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Safety of the Ethanolic Extract *Crateva adansonii* DC. (Capparidaceae) Harvested at Dassa-Zounmè in Central Benin

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Abstract: ***Medicinal plants are widely used worldwide by populations and are a source of new active components. The objective of this work is to assess the toxicity of the ethanolic extract of this plant in order to promote its use in traditional medicine in Benin. Method: The ethanolic extract was obtained after evaporation of the filtrate under vacuum on a rotary evaporator. The toxicity studies took into account on the one hand the determination of heavy metals (Pb, Cd and As) on the other hand the Acute and subacute Toxicities which were carried out according to the OECD guidelines respectively Standards 423 and 407 on Wistar strain female rats. Blood samples were taken from animals for hematological and biochemical analyzes. Finally the organs (liver and kidney) were removed for histological readings. Results: The study of the acute oral toxicity of the ethanolic extract of Crateva adansonii at the single dose of 5.000 mg.kg^{-1} of body weight recorded no death or sign of toxicity during the 14 days of the experimental period. . This shows that the LD_{50} of our extract is greater than 5.000 mg.kg^{-1} pc. As for the subchronic toxicity, it revealed that whatever the dose of the extract administered, no signs of intoxication were observed during the 28 days. The extract Crateva adansonii is therefore not lethal. With the exception of a few rare tubular vacuolar degenerations, rats present a hepatic and renal histological appearance within normal limits. Conclusion: This allows us to conclude the ad hoc use of Crateva adansonii is safe but its prolonged use can be harmful to the human organism.***

Keywords: Toxicity, acute, subchronic, histology, *Crateva adansonii*, heavy metals, Safety, Benin.

1. Introduction

Throughout the world, traditional medicine has seen an increasing interest in recent decades thanks to the study of medicinal plants and their uses by populations. Today, according to the World Health Organization (WHO), almost 80% of the population depend on traditional medicine for primary health care [1]. The study of plants has increasingly become a methodical science used by industries in various fields such as herbal medicine, perfumery, cosmetics, flavoring, etc. [2]. Among these plants is *Crateva adansonii* which is a plant widely used in the Beninese population because of its therapeutic properties [3]; [4]. It is known for its antihypertensive, antibacterial and other properties which, when combined with other plants is capable of solving many multiresistance problems [5], [6], [7]. The objective of this study is to assess the possible effects of prolonged use of *Crateva adansonii* on vital organs such as the liver and kidneys in order to enhance its use in traditional medicine.

2. Materials and methods

2.1 Materials

2.1.1. Plant material

These are exclusively *Crateva adansonii* DC samples. ssp. adansonii harvested in Dassa-Zoumè in central Benin. This plant material has been authenticated at the national herbarium of the University of Abomey Calavi, under the number YH 269 / HNB.

2.1.2. Biological material

The acute and subchronic toxicity studies were carried out according to the OECD guidelines, respectively Standards 423 and 407. The biological material consists of thirty-eight female rats of non-gravid Wistar strain, coming from the laboratory animal facility. Cytogenetic Histo-Embryology and Reproductive Biology of the Institute of Applied Biomedical Sciences (ISBA) Benin. These rats distributed as follows: acute toxicity eight rats and subchronic toxicity thirty-two rats. The rats used have a weight of between 160 g ± 20%.

2.2 Methods

2.2.1 Preparation of the ethanolic extract

The samples dried under laboratory conditions (Θ = 22 ± 3oC) were reduced to powder. 100 g of powder were brought into contact with 500 ml of ethanol with mechanical stirring for 24 hours. The extract was decanted, filtered and then evaporated in vacuo. The extract obtained was dried in an oven at 40 °C before being stored in pill boxes at 4 °C for the various tests.

2.2.2 Procedure for the acute oral safety test

Acute toxicity by oral gavage was performed using an intragastric tube following the guidelines of the [8], Standards 423, taken up by [9]. The rats were divided into two (02) lots of (03) female rats, including one (01) treated lot and one control lot. Before administration, the rats were weighed and fasted for 18 hours with free access to water. The treated batches received the single dose of 5000 mg / kg of bodyweight extract. After the force-feeding, the rats have free access to water and granules. The consumption of granules and water were recorded each day and the rats were weighed on the 7th and 14th day. The rats were constantly observed during the first hours after the force-feeding and then every 24 hours during the experimental period in order to record deaths and clinical signs.

2.2.3 Oral subchronic safety test procedure

Subchronic toxicity is effected by oral gavage using an intragastric probe on female rats following the guidelines of the OECD, Standards 407 [10], [11]. The rats were divided into four (04) groups of eight (08) rats including one (01) control group and three (03) treated groups. Before administration, the rats were weighed and fasted for 18 hours with free access to water. The treated rats received daily doses of 500, 750 and 1000 mg / kg bodyweight of extract, respectively, for 28 days. After each force-feeding, the rats have free access to water and granules. Drinks are taken every day and the rats are weighed on the 7^{th}, 14^{th}, 21^{st} and 28^{th} day. Rats are constantly observed during the first hours after force-feeding and daily during the experiment to record deaths and clinical signs.

2.2.4 Method of assessing the ETM content

The standardized method of the HM 3000 metalyser used to quantify the ETMs is based on cathodic and anodic redissolution voltammetry using disc electrodes. It is a sensitive electro-analytical technique for the determination of minute quantities of metals and derivatives in solution [12]. The indicated dose of buffer and HCl (37%) will be poured into 70 ml of ethanolic extract solution of *Crateva adansonii*. The whole is homogenized followed by the selection of the current dosage and the conditioning of the electrodes for 3 minutes. Then, the method of metered additions was selected. After 3 minutes, 280 µl of standard for the current assay is added and the whole is left to operate for approximately 2 minutes. Finally, the result is displayed in peak and concentration form on the screen of the mini-computer connected to the metalyser.

2.2.5 Biochemical and hematological analysis method

The animals were removed for biochemical analyzes by the retro-orbital sinus puncture technique under slight ether anesthesia [13], [14]. At the end of the treatment, the animals were fasted for 12 hours before being sampled. The blood samples were taken in an EDTA (anticoagulant) tube and a dry tube to measure some blood parameters such as NFS and biochemical parameters such as urea, creatinine and transaminases. The standard protocol used for the measurement of hematological and biochemical parameters is that reported in certain works [15], [14], [11].

2.2.6 Histological method

The technique for making tissue sections used in this work is formalin fixation suitable for observations under light microscopy [16], [17], [18]. It requires seven steps, namely removal, fixation, progressive dehydration, inclusion in paraffin, cutting, coloring and assembly. Following the blood sample, the rats are sacrificed by total drowsiness with chloroform. The kidneys and liver were removed, weighed and immediately introduced into physiological water for rinsing. The organs are then fixed for ten days by immersion in 10% buffered formalin intended to immobilize the cellular and tissue structures, in a state as close as possible to their living state. This fixing phase is followed by dehydration by passage of the fragments in successive ethanol baths of increasing degree and then in a series of toluene baths for cleaning. Dehydration is succeeded by the inclusion in paraffin, a hardening and preservative substance which allows the achievement of fine and regular cuts. The paraffin block obtained in cassettes is obtained. The fine sections (2 to 5 µm thick) of the paraffin block will be made with a microtome. These sections collected on glass slides numbered beforehand. The slides are incubated for 24 hours. Finally, we will proceed with mounting following dehydration (alcohol baths of increasing degree). The haematoxylin and eosin stained sections mounted between slide and coverslip are ready to be observed under an optical microscope.

2.2.7 Statistical analyzes

The data generated are expressed as Average ± Standard Error of Average (SEM). The comparisons between the control values and those of the treated groups were carried out by the "Student" test at the threshold of ($p < 0.05$) according to the ANOVA statistical model with the Epi info 7.2 software. The difference was considered statistically significant when the p-value was less than 0.05.

2.2.8 Ethics Committee

The experimental procedures were carried out after the approval of the ethical guidelines of the Ethics Committee of the Institute of Applied Biomedical Sciences (ISBA). All the experiments were carried out in accordance with the directives for the care and use of laboratory animals and the European Union statutes concerning the handling of laboratory animals (86/609 / EEC) [19], [20].

3. Results

3.1 Results of the acute oral safety test

3.1.1 Clinical signs of intoxication

The acute oral toxicity study in rats of the Wistar strain showed that the ethanolic extract of *Crateva adansonii DC*. at a dose of 5000 mg / kg does not reveal any undesirable effects. No abnormal reactions were recorded during the first four hours after administration of the extract at the single dose of 5000 mg / kg of body weight of extract in the treated groups compared to the control group. During the 14 days of follow-up, no deaths were recorded in the two batches of rats. The behavior of the treated animals

remained normal and comparable to that of the controls. However, a change in behavior, namely the friction of the nose and mouth on the floor of the cage is observed. This however, disappears within 24 hours. These results are consistent with those of [21].

3.1.2 Evolution of the mass of animals

Figure 1 below shows the evolution of the weight growth of the animals during the 14 days of experimentation.

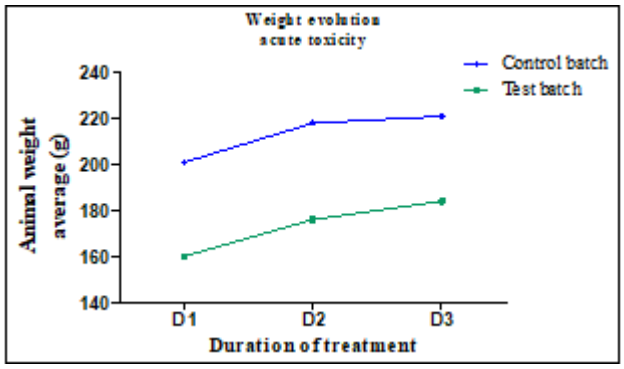

Figure 1: Evolution of the body mass of the animals

All animals experienced positive weight changes during the experiment. The evolution of the body mass of the treated animals did not show any statistically significant difference compared to the control batch (Figure 1).

3.1.3 Water and pellet consumption

The results of the water and granule consumption of the test and treated batches during the two weeks of follow-up are recorded in table 1.

Table 1: Water and granule consumption

Material consumption	*Week*	*Quantity consumed*		
		Témoins	*Test Femelle*	*P-value*
Pellets	1	47.57 ± 16.52	42.429 ± 2.87	0.672
	2	56.71 ± 5.15	54.42 ± 3.30	
Water	1	53.57 ± 2.44	26.42 ± 6.26	0.231
	2	71.71 ± 6.37	49.28 ± 9.32	

Average Results ± Standard Average Error (SEM); * = Significant results: p <0.05

Reading Table 1 shows no statistically significant difference in the consumption of granules and water between the treated batch and the control batch.

3.1.4 Mass of organs removed

After the 14 days of follow-up, the organs (liver; kidneys) are removed and the masses of the treated batch are compared with those of the control batch in Table 2.

Table 2: Mass of organs removed

Organ harvested	*Witness*	*Female Test*	*P-value*
Liver	6.06 ± 0.11	5.52 ± 0.23	0.426584681
Kidneys	0.99 ± 0.079	0.547 ± 0.05*	0.028676757

Average Results ± Standard Average Error (SEM); * = Significant results: p <0.05

The analysis in Table 2 reveals a statistically significant difference between the mass of the kidneys of the treated batch (5000 mg / kg) and of the control batch unlike the mass of the liver which did not show any significant difference.

3.1.5 Haematological parameters

Table 3 above presents the results of the hematological parameters.

Table 3: Hematological parameters

Haematological parameters	*Control batch*	*Female test batch*	*P-value*
RBC	5.98 ± 0.90	5.36 ± 0.67	0.388935334
WBC	7.033 ± 2.38	5.6 3± 1.89	0.469631493
HGB	13.46 ± 0.47	12.96 ± 0.85	0.423716349
HCT	39.56 ± 1.69	36 ± 3	0.347251995
PLT	739 ± 50.86	551 ± 47.64	0.602354821

Average Results ± Standard Average Error (SEM); * = Significant results: p <0.05

The administration of the ethanolic extract of Crateva adansonii at the single dose of 5000 mg / kg of body weight did not show any statistically significant difference on the hematological parameters (white blood cells, number of platelets; red blood cells; hemoglobin) between the treated batch and the control batch.

3.1.6 Biochemical parameters

Table 4 presents the results of the biochemical parameters**.**

Table 4: Biochemical parameters

Biochimical parameters	*Control batch*	*Female test batch*	*P-value*
Urea (g/L)	0.49 ± 0.016	0.39 ± 0.03*	0.04231565
Crea (mg/L)	9.36 ±1.62	8.33 ± 0.39	0.49834465
ASAT (U/L)	147.34 ± 9.37	149.61 ± 6.60	0.80908063
ALAT (U/L)	58.38 ± 7.49	50.88 ±5.26	0.40300778

Average Results ± Standard Average Error (SEM); * = Significant results: p <0.05

The analysis in Table 4 shows that the urea level of the treated batch, although it is within the range of the normal values, presents a statistically significant difference compared to the control batch.

3.1.7 Histological examinations

Figures 2; 3; 4 and 5 presents the results of the histological tests (acute toxicity test) carried out on the liver and the kidneys of the animals.

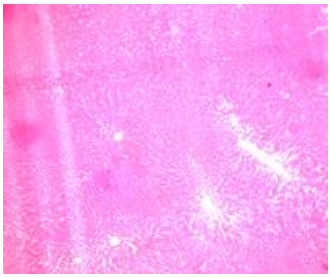

Figure 2: Hepatic histological section
Control batch; HE: X100
Blade quality: fairly good Lobules: Congestion
E Portes: Congestion
Histology within normal limits

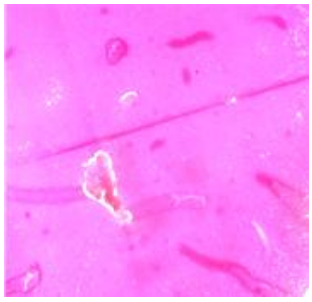

Figure 3: Hepatic histological section batch processed; HE: X 100
Blade quality: Good quality Lobules: Congestion/ siderophages around centrolobular veins
E Portes: Many bile ducts sometimes
Congestive liver, histological in appearance within normal limits .

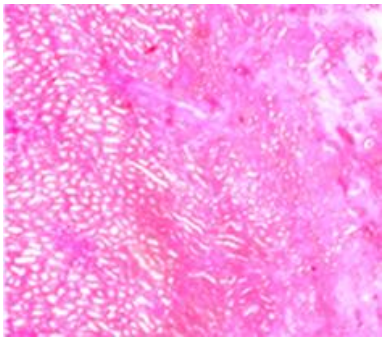

Figure 4: Kidney histological section batch; HE:X 100
Blade quality: fairly Glomeruli: Good
Tubules and interstitium: Featureless
Histology within normal limits

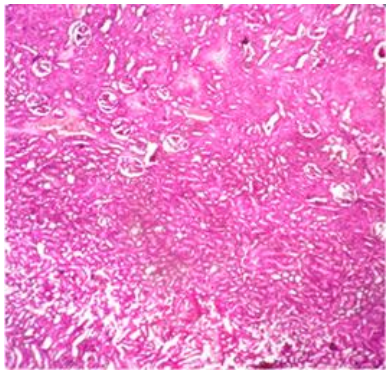

Figure 5: Kidney histological section batch; HE:X 100
Blade quality: fairly Glomeruli: Good
Tubules and interstitium: Some cylinders
Histology within normal limits

Histopathology results from animals with acute toxicity show normal renal and hepatic architecture. Rare congestive aspects are observed in liver sections.

3.2 Results of the oral subchronic safety test

3.2.1 Clinical signs of intoxication

Observation of the behavior throughout the study period made it possible to observe that, whatever the dose (500; 750 and 1000 mg / kg) of the extract administered, no abnormal clinical sign was observed. In animals treated in comparison to the control batch. No case of mortality was recorded either in the control batch or in the treated batches.

3.2.2 Evolution of animal weight

Figure 2 below shows the evolution of the body mass of the different batches treated in comparison to the control batch.

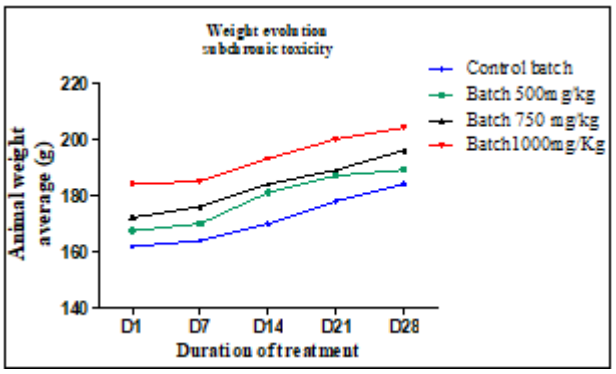

Figure 2: Evolution of body mass subchronic toxicity

During the whole period of the experiment, a monitoring of the body weight of all the animals was carried out every week. This monitoring showed that the animals experienced positive weight growth.

3.2.3 Evolution of water consumption

Table 6 below shows the evolution of the water consumption of the animals during the 28 days of the experiment

Table 6: Water consumption

		Doses		
Week	Control	500mg/Kg	750mg/Kg	1000mg/Kg
1	88,57±8,99	101,71±17,33	115,71±11,33	80,71±10,9
2	94,28±5,34	107,14±4,87	107,14±16,03	90±16,32
3	102,85±11,12	102,85±7,55	120±11,54	87,14±12,53
4	107,14±4,87	112,85±4,87	124,28±7,86	98,57±6,90
average	98,21±8,36	106,14±5,04	116,78±7,31	89,10±7,40
P-value		0,155600033	0,01555978*	0,15411289

Average Results ± Standard Average Error (SEM); * = Significant results: p <0.05

Analysis of the table reveals that the water consumption of the batch having received 750 mg / kg of body weight of extract has a statistically significant difference compared to the control batch.

3.2.4 Evolution of pellet consumption

The evolution of the consumption of granules of the animals during the 28 days of the experiment is presented in Table 7 below.

Table 7: Pellet consumption

		Doses		
Week	Control	500mg/Kg	750mg/Kg	1000mg/Kg
1	67.14±12.30	51.14±4.25	61.14±15.32	64.42±4.57
2	67±4.04	50.85±4.74	60.42±9.07	67.42±8.03
3	72±6.90	53.85±3.67	71.28±4.60	73±7.91
4	73.85±9.35	63.57±6.37	78.71±2.21	83.71±5.34
average	70±3.46	54.85±5.96	67.89±8.75	72.14±8.49
P-value		0.00461763*	0.670142912	0.65682023

Average Results ± Standard Average Error (SEM);
* = Significant results: p <0.05

The table 7 reveals that the consumption of granules in a batch having received the dose of 500 mg / kg of body weight of extract has a statistically significant difference compared to the control batch.

3.2.5 Hematological parameters

The table 8 presents the results of the hematological tests carried out on animals.

Table 8: Hematological parameters

		Doses		
Week	Control	500mg/Kg	750mg/Kg	1000mg/Kg
RBC	7.27±0.07	7.37±0.14	8.51±0.19*	8.08±0.19
WBC	7.8±0.21	6.5±0.56	7.9±0.42	8.2±1.13
HGB	13.45±0.91	14.05±0.49	16.8±0.28*	14.7±0.42
HCT	39.95±2.19	41.9±1.41	48.55±0.07*	47.1±1.41
PLT	620.5±45.96	644.5±64.3	616±124.45	602±77.78

Average Results ± Standard Average Error (SEM); * = Significant results: p <0.05

The analysis in Table 8 shows that the parameters such as the level of red blood cells, of hemoglobin and of hematocrites of the rats having received the dose of 750 mg / kg of body weight of extract have statistically significant differences compared to the batch witness

3.2.6 Biochemical parameters

Table 9 below shows the results of the biochemical parameters

Table 9: Biochemical parameters

	Control	500mg/Kg	750mg/Kg	1000mg/Kg
Urea g/L	0.30±0.04	0.37±0.10	0.32±0.02	0.24±0.014*
Creamg/L	8.18±0.28	9.37±0.51	8.44±0.90	7.06±0.14
ASAT U/L	148.07±49.73	174.42±38.36	126.99±10.8	111.93±0.72
ALAT U/L	84.77±17.84	89.96±15.04	67.68±5.76	85.36±12.71

Average Results ± Standard Average Error (SEM); * = Significant results: p <0.05

From the analysis of Table 9, it appears that the uremia rate of the batch having received the dose of 1,000 mg / kg of body weight of extract has a statistically significant difference.

3.2.7 Mass of organs removed

Table 10: Mass of organs removed

Organs	*Control*	*500mg/Kg*	*750mg/Kg*	*1000mg/Kg*
Liver	5.49±0.08	7.30±0.14	7.08±0.03	9.09±0.04
Kidney	0.47±0.09	0.79±0.07	0.89±0.08*	0.78±0.08

Average Results ± Standard Average Error (SEM);
* = Significant results: p <0.05

The analysis in table 10 reveals a statistically significant difference between the mass of the kidneys of the treated batch (750 mg / kg) and of the control batch unlike the mass of the liver which did not show any significant difference.

3.2.8 Histological examinations

Figures 6; 7; 8; 9; 10; 11; 12; 13 presents the results of the histological tests (subchronic toxicity test) carried out on the liver and the kidneys of the animals.

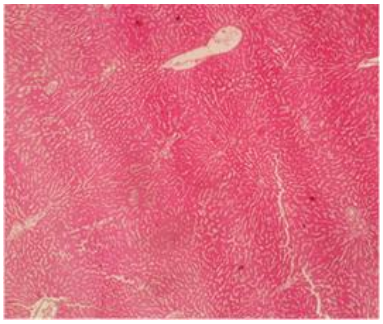

Figure 6: Liver section subchronic toxicity
Control batch; HE X100
Blade quality: Pretty good Lobules: Slight cholestasis.
E Portes: Featureless
Histology within normal limits

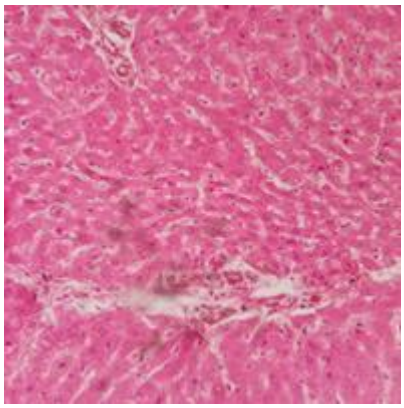

Figure 7: Liver section subchronic toxicity
batch treated 500mg/kg; HE:X400
Blade quality: Pretty good Lobules: Discreet cholestasis; Discreet inflammatory
E Portes: Many biliary canaliculi in some E portes Histological aspect within the limits of normal. Local presence within lobules of a discrete polymorphic inflammatory infiltrate isolated without associated hepatocyte lesions.

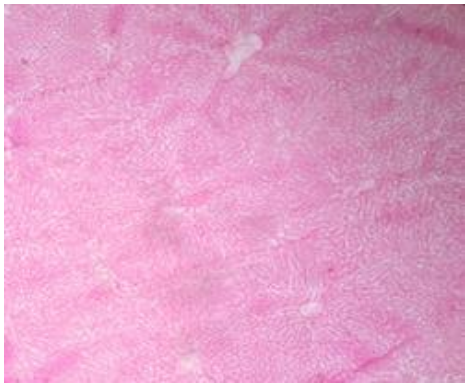

Figure 8: Liver section subchronic toxicity
Control batch; HE X100
Blade quality: Pretty good Lobules: Discrete cholestasis;
E Portes: Presence of some inflammatory cells in the lobules
Histological appearance within normal limits.

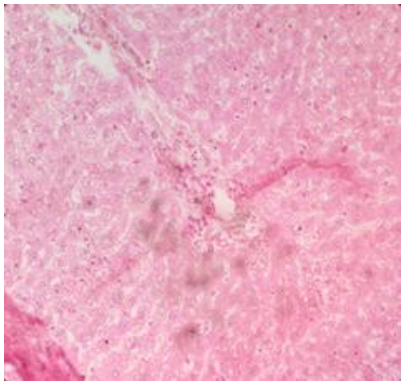

Figure 9: Liver section subchronic toxicity
batch treated 1000mg/kg; HE:X400
Blade quality: Pretty good Lobules: Congestion
E Portes: Discreet inflammatory portal lymphocyte infiltrate without necrotic aspects
Histological appearance within normal limits.

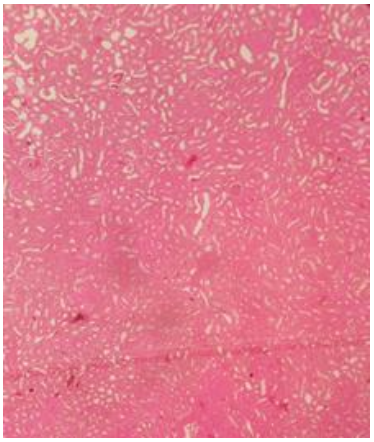

Figure 10: Kidney section subchronic toxicity
Control batch; HE X100
Blade quality: Pretty good Glomeruli: Featureless
Tubules and interstitium: Vacular degeneration aspect of very rare tubules;Luminal expansion of rare tubules
Histology within normal limits

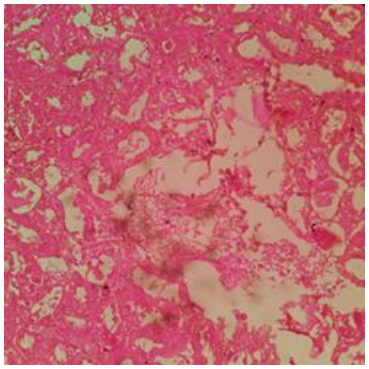

Figure 11: Kidney section subchronic toxicity
batch treated500mg/kg; X200
Blade quality: Pretty good Glomeruli: Featureless
Tubules and interstitium: Vacular atypia of rare renal tubule cells, Luminal expansion of some tubules
Presence of some vacuolar lesions of the renal tubules / Histology within normal limits

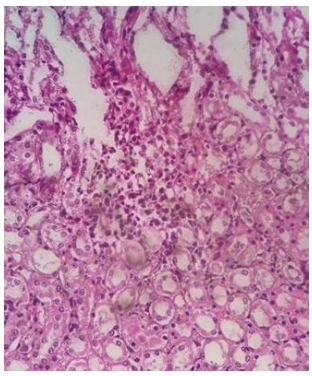

Figure 12: Kidney section subchronic toxicity
batch treated 750mg/kg; X400
Blade quality: Pretty good
Glomeruli: absence of inflammation and cortical fibrosis
Tubules and interstitium: Congestion, Vuolar degeneration, rare cylinders, Focal presence of a cluster of inflammatory cells made of lymphocytes and plasma cells centered by a few renal tubules in necrosis
Light focal tubulointerstitial nephritis

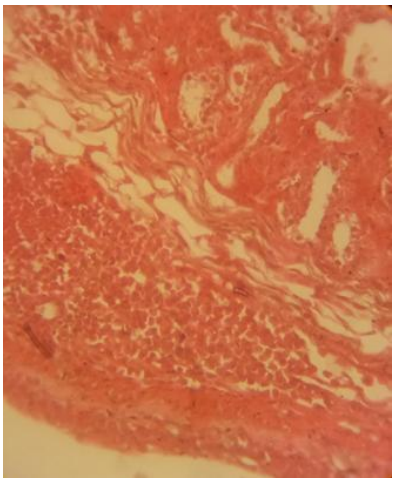

Figure 13: Kidney section subchronic toxicity
batch treated 1000mg/kg; X400
Blade quality: fairly Glomeruli: Pretty good
Tubules and interstitium: discreet vacuolar degeneration, Moderate lympho-plasmocytic inflammatory infiltrate organized in clusters with para-cortical localization without associated necrosis

Moderate to severe paracortical lympho-plasma cell inflammation, discreet tubular vacuolar degeneration

The analysis figures 6;7; 8; 9; 10; 11; 12 ant 13 shows overall a normal appearance of the hepatic and renal cells of the animals. Some rare atypies have been observed in places. The rats exposed to the different doses (500; 750; 1000 mg/kg of PC) have a hepatic and renal histological appearance within the limits of normal.

3.2.9 Result of Metallic Trace Elements

Table 12 below shows the ETM content dosed in the extract

Table 12: Metallic Trace Elements

ETM	Concentration (ppm)		Normes OMS (ppm)	Rapport
Pb	0.00789	7.89	≤ 10	≈ 1267
Cd	0.00165	1.65	≤ 0.3	≈ 182
As	Indetermined	Indétermined	≤ 1	-

The ETM assay reveals the presence of Pb and Cd in variable proportions. The presumptive dosage of As was found to be negative (Table 12). The concentrations of Pb and Cd are respectively around 1267 and 182 times lower than the WHO standards in force.

***Abbreviations**: Crea, Creatinine; ASAT, aspartate aminotransferase ; ALAT, alanine aminotransferase, RBC, red blood cells; WBC, White blood cell count; HGB, hemoglobin concentration; HCT, haematocrit; PLT, platelet count; ETM, Metallic Trace Elements; Pb, lead; Cd, cadmium; As, arsenic.*

4. Discussion

Observation of the behavior of the animals during the study period made it possible to observe that, whatever the dose of the extract administered, no abnormal behavior was observed. No deaths were also observed in both the acute and subacute toxicity batches. This testifies to the non-lethality of the extract of *Crateva adansonii* at the doses used. The lethal dose of the extract is greater than 5000mg / kg of body weight. These results confirm those of [21] which led to the same results on the methanolic extract of *Crateva adansonii*. The toxicity test results show that all of the animals experienced weight gain during the experiment. Weight change is used as a general indicator of the adverse effects of chemical compounds [22]. Thus weight gain is correlated with the physiological state of the animal and can be explained by the absence of clinical signs of toxicity such as drowsiness, anorexia [23]. This plant is known for its richness in nutrients, since it is used as a vegetable in certain countries [24]. These results are consistent with those of [21] who recorded a statistically insignificant increase ($p > 0.05$) in the weight of the animals during the entire period of the experiment. The results of the subchronic toxicity test showed a statistically significant difference in water and granules in the batch having received the dose 750 mg / kg of body weight of extract. As for acute toxicity, it also did not show any statistically significant difference between the batch tested and the control batch. From these analyzes, the consumption of pellets and water by rats is neither a function of the type of toxicity nor dependent doses. In view of the disparity observed in the evolution of water and granule consumption, these variations cannot be linked to the effects of the plant. They would be explained by natural predispositions of the organism of the rats. By way of comparison, these results are consistent with those of [25] who reported statistically insignificant variations in rats treated at the same doses with the ethanolic extract of another plant, *Momordica charantia*. The haematological examination carried out at the doses (500 mg / ml; 1000 mg / ml) did not show any modification in the level of the hematopoietic line. As for the batch fed at 750 mg / kg, the levels of red blood cells, hemoglobin and hematocrit show significant increases ($P < 0.05$). Hematological variations are the first indicators of toxic effects on tissues. In animals, blood is the most important tissue. It is at this level that the various changes caused by metabolic processes are noticed [25]. In the present study, an increase in the average level of hemoglobin and red blood cells has been reported. This would translate into better stimulation of the production and / or maturation of erythrocytes. In a comparative approach, the effects of the latter are comparable to those of [26] with the aqueous extract and to those observed on albino rats force-fed with the hydroalcoholic extract of *Capparis tomentosa* (Capparidaceae) the results of which did not show any significant changes ($P > 0.05$) on hematological parameters such as the number of RBC red blood cells, PCV white blood cells, hemoglobin level compared to the control group [27]. In this work, the usual renal (urea; creatinine) and hepatic (ASAT; ALAT) markers are evaluated to apprehend possible effects of the extract on these target organs. These biochemical parameters are the main indicators of hepatorenal pathologies [28]. The assay of the biochemical parameters show that the urea content of the batches treated at 1000 mg / kg and 5000 mg / kg present a statistically significant difference compared to the control batches. On the other hand, the biochemical parameters (creatinine and transaminases) did not show any significant difference in the two cases (acute and subacute toxicity). The values of these biochemical parameters did not undergo significant variations compared to the controls. This shows a good tolerance of the animals with regard to the ethanolic extract of *Crateva adansonii*. These results are consistent with those of [26] who had similar results on the aqueous extract of *C. adansonii* who used concentration ranges varying from (325 - 1300 mg / kg of body weight) aqueous extract. Histological sections of the liver show some siderophages around centrolobular veins and rare congestions. Rare bile ducts are sometimes seen. In conclusion, the liver presents an architecture whose histological aspect is within the limits of normal. As for the kidney of the test batch, its cut presents a good distribution of the normal size glomeruli in the cortex. Some cylinders are observed in Tubules and interstitium. In short, its histology within the limits of normal. Histological sections of the liver at the level of subchronic toxicity show that apart from a discrete inflammatory infiltrate made of rare lymphocytic and sometimes eosinophilic neutrophils without hepatocyte necrosis associated with the level of rats force-fed at 500 mg / ml, no abnormality significantly

different from that observed in the control lot was not identified. By way of comparison, these results corroborate those of [26] who obtained similar results on rats with the aqueous extract of *C. adansonii*. At the kidney level, compared to the control batch, the force-fed batches have a few particulars, namely:

The batch fed at 500 mg / kg of CP presents some lesions of vacuolar degeneration of the renal tubules. The batch force-fed at 750 mg / kg presents a heap of inflammatory cells made up of lymphocytes and plasma cells centered by a few renal tubules in necrosis. We could speak of acute nephritis of the interstitial tubules. The batch force-fed at 1000 mg / kg presents a moderate lympho-plasmocytic inflammatory infiltrate organized in clusters with paracortical localization without associated necrosis.

5. Conclusion

The objective of our study is to study the acute and sub-chronic toxicity in order to evaluate the possible clinical signs of intoxication, hematological and / or biochemical on various organs linked to the repeated use of *Crateva adansonii DC*. At a single dose of 5000mg / kg of body weight, this herb has shown no signs of toxicity. Subchronic toxicity has shown that the extract of this plant does not contain, at pharmacological doses (500mg; 750mg and 1000mg), lethal substances or toxic for the hematological and biochemical parameters studied over 28 days in repeated single-daily administrations. As for the histological sections, some rare lesions (vacuolar degeneration of a few tubules) are reversible. This allows us to conclude the ad hoc use of *Crateva adansonii* is safe but its prolonged use can be harmful to the organism.

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