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Koffi Oi Koffi Vincent
UPR Endocrinology and Reproductive Biology, Laboratory of Biology and Health, UFR Biosciences, Felix Houphouët- Boigny University, 22 BP 582 Abidjan, Côte d'Ivoire

Kouakou Koffi Roger
Biology Laboratory, Department of Sciences and Technology, UFR Medical Sciences, Alassane Ouattara University, Bouake, Côte d'Ivoire

Siapo Yao Martin
UPR Endocrinology and Reproductive Biology, Laboratory of Biology and Health, UFR Biosciences, Felix Houphouët- Boigny University, 22 BP 582 Abidjan, Côte d'Ivoire

Zougrou N'guessan Ernest
UPR Endocrinology and Reproductive Biology, Laboratory of Biology and Health, UFR Biosciences, Felix Houphouët- Boigny University, 22 BP 582 Abidjan, Côte d'Ivoire

Kablan Kassi Jean Jacques
UPR Endocrinology and Reproductive Biology, Laboratory of Biology and Health, UFR Biosciences, Felix Houphouët- Boigny University, 22 BP 582 Abidjan, Côte d'Ivoire

Djinandji Gnamien Marie-Claire
UPR Endocrinology and Reproductive Biology, Laboratory of Biology and Health, UFR Biosciences, Felix Houphouët- Boigny University, 22 BP 582 Abidjan, Côte d'Ivoire

Kouakou Koffi
UPR Endocrinology and Reproductive Biology, Laboratory of Biology and Health, UFR Biosciences, Felix Houphouët- Boigny University, 22 BP 582 Abidjan, Côte d'Ivoire

Corresponding Author:
Koffi Oi Koffi Vincent
UPR Endocrinology and Reproductive Biology, Laboratory of Biology and Health, UFR Biosciences, Felix Houphouët- Boigny University, 22 BP 582 Abidjan, Côte d'Ivoire

Evaluation of the acute and subacute toxicity of *Kigelia africana* bark extracts on Wistar rats

Koffi Oi Koffi Vincent, Kouakou Koffi Roger, Siapo Yao Martin, Zougrou N'guessan Ernest, Kablan Kassi Jean Jacques, Djinandji Gnamien Marie-Claire and Kouakou Koffi

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Abstract
Kigelia africana is a plant present in almost all of Ivory Coast, it has several therapeutic virtues in traditional medicine. For a better use of the bark of this plant we have carried out scientific research. The objectif of this research is to determine the actions of aqueous substances of the bark of *Kigelia africana* on the hematological and biochemical parameters of female rats. The aqueous substance were obtained by maceration. The results obtained indicated that the substances contain bioactive elements which would give the bark pharmacological properties. The bark of *Kigelia africana* is safe for health because the LD_{50} of the products is above 5000 mg/mc. Likewise, the weekly use of extracts revealed their hepato- and cardio-protective activities. A drop in the percentage of urea and creatine in administered rats was observed as well as a gain in the percentage of blood platelets in the treated rats. These results show that these bark extracts did not generate any damage during the study period at the different doses studied.

Keywords: Acute and sub-acute toxicity, haematological and biochemical compounds

1. Introduction
Medicinal plants have been used for a long time in the fight against the majority of diseases in African societies (Telefo *et al.*, 2011; Lawin *et al.*, 2016) [1-2]. The WHO believes that nearly 80% of the world's population primarily has the advantage of using plants to heal themselves (WHO and FAO, 2002) [3]. Bouzouita (2016) [4] indicates that the strong demand for plants gave birth to phytotherapy, which is a medicine in its own right which shows that plants could be authentic medicines. However, the purpose of a subject in pharmacology is not completely acceptable to authorize its possible appearance in therapy. Indeed, in addition to the purpose, there must not be poisonous and harmful consequences for the body for the capacity used. It is therefore necessary to develop the risk benefit rate in the therapeutic use of each material (Bounihi, 2015) [5]. This can only be carried out by means of two types of research, on the one side the determination in animals (experimental pharmacology) and in humans (beneficial effects), and on the other side a search for security in humans. animal (toxicology) and in humans adverse effects (Antonious *et al.*, 2006; Buenz, 2006) [6-7]. Toxicology therefore has an action of observation on the non-harmful use of medicinal plants. In conclusion, it must make phytotherapy and the consumption of plants with a certain level of insurances and security (Bounihi, 2015) [5]. In Ivory Coast, among the plants used in herbal medicine for the treatment of certain pathologies, we find *Kigelia africana* (Lam). Benth. The present study therefore aims to determine the toxicity of the aqueous extract of *Kigelia africana* bark on wistar rats.

2 Materials
2.1 Plant Materials
The plant material is composed of the bark of *K. africana* harvested in May in the commune of Daoukro (department of Iffou, Center-East Ivory Coast). A sample of *K. africana* was identified at the Center National Floristique (CNF) of the University Felix HOUPHOUËT-BOIGNY under the respective numbers 8937. The choice was made on the bark of this plant, because it is used by the Ivorian population in a traditional way for the treatment of cases of infertility and cases of cessation of menses (Mohnen, 2008) [8].

2.2 Animal material
The animal species used composed of Rattus norvegicus species (Muridae) of the Wistar strain.

These rats come from the animal store of the Ecole Normale Supérieure (ENS) in Abidjan. They were fed avery day add libitum. This species was selected because it is the animal model for studies in toxicology and pharmacology.

2.3 Preparation of extracts

The collected bark of *K. africana* is rinsed in tap water with great force. They were dried in the laboratory without the presence of sunlight at a temperature for (30±2 °C) for four weeks. The dried bark is reduced to powder using and electric mixer-grinder of the IAMAG-RCT® type. A quantity of 50 g of this powder was marinated in 1.25 L of distilled water for five repetitions of three minutes each in a blender (Single®, Singapore). The decoction collected was passed through a sieve three time on white cloth then successively on Wattman No. 1 paper. The collected substrate was put in a sauna at 50 °C for 48 hours to obtain a brown-colored dry substance (Zirihi *et al.*, 2003) [9].

2.4 Phytochemical screening of the different extracts

The different elements (sterols, polyterpenes, alkaloids, tannins, polyphenols, flavonoids, quinones and saponins) were extracted in the different preparations according to the standard coloring methods described by Wagner and Bladt (2001) [10], Békro *et al*. (2007) [11].

2.5 Effects of acute toxicity

The acute toxicity study was carried out according to OECD guideline 423 (2001) [12]. As for carrying out the present test, nine female rats aged 8 to 12 weeks, nulliparous, non-pregnant and then virgin, weighing 120 to 140 g, were used. The rats were deprived of food on the day preceding the experiment, while freely benefiting from water. The masses determined, the rats were divided into two groups (a control group and a treated group) with three animals per group. Each rat in the control group received 1 ml of distilled water while in the treated group each animal received a single concentration of aqueous extract of *K. africana*. For this research, the initial limit concentration of 2000 mg/kg bw was selected from the following concentrations: 50, 100 and 2000 mg/kg bm. Each rat received 1ml/100 g body mass with a concentration of 2,000 mg/kg mc of aqueous substance of *K. Africana* orally using an appropriate gastric catheter.

After treatment, the animals were examined separately, at least once during the first 30 min and regularly during the first 2 days. Four hours after access to food, the animals were examined again for possible toxicological signs. Daily, for 2 weeks, the animals were observed. Signs such as tremor, convulsion, salivation, diarrhea, lethargy, sleep, coma and death have been noted. The skin, hair, eyes and mucous membranes, as well as the respiratory system were analyzed. The animals were finally skinned and vital organs such as the liver, kidney, heart and lungs were removed and their mass determined.

2.6 Effects of subacute toxicity

Subacute toxicity was performed according to OECD guideline 407. A total of 20 rats, two months old with a mass of 120 to 140 g, were divided into four groups of 05 animals (5 rats/group). Group 1 received 1 ml/100 g mc (body weight) of distilled water while groups 2, 3 and 4 received respectively 50, 100 and 200 mg/kg mc of *K. africana* extract for 28 days. The animals were weighed every two days and their behavior was examined. On the last day of the experiment, the rats were sacrificed by headlessness following ether algesia. Organs such as the liver, kidney, heart and lungs were removed to determine their mass.

2.6.1 Determination of hematological parameters

A quantity of blood from each rat was collected in EDTA tubes and in dry tubes for the determination of hematological and biogenic parameters respectively. The hematological parameters were measured using a Sysmex R (Japan).

3. Results

3.1 Assessment of acute toxicity

No clinical signs of toxicity were observed during the 2 weeks of observation after treatment in a single oral concentration of 2000 mg/kg bw of aqueous substance of *K. africana*. These observations included drowsiness, salivation, tremor, convulsion, coma, lethargy, diarrhea, morbidity and mortality. According to guideline 423 of the Organization for Economic Co-operation and Development (OECD), the LD_{50} would be greater than 5000 mg/kg bw. Thus, the aqueous substance of *K. africana* would be classified in category 5, therefore unclassified, according to the classification of the harmonized globalization system (SHG). The aqueous extract of the bark of *K. africana* would therefore be non-toxic in à single dose.

3.11 Effect of *Kigelia africana* substance on the weight of rats during 14 days of treatment.

During the 02 weeks of administration, the gain in body mass of the rats varied from 0 to 30.28±4.16% and 31.42±2.60% respectively in the controls and the rats treated with *K. africana* product. Statistical analysis showed no significant difference (p>0.05) between the body mass gain of control rats and that of rats administered with aqueous substance of *K. africana* during the 14 days of treatment (Figure 1).

3.1.2 Effects of *Kigelia africana* substance on the weight of rat organs

The relative mass of the kidney of the rats having received the single concentration of 2000 mg/kg of mc of the aqueous substance of *K. africana* was 0.836±0.21 g/kg. This mass presents no significant difference (p> 0.05) compared to that obtained from the controls which was 0.876±0.20 g/kg.

At the liver level, the mass in animals administered with the aqueous substance of *K. africana* was 3.83±1.580g/kg. This result reveals no significant difference (p>0.05) between the mass of the treated rats and that of the control rats whose mass value was 2.91±1.032 g/kg.

Regarding the heart, administration of the aqueous substance of *K. africana* gave a mass of 0.454±0.44g/kg. This result revealed no significant difference (p> 0.05) between the heart mass of the treated rats and that of the control rats, the value of which was 0.465±2.90 g/kg.

3.2 Evaluation of subacute toxicity

No change in behavior of animals treated with different concentrations compared to controls was noted.

3.2.1 Effect of *Kigelia africana* products on the weight of rats during 04 weeks of administration

The results indicated that at the low concentration of 50 mg/kg bm, K. africana substance gives the smallest bm gain value of 11.75%. While at the highest concentration of 200 mg/kg mc, the value obtained was the highest with 12.95%. Furthermore, the statistical analysis showed that the gain in body mass obtained with the different concentrations of K. africana product is not statistically different from that of the control which is 13.86% (p>0.05), (Figure 2).

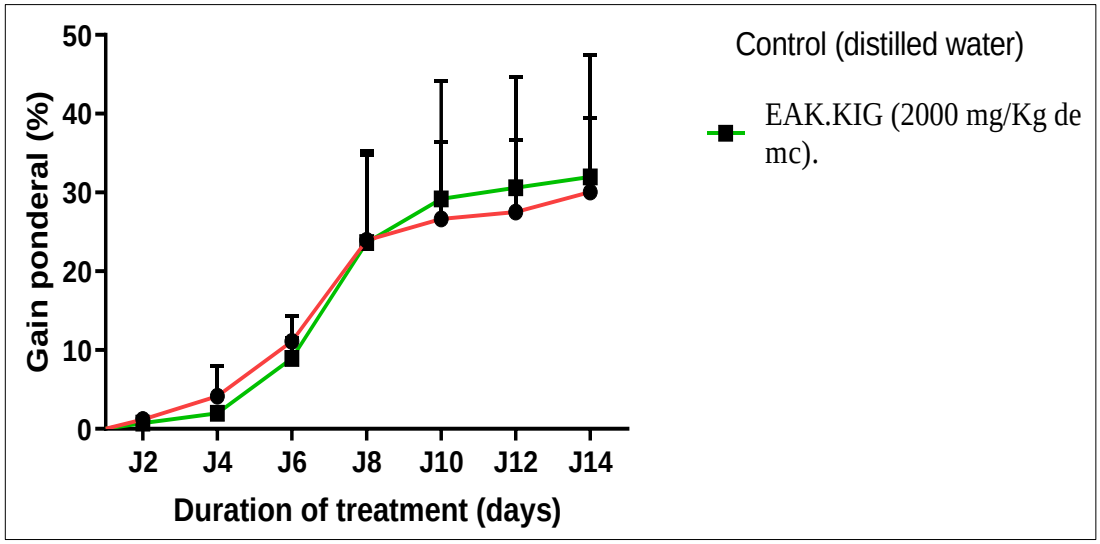
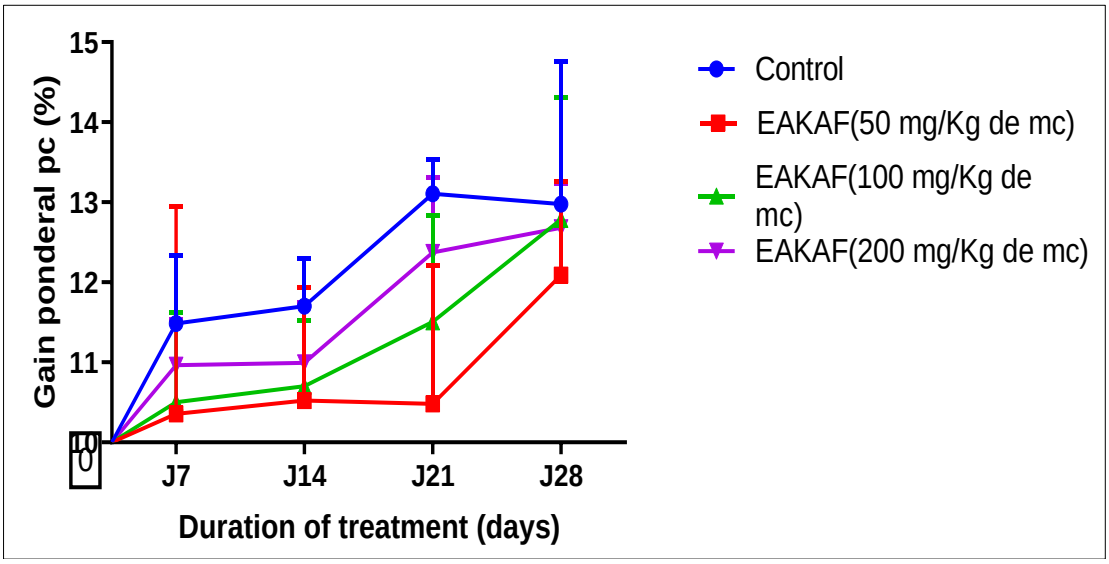


Fig 1: Effect of the aqueous substance of *K. africana* on the body mass of rats mc: body mass



EAKAF: Aqueous substance of *Kigelia africana*
MC: body mass

Fig 2: Effect of the different concentrations of the aqueous substance of *K. africana* administered orally on the body masses of adult rats

3.2.2 Effect of *Kigelia africana* products on the organs mass of rats after 28 treatment

Administration of the aqueous substance of *K. africana* led to a variation in kidney mass, going from 0.256±0.007 at the concentration of 50 mg/kg bw to 0.258±0.007g/100g bw at the concentration of 200 mg /kg of mc. Liver also varied from 3.373±0.049 at 50mg/kg bw to 3.285±0.065 g/100 g bw at 200mg/kg bw. The heart also varied respectively from 0.338±0.008 at the 50 mg/kg bw concentration to 0.317±0.005 g/100 g bw at the 200mg/kg bw concentration and from 0.619±0.054 at 50mg/kg bw to 0.196±0.086 g/100g of mc to 200mg/kg of mc. As for the lung, the lowest concentration gave 0.619±0.054 g/100g at 50 mg/kg bw and 0.196±0.086 g/100g bw at the concentration of 200mg/kg bm. These results do not show a significant change (p>0.05) between the mass of the kidney, liver and heart compared to that of the control. On the other hand, the mass of the lung experienced a significant decrease compared to the control (Table 1).

Table 1: Effet of the aqueous substance of *K. africana* on the mass of the vital organs of rats after 04 weeks of treatment

Doses de *K. africana* (mg/kg de mc)	Kidneys	Liver	Heart	Lungs
0 (Control)	0,473±0,003	3,690±0,017	0,346±0,005	0,619±0,008
50	0,286±0,007	3,373±0,049	0,338±0,008	0,619±0,054
100	0,266±0,005	3,335±0,091	0,319±0,004	0,593±0,054
200	0,258±0,007	3,285±0,065	0,317±0,005	0,196±0,086**

The values bearing the "*" sign in each column indicate a significant change with a significance level of 5% in the ANOVA test. Turkey's multiple comparison was used to separate differences between different cocentration when a difference is observed.

3.3 Effects of the aqueous substance of *K. africana* on hematological parameters

The hematological parameters which are white blood cells, red blood cells and hematocrit level in the rats having obtained the aqueous substance of *K. africana* at a concentration of 50 mg/kg of mc were respectively 12.17±0, 31 × 103/ml,

8.17±0.31 × 106/ml and 14.11±0.36 g/dl. At the concentration of 100 mg/kg of mc these parameters were respectively 12.17±0.27 × 103/ml, 8.17±0.90 × 106/ml and 15.45±0.32 g/dl. As for the concentration of 200 mg/kg of mc the values obtained were respectively 12.37±0.74 × 103/ml, 8.37±0.63 × 106/ml and 15.80±0.69 g /dl. All capacities administered (50, 100 and 200 mg/kg bw) did not induce any significant variation (p> 0.05) in the hematological parameters of the treated rats compared to their respective controls 10.20±0.74 × 103/ml, 7.09±0.11 × 106/ml and 14.12±0.52 g/dl. Likewise, the mean globular volume, the corpuscular content and the mean corpuscular hemoglobin concentration in animals administered with the aqueous product of *K. africana* at a concentration of 50 mg/kg of mc gave respectively 53.38±0, 97 fl, 16.74±0.92 pg and 32.42±0.42 g/dl. At the concentration of 100 mg/kg mc, it was obtained respectively 54.18±0.42 fl, 16.37±0.67 pg and 32.87±0.77 g/dl. The concentration of 200 mg/kg mc gave 54.92±0.49 fl, 17.00±0.31 pg and 33.93±0.66 g/l respectively. These different values presented no significant variation (p> 0.05) compared to those of the respective controls whose values were 52.80±0.88 fl, 15.92±0.89 pg and 32. 02±94.07 g/dl respectively. In contrast, blood platelet levels were 793.87±140.34 × 103/ml, 995.00±109.19 × 103/ml and 1094.97±103/ml in rats treated at the respective capacities 50, 100 and 200 mg/kg mc of *K. africana* extract. These levels are highly significant (p> 0.05) compared to that of the controls which is 793.87±100.97 × 103/ml (Table 2).

Table 2: Effet of the aqueous substance of *K. africana* on hematological parameters in rats after 28 days of administration

Doses de (*K. africana*) (mg/kg.mc)	G.B (×10°3/ ml)	G.R. (×10°6/ml)	H.G (g/dl)	HCR (%)	VGM (fl)	TCMH (pg)	CCMH (g/dl)	PLQ (10°3/ml)
0 (témoin)	10,20±0,74	7,09±0,11	14,12±,52	45,59±0,87	52,80±0,88	15,92±0,89	32,02±94,07	793,87±172,39
50	12,17±0,31	8,17±0,31	14,11±0,36	46,00±0,81	53,38±0,97	16,74±0,92	32,42±0,42	794,25±140,34
100	12,17±0,27	8,17±0,90	15,45±0,32	46,91±0,35	54,18±0,42	16,37±0,67	32,87±0,77	995,00±109,19*
200	12,37±0,74	8,37±0,63	15,80±0,69	47,00±0,37	54,92±0,49	17,00±0,31	33,93±0,66	1094,85±100,97*

The values bearing the "*" sign in each column indicate a significant change with a significance level of 5% in the ANOVA test. Turkey's multiple comparison was used to separate differences between different capacities when a difference is observed.

3.4 Effect of the aqueous substance of *K. africana* on biochemical parameters

The creatinine levels were 0.70±0.04 g/l, 0.65±0.06 g/l and 0.56±0.06 g/l in the rats having received the respective concentrations of 50, 100 and 200 mg/kg mc of product. The urea values were 0.463±0.058 g/l, 0.3850±0.080g/l and 0.344±0.070 g/l at these same concentrations. As for glycerol, the values were 0.46 3±0.058 mmol/l, 0.562±0.040 mmol/l and 0.812±0.057 mmol/l. These nephrotic parameters in rats administered with different capacities of aqueous substance of *K. africana* presented a significant decrease (p< 0.05) compared to their respective controls 0.123±0.034mmol/l (Table III). The lipid and protein parameters of the rats treated with different previous concentrations of *K. africana* substance, showed no significant difference (p > 0.05) between the levels of cholesterol, Total protein and HDL compared to their respective controls. Furthermore, a highly significant increase (p<0.001) in the triglyceride level was examined in animals administered at concentrations of 100 and 200 mg/kg bw compared to that of the controls (Table 4).

Table 3: Effects of different concentrations of aqueous substance of *K. africana* on nephrotic parameters in rats after 04 weeks of administration

Doses (mg/kg de mc)	CREAT (g/l)	UREE (g/l)	A U (mg/l)	GLY (mmol/l)
0 (Control)	0,992±0,033	0,871±0,740	5,97±0,170	0,123±0,034
50	0,706±0,043*	0,463±0,058*	5,585±0,064	0,463±0,058*
100	0,659±0,060*	0,385±0,080*	5,692±0,033	0,562±0,040*
200	0,565±0,065*	0,344±0,070*	5,047±0,020	0,812±0,057*

Values were expressed as the mean±Error of the Mean (ESM). The Turkey test used allowed comparisons to be Controls. *: significant change at p<0.05; The absence of an asterisk on the values indicates that there is no significant difference p>0.05., A. uric acid: Uric acid; CREAT: Creatine; A U: Uric acid., GLY: Glycerol; E.D: Distilled water.

Table 4: Effects of different concentrations of aqueous substance of *K. africana* on protein and lipid parameters in rats

Dose (mg/kg de mc)	CHOL (g/l)	TG (g/l)	PT (g/l)	HDL (g/l)
0 (Témoin)	0,97±0,052	0,887±0,059	83,858±1,733	0,77±0,020
50	0,984±0,061	0,976±0,141	84,316±4,501	0,802±0,193
100	0,99±0,033	1,299±0,024	85,291±1,893	0,841±0,936
200	0,99±0,034	1,883±0,073	85,808±4; 348	0,92±0,109

Data were expressed as the mean±Error of the Mean (ESM). The Turkey test was used to make differnces to Controls. *: significant difference at p<0.05; not having an asterisk on the numbers shows that there is no significant change p > 0.05; HDL: High density lipoprotein; Tg: Triglyceride; TP: Total Protein; CH0L: Cholesterol.

The liver parameters of Aspartate Amino-Transferase, Alamine Amino-Transferase, Total Bilirubin and Conjugated Bilirubin were determined in rats treated at concentrations of 50, 100 and 200 mg/kg bw of the substance aqueous of *K. africana*. The analysis revealed no significant change (p>0.05) between the parameters of the treated and those of the controls (Table 5).

Table 5: Effects of different concentrations of aqueous product of *K. africana* on liver parameters in rats after 04 weeks of treatment

Dose (mg/kg de mc)	ASAT (UI/l)	ALAT (UI/l)	BT (mg/l)	BC (mg/l)
0 (Témoin)	172,350±4;283	50,85±0,025	6,315±0,028	1,741±0,104
50	173,375±3,072	50,962±7,438	6,415±0,080	1,834±0,065
100	174,5±3,625	50,975±2,797	6,519±0,060	1,884±0,077
200	174,992±2,798	51,087±3,078	6,523±0,068	1,994±0,065

The absence of an asterisk on the data in the same vertical show that there is no significant difference p > 0.05. ALT: Alanine-Amino transferase; ASAT Aspartate amino transferase; BT: Total bilirubin; B.C: Conjugated Bilirubin

4. Discussion

The treatment of the unique concentration of 2000 mg/Kg mc of *Kigelia african* product a to rats in the toxicity study, did not cause any change in behavior, no sign of intoxication. In addition, no mortality was recorded during the 2 weeks of the trial. The substance of *K. africana* would therefore not be toxic in a single concentration of 2000 mg/kg of mc. After 02 weeks of the acute toxicity evaluation test, the LD_{50} of the *K. africana* substance would be above 5000 mg/kg of body weight orally. According to the globally harmonized classification system OECD (2001) [12], *K. africana* product can be in category 5 or unclassified. Several other authors have also shown in certain plants that the LD_{50} would be above 5000 mg/kg of body weight after oral administration. This is the case of Blahi (2017) [13] who showed that the LD_{50} of the leaves of the Sarcocephalus latifolius plant (Rubiaceae) would be greater than 5000 mg/kg bw. Kouakou *et al.* (2018) [14] also showed that the LD_{50} of the leaves of the Moringa oleifera plant (Moringaceae) would be above 5000 mg/kg bw.

The body mass gain of rats treated at different concentrations (50, 100 and 200 mg/kg body mass) of *Kigelia africana* has not indicated any significant change compared to that of control rats. This result shows that the unique concentration of 2000 mg/Kg body mass of the aqueous substance of *K. africana* would not influence the body mass of the treated rats.

The relative mass of the organs also revealed no significant variation ($p>0.05$) compared to the control at the end of the 2 weeks of observation. This result also shows that the unique concentration of 2000 mg/Kg body mass of the aqueous substance of *K. africana* would have no impact on organ mass. Subacute toxicity concerns harmful effects due to the repetition of concentrations which would produce toxic effects in the long term. According to OECD (1979) [15] due to accumulation of the product in the tissues or by other mechanism, late effects may occur. Daily administration for 28 days orally at repeated concentrations of the aqueous substance of *K. africana* showed no significant modification on the evolution of the body mass of the treated rats. This observation could indicate that the extract did not modify the metabolic processes of the treated animals which could subsequently affect body mass. The same results were also obtained by Zougrou *et al.* (2018) [16] who indicated that with the concentrations of 50 and 100 mg/kg bw of the aqueous substrance of *Cnestis ferruginea* (Connaraceae) applied to rats for 30 days, no No harmful effect was observed and the metabolic processes of the treated animals were similar to controls.

The analysis of the hematological parameters of rats treated with the aqueous substance of *K. africana* revealed no significant modification ($p>0.05$) of the different variables (the number of white blood cells (WBC), red blood cells (RBC), hemoglobin (HG), hematocrit rate (HCR), mean corpuscular volume (MCV), mean corpuscular hemoglobin content (TCMH) and mean corpuscular hemoglobin concentration (CCMH)). Conversely, a significant change ($p<0.05$) in blood platelets (PLQ) was noted. For the level of blood platelets, their increase could reveal the anti-infectious immune effect of *K. africana* products. Blood platelets are, in fact, sentinel cells which contribute significantly to anti-infectious immunity (Chabert *et al.*, 2017) [17]. Furthermore, *K. africana* due to its high flavonoid content, shows its ability to modulate megakaryopoiesis, which is the system of production and regulation of platelets (Roegsumran *et al.*, 2000) [18]. These results are the same with those work of Alrawaiq and Abdullah (2014) [19] who showed that following the oral administration of quercetin to rats, the level of blood platelets increased.

Analysis of biochemical parameters showed a significant drop ($p<0.05$) in urea and creatinine levels. These effects obtained are similar to those of the work of Narhari *et al.* (2015) [20] in the study of the acute and subacute toxicity of Terminalia citrina leaf substance. On the other hand, no significant variation was observed in ALT and AST levels. Indeed, ALT is a specific liver enzyme in dogs, cats, rabbits, primates and rats (Farah *et al.*, 2011) [21]. It can provide a quantitative assessment of the degree of damage suffered by the liver (Hilaly *et al.*, 2004) [22]. As for AST, in addition to the liver, it is also present in the heart, skeletal muscles, lungs and kidneys. It is also an indicator of the destruction of hepatocytes. (Bleu *et al.*, 2011) [23]. The reduction in urea and creatinine levels and the non-variation of AST and ALT in the present study therefore indicates that the aqueous substrance of *K. africana* at the doses studied does not cause any toxic effects on the liver and kidney, or heart damage.

Triglycerides are reserve lipids. They are provided by food or produced in hepatocytes from sugar and alcohol when these are found in high quantities in the diet (Bidié *et al.*, 2011) [24]. An increase in their serum concentration above 150 mg/dl may be a sign of hyperlipidemia, cholestasis, pancreatitis, nephrotic syndrome, administration of glucocorticoids. Indeed, high serum triglyceride concentrations constitute a major danger for heart disease and diabetes (Cornus, 2010) [25]. The triglycerides of animals administered the aqueous product of *Kigelia africana* at different capacities showed no significant change compared to those of control animals. Likewise, the serum concentration of triglycerides in those treated is below the normal serum concentration. Therefore, the extract could have cardioprotective effects. The cardioprotective effect could be explained by the richness of *K aficana* substance in alkaloids. Indeed, alkaloids have the concentrations to positively influence the cardiovascular system by reducing fat mass (Schmeda-hirschmann *et al.*, 2000) [26]. These results are identical to those obtained by Pillai *et al.* (2011) [27] who after administration of the substance of Plectranthus amboinicus (Lamiaceae) observed no significant variation in serum triglyceride concentration. Zougrou *et al.*, (2018) [16] noticed contrary results in the research of the aqueous substance of *Cnestis ferruginea* leaves.

The cholesterol level of the different groups of treated animals did not cause any significant modification comparatively to the controls. However, this rate remains high in animals treated at concentrations of 100 and 200 mg/kg mc of the aqueous substance compared to those of control animals. The increase

in cholesterol observed, particularly in animals treated at both concentrations (100 and 200 mg/kg bw), would probably be justified by the action of secondary metabolites present in the aqueous substance, which activates the release of cholesterol at level of adipose tissue and fat. Cholesterol is subsequently converted into steroids like estradiol and progesterone. These steroid hormones are synthesized by a common precursor, cholesterol. Blahi (2017) [13] observed the same results in the study of the effects estrogenic of Sarcocephalus latifolius. On the other hand, these are distinct differ from those of Ngoungoure *et al.* (2018) [28] who obtained a reduction in cholesterol levels in animals treated with aqueous products of Anthocleista schweinfurthii compared to those treated only with estradiol.

5 Conclusion

The study of the acute toxicity of the aqueous substance of the bark of *K. africana* carried out according to OECD guideline 423 did not show any apparently toxic sign on the behavior and on the vital organs of rats at concentration limit of 2000 mg/Kg of mc. The LD_{50} was therefore estimated to be greater than 5000 mg/Kg of mc. The evaluation of subacute toxicity through OECD guideline 407 at concentrations of 50, 100, 200 mg/kg bw did not generally show any sign of toxicity both in terms of behavior and physiological level, after 28 days of administration. From these results, it appears that the aqueous substance of *K. africana*, although made up of several secondary metabolites, would not be toxic orally. The product did not cause any variation in cholesterol levels and HDL levels. This shows that the product would have a nephroprotective and cardioprotective effect. These results obtained with the aqueous substance of *K. africana* would justify on the one hand the use of this plant in popular medicine.

6. Reference

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