/mg protein)	46.55±10.48^{a}	53.43±8.95^{a}	63.15±9.98^{b}	50.28±11.66^{a}	67.32±8.33^{a}	77.46±11.30^{ab}	86.56±10.35^{b}	71.47±11.85^{ab}
	TBARS (nM MDA/mg protein)	3.26±0.39^{a}	3.01±0.36^{a}	2.85±0.20^{a}	4.26±0.36^{b}	3.07±1.19^{ab}	2.63±0.53^{ab}	2.40±0.69^{a}	3.93±1.04^{b}
Lungs	CAT (nM of H_2O_2/min/mg protein)	705.65±24.13^{a}	1794.34±29.21 b	2050.2±13.35^{b}	685.24±22.16^{a}	3198.93±28.79 a	2024.15±34.43 a	3529.7±20.63^{a}	2025.34±29.39 a
	SOD (Unité/mg protein)	1780.85±7.29^{a}	1811.14±7.47^{a}	2026.32±7.26^{a}	1951.82±5.77^{a}	2252.07±7.33^{a}	2284.81±7.80^{a}	2592.78±7.15^{a}	2188.31±5.06^{a}
	GSH (µM/mg protein)	0.89±0.57^{a}	1.40±0.32^{ab}	2.92±0.53^{c}	2.02±0.40^{b}	4.02±1.71^{a}	4.43±1.92^{a}	5.14±1.88^{a}	4.29±2.00^{a}

AQ300: aqueous extract at a dose of 300 mg / kg; AQ500: aqueous extract at a dose of 500 mg / kg; AQ800: aqueous extract at a dose of 800 mg / kg; MC and FC: TBARS: substances reactive with thiobarbituric acid. MDA: malondialdehyde. GSH: thiol group. SOD: superoxide dismutase. CAT: catalase. CN: negative control; Values are means ± standard deviation, n = 5. Values in the same line with different letter at superscript are significant (p<0.05) different.

Effect of oral administration the leaves extract of *Solanum aethiopicum* on the micrographs of selected target organs.

Liver



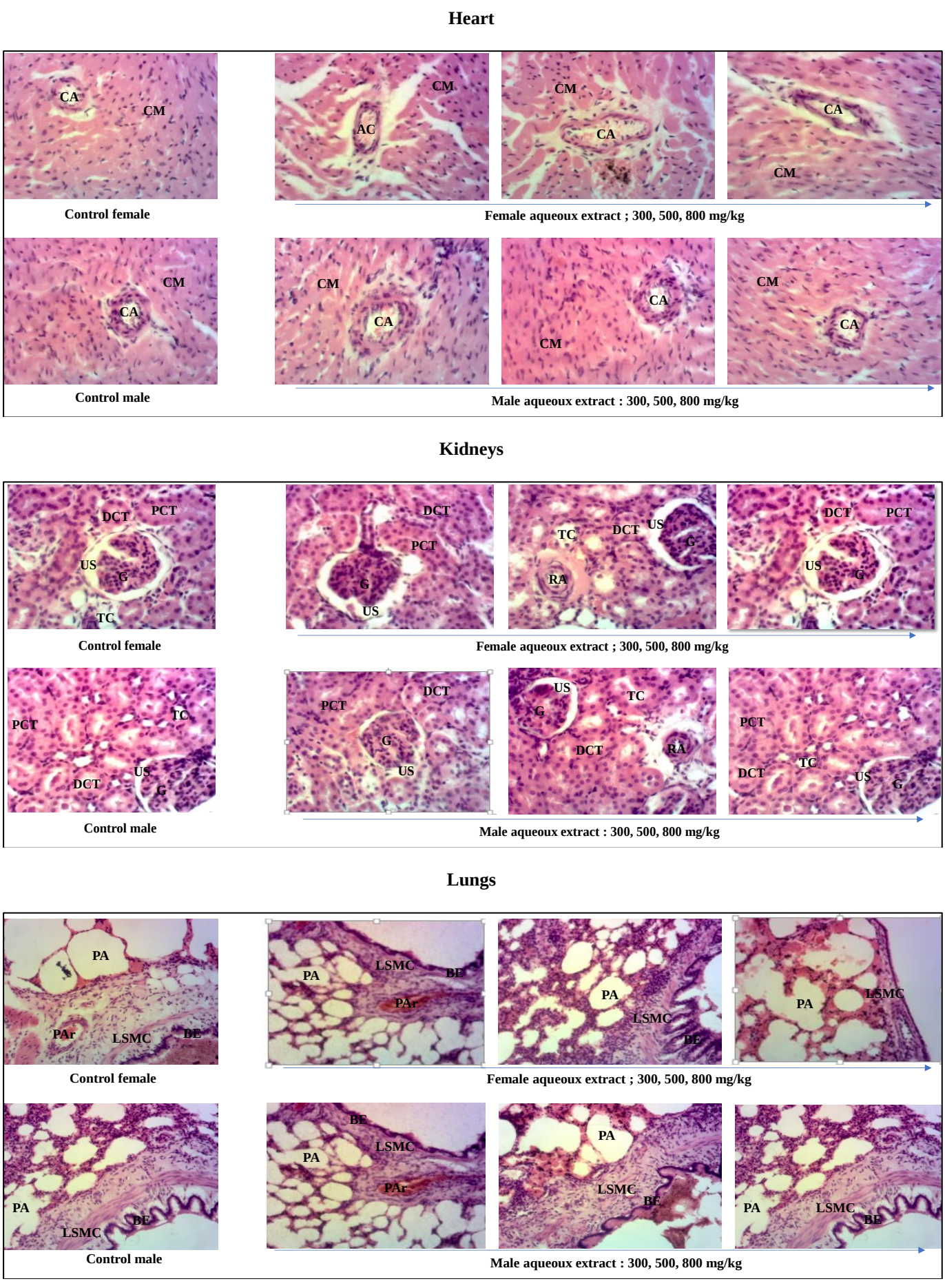


Fig 1: Photomicrographs of the liver, heart, kidney and lung of male and female rats.
BHP: Branch of the hepatic portal vein; HN: Hepatocyte nucleus; BHA: Branch of the hepatic artery; GC: Gallic canaliculus; CM: cardiac myocyte; CA. Cardiac artery DCT: Distal convoluted tubule; PCT: Proximal convoluted tubule; US: Urinary space; G: Glomerulus; RA: Renal artery; TC: Tubular clarification; PA: Pulmonary alveolus; PAr: Pulmonary arteriole; LSMC: Layer of smooth muscle cells; BE: Bronchial Epithelium; Magnification 200x.

Treatment with the aqueous extract of *S. aethiopicum* leaves at doses of 300, 500 and 800mg / kg/ bw cause no tissue disorders in the organs studied. This result shows an hepato-reno-cardioprotective properties of leaves extracts of *S. aethiopicum* aqueous. Different results were obtained by Parasuraman *et al.* [46] who found that administration of ethanolic extract of *Solanum trilobatum* leaves at the doses of 200 and 400 mg/kg to rats caused tissue disorders in the kidneys, lungs and liver. Plant species and occurence of phytochemicals could explain this difference [41].

Conclusion

The purpose of this study was to evaluate the acute and sub-acute toxicity of *Solanum aethiopicum* LINN GILO aqueous leave extract in rats. The lethal dose was greater than 5000 mg/kg/bw. The aqueous extract at doses of 300, 500 and 800 mg/kg/ bw reduced blood lipids, sugar and proteinuria. It increases red blood cells, hemoglobin, leukocytes, lymphocytes, protects the liver, heart, kidneys and lungs from tissue damage and oxidative stress. *Solanum aethiopicum* LINN GILO leaves extract at doses of 300, 500 and 800 mg/kg/bw is non-toxic and could be used in treatments of various diseases.

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