EVALUATION OF ACUTE AND SUB ACUTE TOXICITY OF STEM BARK AQUEOUS EXTRACT OF ANTHOCLEISTA SCHWEINFURTHII (LOGANIACEAE)

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ABSTRACT

Anthocleista schweinfurthii is a plant of the Loganiacea family. Many studies performed on it, related that the plant presents a wide variety of therapeutic effects, specially, cytoprotective effects on gastric mucosa, milky stimulator and anti-malarial virtues. This study aimed to evaluate the toxic profile of the aqueous extract obtained from the bark of this plant. Acute toxicity using a single dose of 2000 mg/kg was administered to mice and effects were observed for 14 days. The sub-acute toxicity of the aqueous extract at doses 250 mg/kg, 500 mg/kg and 1000 mg/kg, was also studied on male and female rats for 28 days. The control group, constituted of healthy rats, received the same amount of distilled water. At the end of the treatment, physical, haematological, biochemical and histological parameters were evaluated. The results obtained show no death and no significant variation (p>0.05) in the behavioral and morphological parameters. Similarly, the sub acute test shows no significant variation, at all doses, in the evaluated parameters. In conclusion, the aqueous extract of the A. schweinfurthii can be classified in the category of non-toxic substances since its 50 % lethal dose (LD₅₀) is superior to 2000 mg/kg.
KEYWORDS: toxicity, *Anthocleista schweinfurthii*, aqueous extract, Loganiaceae.

**INTRODUCTION**

*Anthocleista schweinfurthii* is the plant belonging to the Family Loganiaceae. [1] The genus *Anthocleista* includes 14 species and occurs in tropical Africa, Comoros and Madagascar. It occurs on moist soils in secondary forests, forest-galleries, thickets and sometimes swampy areas or rain forests, 400 - 1800 m. [1,2,3] Known as "bopolopolo" language Douala in Cameroon [4], "Abanga'a " in languages *Tumu Fang* (Cameroon, Gabon, Equatorial Guinea). *Anthocleista schweinfurthii* is used in Gabon by bapunus peoples to improve lactation in new mothers. The stem bark decoction is used in the treatment of hernia and female infertility in Congo. [3,5] In Cameroon, bark decoction is used to treat stomach aches. The decoction of the roots is used to treat ovarian problems, venereal disease, bronchitis and fever. It is taken as a purgative to trigger delivery. In Tanzania, the decoction of the roots is used in treatment against malaria, abscesses and as an anthelmintic. The young leaf juice, powdered root or bark pulp are used to facilitate wound healing. [2] Women suffering from vaginal prolapse using the decoction of leaves bath. While the twig bark decoction and leaves can be eaten as a febrifuge. [6] It has been proved that the aqueous extract of the root bark of *Anthocleista schweinfurthii* contain a substance responsible for vasoconstriction and increases the contractions of the cardiac muscle fibers. [7] However, the toxicity of *Anthocleista schweinfurthii* has not been intensively studied in order to ascertain the limits of it application. The aim of this study was to investigate the acute and sub acute toxicity effects of the aqueous stem barks extract of this plant.

**MATERIALS AND METHODS**

**Plant material**

*Anthocleistha schweinfurthii* was harvested in July 2013 in South Cameroon region, Ambam subdivision (Mefoup). Botanical identification was done in the National Herbarium, Yaoundé, by Jean Michel Onana, by comparing with existing herbarium specimen No. 53944 / NHC. The barks were dried at room temperature in the laboratory, away from sunlight, and were then ground in a bark powder moulin.700g was introduced in 5 liters of distilled water and boil for 30 minutes. After cooling, the solution was filtered using a Whatman paper n° 3. The filtrate obtained was dried in a convection oven at a temperature of 50 ° C for 2 days. The powder obtained (50 g) was used for toxicity tests.
Experimental animals
Male and female Swiss mice weighing 20 ± 2 g were used for acute toxicity and young Wistar rats weighing 76 -100 g for sub acute toxicity. These animals were raised in the Animal house of the Higher Teachers’ Training College, University of Yaoundé I. They were fed a standard laboratory diet (NAAPCAM Sarl, Yaoundé, Cameroon) and given fresh water ad libitum. Before the experiments (acute toxicity), they were starved for 12 h in wire mesh bottom cages to prevent coprophagy but allowed free access to water. Prior authorization for the use of Laboratory Animals was obtained from the Cameroon National Ethics Committee (Reg. N° FWAIRB00001954). The use, handling and care of animals were done in adherence to the European Convention (Strasbourg, 18.III.1986) for the protection of vertebrate animals used for experimental and other purposes (ETS-123), with particular attention to Part III, articles 7, 8 and 9.

Acute toxicity
The acute toxicity was performed according to the sequential method of OECD (Organization for Economic Co-operation and Development). Using a stomach tube, the A. s. extract was administered to three female mice (20 – 23g) with a single dose (2000 mg / kg). The control group received vehicle. The same method and the same dose was repeated 48 hours later, on 3 additional animals. Thereafter, all animals were observed carefully for 14 days during which mortality, body weights and gross behavioral change were noted daily. [8]

Sub acute toxicity
Young Wistar rats (76-100 g) in six groups of 12 animals (6 males and 6 females) for each dose level of Anthocleista schweinfurthii were used in these tests. Sub acute toxicity was evaluated after single daily administration of extract at 250, 500 and 1000 mg / kg orally for a period of 4 weeks. The satellite group was also treated with the extract of A. schweinfurthii (1000 mg/kg) for 4 weeks but these animals were sacrificed 2 weeks after stopping treatment. The satellite control and control groups received vehicle, control and satellite were sacrificed 2 weeks after treatment. All rats were maintained under identical conditions with food and water ad libitum for the entire period with close observation. Toxicity was evaluated in terms of corporal and organ weights, gross behavior, gross and histological appearance of vital organs (heart, kidney, liver, stomach, spleen, lungs, ovary, testicle and adrenal gland). The plasma from EDTA blood prepared was carefully collected for blood chemistry and enzyme analysis (total protein, AST, ALT, creatinine, bilirubin, urea, total cholesterols, triglycerides)
using Commercial kits (Fortress) and glycaemia using a glucometer (Accurends, Roche Diagnostics GmbH, D-68298, Mannheim, Germany). The Haematological parameters (white blood cell count, red blood cell count, platelet count, hemoglobin, haematocrit, lymphocytes, monocytes and granulocytes) were evaluated using a Coulter counter.[8, 9, 10]

**Statistical analysis**

The results were reported as mean ± SEM. The statistical significance was determined by using one way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparison tests. P values less than 0.05 were considered as significant.

**RESULTS**

**Acute toxicity**

Administration of a single dose of aqueous extract of *Anthocleista schweinfurthii* (2000 mg/kg) in mice did not result in any deaths in the first stage. 48 hours later, carrying out a second test did not result in any deaths. After 14 days of observation, no changes were observed in mice regarding: coat color, appearance, saddles, reflexes, alertness, heart rate, respiratory rate, sensitivity to noise and sensitivity to touch. The aqueous extract is *Anthocleista schweinfurthii* categorized 5 which includes substances with LD$_{50}$ is greater than 2000 mg/kg according to OECD guideline 423, 2001.

**Sub acute toxicity**

The extract of *Anthocleista schweinfurthii* (250 mg/kg, 500 mg/kg and 1000 mg/kg) administered daily to rats caused no adverse effects in animals treated for 28 days of administration. The body weight of rats treated with the extract showed no significant change compared to group control. The relative weight of vital organs showed no dose-dependent variation for all doses of extract compared to the group control. However, a significant decrease in stomach weight was observed in rats of the satellite group. The relative weight of the right kidney and liver were significantly decreased in satellite lots and control satellite (Table 1).
Table 1: Effect of the stem bark aqueous extract of *Anthocleista schweinfurtii* on rat organ weights (values expressed as the percentage of organ weight over the body weight)

<table>
<thead>
<tr>
<th>Organs</th>
<th>Control</th>
<th>A.s. 250mg/kg</th>
<th>A.s. 500mg/kg</th>
<th>A.s. 1000mg/kg</th>
<th>Satellite</th>
<th>Sat. C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>4.07±0.18</td>
<td>3.74±0.09</td>
<td>3.77±0.12</td>
<td>3.84±0.11</td>
<td>3.48±0.13*</td>
<td>3.42±0.05**</td>
</tr>
<tr>
<td>Right kidney</td>
<td>0.44±0.02</td>
<td>0.42±0.01</td>
<td>0.41±0.01</td>
<td>0.41±0.01</td>
<td>0.35±0.01**</td>
<td>0.37±0.01**</td>
</tr>
<tr>
<td>Left kidney</td>
<td>0.41±0.02</td>
<td>0.42±0.01</td>
<td>0.39±0.01</td>
<td>0.38±0.01</td>
<td>0.42±0.03</td>
<td>0.36±0.01</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.08±0.06</td>
<td>0.99±0.02</td>
<td>1.03±0.04</td>
<td>1.05±0.03</td>
<td>0.86±0.03**</td>
<td>0.95±0.02</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.87±0.03</td>
<td>0.78±0.06</td>
<td>0.71±0.03*</td>
<td>0.74±0.02</td>
<td>0.65±0.02</td>
<td>0.72±0.03</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.39±0.03</td>
<td>0.41±0.01</td>
<td>0.36±0.02</td>
<td>0.39±0.02</td>
<td>0.37±0.01</td>
<td>0.37±0.02</td>
</tr>
<tr>
<td>Heart</td>
<td>0.39±0.01</td>
<td>0.37±0.01</td>
<td>0.35±0.01</td>
<td>0.36±0.01</td>
<td>0.32±0.01**</td>
<td>0.35±0.01</td>
</tr>
<tr>
<td>Right a. g.</td>
<td>0.01±0.00</td>
<td>0.02±0.00</td>
<td>0.03±0.01</td>
<td>0.02±0.00</td>
<td>0.02±0.00</td>
<td>0.02±0.00</td>
</tr>
<tr>
<td>Left a. g.</td>
<td>0.02±0.00</td>
<td>0.02±0.00</td>
<td>0.03±0.01</td>
<td>0.02±0.00</td>
<td>0.02±0.00</td>
<td>0.02±0.00</td>
</tr>
<tr>
<td>Right testicle</td>
<td>0.66±0.03</td>
<td>0.71±0.05</td>
<td>0.74±0.02</td>
<td>0.65±0.03</td>
<td>0.66±0.03</td>
<td>0.71±0.03</td>
</tr>
<tr>
<td>Left testicle</td>
<td>0.67±0.04</td>
<td>0.71±0.05</td>
<td>0.84±0.02</td>
<td>0.72±0.01</td>
<td>0.67±0.03</td>
<td>0.75±0.01</td>
</tr>
<tr>
<td>Right ovary</td>
<td>0.04±0.00</td>
<td>0.03±0.00</td>
<td>0.03±0.00</td>
<td>0.03±0.00</td>
<td>0.03±0.00</td>
<td>0.04±0.00</td>
</tr>
<tr>
<td>Left ovary</td>
<td>0.04±0.00</td>
<td>0.03±0.00</td>
<td>0.04±0.00</td>
<td>0.03±0.00</td>
<td>0.03±0.00</td>
<td>0.04±0.00</td>
</tr>
</tbody>
</table>

Sat. C: Satellite control; a.g: adrenal gland; * Significantly different from control, p<0.05; ** Significantly different from control, p<0.01

Table 2 shows that *Anthocleista schweinfurthii* extract, at all doses, did not significantly alters the rate of blood cells. However, platelets decreased significantly in all rats treated with the extract, the decrease was very significant in animals of the satellite group.

Table 2: Effect of the stem bark aqueous extract of *Anthocleista schweinfurthii* on hematological parameters in rat.

<table>
<thead>
<tr>
<th>Type of cell</th>
<th>Control</th>
<th>A.s. 250mg/kg</th>
<th>A.s. 500mg/kg</th>
<th>A.s. 1000mg/kg</th>
<th>Satellite</th>
<th>C.Sat.</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC(10^6/mm³)</td>
<td>6.00±0.18</td>
<td>5.96±0.043</td>
<td>6.38±0.044</td>
<td>5.68±0.57</td>
<td>5.32±0.42</td>
<td>6.71±0.55</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>35.13±1.62</td>
<td>34.14±2.06</td>
<td>38.07±1.08</td>
<td>34.61±2.33</td>
<td>34.29±2.21</td>
<td>35.06±1.90</td>
</tr>
<tr>
<td>Haemoglobin(g/dl)</td>
<td>12.39±0.47</td>
<td>13.24±0.90</td>
<td>13.15±0.74</td>
<td>11.60±1.67</td>
<td>12.01±1.53</td>
<td>10.43±1.61</td>
</tr>
<tr>
<td>Platelet(10^3/mm³)</td>
<td>484.50±17.67</td>
<td>382.40±26.43*</td>
<td>384.40±27.12*</td>
<td>354.40±22.80**</td>
<td>273.30±24.47***</td>
<td>410.50±23.23</td>
</tr>
<tr>
<td>WBC(10^3/mm³)</td>
<td>8.04±0.84</td>
<td>7.72±0.68</td>
<td>8.44±0.94</td>
<td>6.79±1.31</td>
<td>6.28±1.68</td>
<td>6.01±1.24</td>
</tr>
<tr>
<td>Lymphocyte(%)</td>
<td>86.13±1.75</td>
<td>87.33±1.83</td>
<td>87.53±1.13</td>
<td>88.41±2.16</td>
<td>86.03±2.28</td>
<td>87.51±2.03</td>
</tr>
<tr>
<td>Monocyte(%)</td>
<td>8.83±0.64</td>
<td>9.13±0.95</td>
<td>9.54±0.94</td>
<td>8.68±1.15</td>
<td>7.22±0.99</td>
<td>7.97±1.27</td>
</tr>
<tr>
<td>Granulocyte (%)</td>
<td>2.47±0.26</td>
<td>2.84±0.29</td>
<td>2.27±0.30</td>
<td>1.72±0.33</td>
<td>2.45±0.33</td>
<td>2.34±0.29</td>
</tr>
</tbody>
</table>

RBC: red blood cell; WBC: white blood cell; Sat. C: Satellite control; * Significantly different from control, p<0.05; ** Significantly different from control, p<0.01

Biochemical parameters such as blood glucose, alanine aminotransferase (ALT), cholesterol, creatinine and bilirubin showed no significant change in the rats treated with the extract. Urea significantly decreased in animals treated with extract at dose 250 mg/kg, aspartate
aminotransferase (AST) showed a significantly higher activity in rats treated with the extract at 500 mg/kg. The extract at a dose of 1000 mg/kg caused a significant increase in plasma proteins, but this rate of plasma proteins is back to normal two weeks after stopping treatment (satellite group). The plasma triglyceride levels significantly increased in rats treated with the extract at a dose of 1000 mg/kg, the plasma levels of triglycerides persisted two weeks after stopping treatment (satellite group) (Table 3).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>A.s. 250mg/kg</th>
<th>A.s. 500mg/kg</th>
<th>A.s. 1000mg/kg</th>
<th>Satellite</th>
<th>Sat.C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycaemia (mg/dl)</td>
<td>87.40±3.02</td>
<td>84.40±2.20</td>
<td>83.20±2.92</td>
<td>83.40±4.45</td>
<td>95.60±2.51</td>
<td>94.40±3.19</td>
</tr>
<tr>
<td>AST (UI/l)</td>
<td>197.66 ±7.55</td>
<td>206.95±7.80</td>
<td>230.31±6.41*</td>
<td>222.94±8.08</td>
<td>202.11±8.47</td>
<td>215.53±2.08</td>
</tr>
<tr>
<td>ALT (UI/l)</td>
<td>52.90±2.85</td>
<td>48.62±1.16</td>
<td>53.94±4.63</td>
<td>61.98±3.86</td>
<td>65.46±5.80</td>
<td>55.52±4.83</td>
</tr>
<tr>
<td>Total protein (mg/dl)</td>
<td>161.11±12.97</td>
<td>135.71±8.46</td>
<td>169.87±26.19</td>
<td>246.59±20.02**</td>
<td>173.88±13.86</td>
<td>178.39±4.19</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>115.19±6.43</td>
<td>91.36±6.48</td>
<td>101.86±9.64</td>
<td>159.67±12.42**</td>
<td>180.72±11.97**</td>
<td>120.84±11.05</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>2.09±0.36</td>
<td>1.97±0.42</td>
<td>2.19±0.58</td>
<td>1.47±0.08</td>
<td>2.28±0.25</td>
<td>1.78±0.34</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>31.85±3.34</td>
<td>14.09±1.15**</td>
<td>25.12±1.85</td>
<td>36.34±2.13</td>
<td>27.71±2.69</td>
<td>33.14±3.16</td>
</tr>
<tr>
<td>Bilirubine (mg/dl)</td>
<td>98.63±11.87</td>
<td>108.96±8.35</td>
<td>72.50±9.63</td>
<td>120.81±10.95</td>
<td>113.25±12.09</td>
<td>82.75±6.11</td>
</tr>
</tbody>
</table>

Sat. C: Satellite control; * Significantly different from control, p<0.05; ** Significantly different from control, p<0.01

The texture and color of the vital organs (liver, kidney, heart, spleen, adrenal glands, stomach, lungs, testes, ovaries) animals receiving the extract of Anthocleista schweinfurthii for 4 weeks showed no significant change compared to control rats. Histological analysis of liver and kidney showed no abnormalities in rats treated with the extract.

**DISCUSSION**

Anthocleista schweinfurthii is a plant used in traditional medicine for the treatment of diseases such as malaria, cancer, venereal disease, bacterial infections and ulcers. However, many published studies have reported potential toxic effects of natural products; it is necessary to characterize the effects of this plant on biological systems, including its toxicological effects. In this work, the study of acute oral administration of a single dose of 2000 mg/kg of the aqueous extract of Anthocleista schweinfurthii caused no deaths. Based on the toxicity scale Hodge and Steiner and the recommendations of the OECD Bulletin No. 423 (2001), this plant extract can be considered as low toxicity, presents a higher LD50 superior to 2000 mg/kg; and corresponds to the class "Not classified", that is non-toxic. This result suggests that A. schweinfurthii aqueous extract has a substantial margin of safety.
given the effective doses (250-500 mg/kg) (unpublished) that are significantly lower than 2000 mg/kg. To assess the impact of prolonged exposure to the extract, sub acute toxicity studies were conducted on young male and female rats.

The general observation of the animals during the experiment revealed no change in coat color, appearance, saddles, locomotion, and sensitivity to noise and touch. Similarly, the absence of drowsiness and aggression were noted. These results suggest that the aqueous extract of A. schweinfurthii would have no influence on the behavior and physical appearance of the animals. The absence of diarrhea indicates that the extract does not stimulate intestinal peristalsis. [16] Corporal weight changes are used as indicators of adverse effects of toxic substances. [17,18] The observed results showed tangible gain comparable to that of untreated animals within 28 days of treatment, and in the two weeks following discontinuation of therapy. This reflects a change that is not related to the administration of the plant extract. The experience that began with young animals shows normal growth, show that the extract would not have led to changes in the cartilage and growth hormones.

In general, changes in body weight of treated animals, as well as the vital organs (liver, kidneys, lungs, adrenal glands, testicles, ovaries, spleen, stomach and heart), are indicators of a substance with high toxicity. [17,19] The results showed a significant (P <0.01) diminution of the relative weight of the heart and stomach in satellite group. Indeed, the work of Kabamba et al. [7] showed that the aqueous extract of A. schweinfurthii has positive inotropic properties (increase of the amplitude of the contractions of the heart) of the isolated frog heart. This inotropic activity is explained by the presence of cardiac glycosides (cardenolides) in this plant extract. [7] However, the high-dose extract (1000 mg/kg) causes (satellite group) a significant (p <0.05) diminution of heart weight, two weeks later. This decrease in heart weight was due to a toxic concentration of certain compounds of the extract used in high doses (1000 mg/kg).

In general, increase in relative liver weight is due to inflammation. [20] Table 1 shows a decrease in the relative liver weight in rats treated with the extract dose of 1000 mg/kg and this reduction persisted during the two weeks following discontinuation of treatment with the extract at a dose 1000 mg/kg. The decrease of liver weight observed in these rats result to decreased hepatic metabolism. [20] Indeed, hepatic transaminases involved in the metabolism of amino acids and carbohydrates. They have a wide tissue distribution, but ALT is specific to the liver. Generally, damage of the liver parenchyma induced elevation of transaminases in
blood so any increase is a sign of a first cell damage that induces the influx of these enzymes in serum. \[21\] Table 3 shows no significant change in ALT (alanine aminotransferase), suggesting that the liver has not suffered significant damage. This is confirmed by the fact that the liver of satellite group rats also presented a weight loss. The *Anthocleista schweinfurthii* extract would not be responsible for the decrease in liver weight observed in these rats.

The relative weight of the stomach significantly decreased in rats in the two weeks following discontinuation of treatment with the extract at a dose of 1000 mg/kg. The stomach is a target organ of *Anthocleista schweinfurthii* extract, this would translate a detrimental effect of the extract on the stomach due to prolonged exposure at high doses can be linked to a slow metabolism of the plant extract.

Haematological parameters give information on hematopoietic function (evaluation of cells of the myeloid lineage) and the determination of the occurrence of any allergies (white blood cell studies). \[22\] The observed results showed no significant change in the rate of red blood cells in rats treated with the extract of *A. schweinfurthii*. These results are similar to those obtained with the extract of *Ocimum suave*, \[10\] *Carica papaya* \[19\] and those of the work of Ihedioha et al. \[23\] A decrease in blood platelets reduces blood clotting ability, which would lead to severe and prolonged bleeding. \[24\] A significant decrease of platelets was observed in rats treated with the extract at all doses, this reduction persisted 2 weeks after discontinuation of treatment at a dose of 1000 mg/kg. This result would indicate a higher risk of bleeding due to prolonged administration of the plant extract.

In order to evaluate discomfort reactions in the body cope with stress, to a state of deprivation, biochemical assay of plasma parameters was carried out. The lipid profile is an indicator of lipid metabolism in the liver. \[25\] The increase in serum triglyceride levels is due to liver dysfunction and may cause cardiovascular problems. Triglycerides increased significantly (P <0.01) in rats treated with the extract (1000 mg/kg), this effect persisted in the two weeks following discontinuation of therapy. This would suggest that the *A. schweinfurthii* extract might disturb hepatic lipid metabolism and cause cardiovascular problems.

Almost all of the plasma proteins are synthesized in the liver. A low plasma level would indicate either liver disease (cirrhosis, cancer), or nephrotic syndrome that is to say an
excessive shedding of plasma proteins by the kidneys. While high levels of plasma proteins suggests liver disease or an inflammatory or immune response in general. [20] Serum proteins have increased significantly (P <0.01) in the group treated with the extract at a dose 1000 mg/kg which is returned to normal within two weeks following discontinuation of treatment, which shows that this effect is reversible (Table 3). This would show that the A. Schweinfurthii extract, dose 1000 mg/kg, or cause liver inflammation, an allergy but this effect is reversible.

The study of fasting blood glucose gives information on the state of functioning of the liver and pancreas. However, the liver provides storage and release while the pancreas information on the availability and deficiency. [26,27] No significant variation was observed in animals treated with the extract of A. schweinfurthii. This result indicates that this extract does not change the functioning of the liver and pancreas.

Creatinine gives information on the degree of renal filtration. It is a constituent of muscle proteins, which is eliminated only by the kidney. It is thus a marker of renal function. [10] His serum values may vary as a result of kidney extra factors (excessive protein intake in the diet, the importance of muscle catabolism related to body mass, age). The increase in the creatinine level reflects a functional defect nephron. [28] Creatinine levels have no significant variation (p <0.05) in rats treated with the extract, this suggests that the extract of A. schweinfurthii does not influence renal function.

The urea, product of the protein catabolism, is eliminated by the kidney. His blood level reflects kidney function. However, it can be changed by extra-renal parameters (fever, protein-rich food intake). A significant decrease in urea-treated rats at the dose of 250 mg/kg was noted. This decrease is not dose-dependent; this would suggest that this effect may not be related to the extract. Therefore, the aqueous extract of A. schweinfurthii does not significantly affect the renal function.

Total plasma bilirubin reflects both hepatic and renal function. The liver converts non-conjugated bilirubin to conjugated bilirubin. Then, the kidney excretes conjugated bilirubin. The change in plasma bilirubin shows a hepatic or renal dysfunction. [20] Table 3 shows that the plasma bilirubin was no significant changes in the animals treated with the extract of A. schweinfurthii compared to the control group. So, this extract does not significantly affect liver function and kidney function.
These biochemical data are confirmed by histological analysis of liver and kidney which showed no abnormalities in liver and kidney tissues of rats exposed to the extract of *A. schweinfurthii* for 28 days. Based on these results, the administration of the aqueous extract of the bark of *A. schweinfurthii* would have resulted in no changes in the liver and kidneys and the general condition of the animals.

**CONCLUSION**

Our study shows that the LD$_{50}$ of the *A. schweinfurthii* extract is greater than 2000 mg/kg, so this extract is classified as poorly toxic substances. A study with three dose levels (250mg/kg, 500mg/kg, 1000mg/kg) administered daily to the animals, for a period of 28 days, did not result in any change in behavior, liver function and renal function for the dose 250 mg/kg and 500 mg/kg. Only the dose of 1000 mg/kg caused an increase in plasma triglyceride level. Thus, the effective therapeutic dose (250 mg/kg and 500 mg/kg) having made a cytoprotective effects (unpublished) on the gastric mucosa, would be non-toxic in repeated administration for 28 days.

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