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Influence of an aqueous extract of *Sacoglottis gabonensis* (Baille) urban (Humiriaceae) stem bark, a plant used in the traditional treatment of Buruli ulcer, on anthropometric and hematological parameters in Wistar rat

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Abstract
Sacoglottis gabonensis is a medicinal plant used in the treatment of Buruli ulcer in Côte d'Ivoire. The stem bark aqueous extract of this plant has a lethal dose 50% (LD_{50}) higher than 5000 mg/kg body weight (b.w.) in mice and is nontoxic for rats when administered subacutely. To assess the subchronic toxicity of this extract, it is administered, by oral route, daily for 90 days to rats at the doses of 3.5; 35 and 350 mg/kg b.w. while the control group rats were gavaged with distilled water. The amounts of food and water consumed by rats were monitored every day. The rats were weighed once per week. Blood samples and blood smear were taken at the end of every month. Results showed that *S. gabonensis* extract (3.5 and 35 mg/kg b.w.) did not influence anthropometric parameters while a significant decrease of these parameters was observed in the rats treated with the dose of 350 mg/kg b.w. of this extract. Administration of the extract did not alter most of the hematological parameters. However, all the doses of *S. gabonensis* extract increased thrombocyte levels and neutropenia at 350 mg/kg b.w. only. The blood smear didn't show any abnormality in erythrocyte cells' size, shape and staining of the rats treated with *S. gabonensis* stem back extract. In sum, this study revealed that the aqueous extract of *S. gabonensis* stem bark is nontoxic on blood cells, at a therapeutic dose 3.5 mg/kg b. w. for 90 days-administration in rats.

Keywords: *Sacoglottis gabonensis*, subchronic toxicity, anthropometric parameters, hematological parameters, rat

1. Introduction
Buruli ulcer is a public health problem, despite advances in modern medicine [24-16]. This skin disease caused by *Mycobacterium ulcerans* is particularly observed in West Africa where the prevalence is about 50% with the majority of cases are children [19]. Côte d'Ivoire is one of the most endemic country with over 2000 new cases per year [9]. Indeed, the National Buruli Ulcer Control Program, in Côte d'Ivoire (PNLUB), reported 25,617 cumulative cases from 1978 to 2006 [20]. Moreover, in 2008, The World Health Organization reported about 30,000 cases in Côte d'Ivoire [18]. In order to discover new molecules likely to treat this pathology, research has been initiated on *Sacoglottis gabonensis* (Humiriaceae). It's traditionally used in the treatment of Buruli ulcer in Côte d'Ivoire. *S. gabonensis* is a tree about 25 m high with dark and rough barks. It is widespread in rain forests in both west and central Africa [2]. At the ethnobotanical level, the treatment of Buruli ulcer with *Sacoglottis gabonensis* consists in using the decoction of the stem bark of the plant as a drink and in local application [23]. In addition, the aqueous extract of stem bark of this plant had an inhibitory effect on different strains of *Mycobacterium ulcerans* [10]. In addition, the acute and subacute toxicity tests performed in mice and rats respectively, showed that this extract has an LD_{50} higher than 5000 mg/kg b.w. These tests also showed that it promotes an increase in thrombocytes during the third and fourth weeks of administration [11]. This work aims at further studying subchronic toxicity of the aqueous extract of the stem bark of *Sacoglottis gabonensis* by assessing its effects on anthropometric and hematological parameters for 90 days in Wistar rats.

2. Material and Methods

2.1 Plant material

The stem barks of *S. gabonensis* were harvested in November 2016, in Ingrakon, in the department of Alépé, located about 45 km far from Abidjan. A sample was identified and kept at the herbarium of the National Floristic Center of Abidjan (Côte d'Ivoire), under the number of 131.

2.2 Animal

Albino rats, *Ratus norvegicus*, aged from six to eight weeks and weighing between 73 and 103 g were used. The rats were raised in the animal house of the Laboratory of Physiology, Pharmacology and Pharmacopoeia of Nangui Abrogoua University according to the good practices of the laboratory [17] at a temperature of 22° C ± 2. They were exposed to 12 h dark/light cycle and fed with IVOGRAIN® pellets food and given water *ad libithum.*

2.3 Preparation of the stems bark aqueous extract of *Sacoglottis gabonensis*

The aqueous extract is prepared according to the method described by Koné *et al.* [11]. The fresh stem barks of *S. gabonensis* were harvested, carefully cleaned and then dried for three weeks at room temperature (25 °C±2). The dried barks were powdered using an electric grinder (Mark Culatti, France). Four hundred grams (400 g) of stem bark powder were mixed with 2 L of distilled water, then the whole were boiled for 30 minutes. The decoction obtained was filtered on hydrophilic cotton and Whatman filter paper (n°1). Water was evaporated and the extract was dried using an oven (Mark J.P. Selecta S. Spain) at 50 °C for 48 hours. A quantity of 31 g of black-brown powder with a yield of 7.75% is obtained and stored in a refrigerator at 7 °C until use.

2.4 Subchronic toxicity study

Guideline 408 of OECD [17] was used to evaluate subchronic toxicity of the stem bark aqueous extract of S. *gabonensis*. Thus, eighty (80) rats were randomly divided into 4 batches of 20 rats each including three test groups and one control group. Each group contained ten males and ten females. A solution volume of 2 mL/100 g b.w. is administered to the rats orally. The control group (A) received distilled water. Batches B, C and D received respectively 3.5; 35 and 350 mg/kg b.w. of the stem bark aqueous extract of *S. gabonensis*. The dose of 3.5 mg/kg b.w. was the therapeutic dose of the traditional practitioner. Satellite group containing ten rats in the batch A and ten rats in batch D were added in order to check the reversibility, the persistence or late onset of toxic effects 30 days after stopping administration.

2.5 Determination of anthropometric parameters

Consumption of food and water are determined daily. Weighing is done at the end of each week of administration.

2.6 Blood samples

Under ether anesthesia, blood was obtained from the rats' retro-orbital sinus using a sterile pipette before any treatment every month [13]. Blood were taken in all the rats before the administration of the different doses, then monthly. The blood samples were collected in tubes containing Ethylene Diamine Tetra acetic (EDTA) for hematologic parameters analyses using an autoanalyser (Sysmex XT-2000i, Japan) and blood smears stained with May-Grünwald Giemsa.

2.7 Statistical analyzes

The results obtained were statistically analyzed using Graph pad Prism software version 5.01 [7]. The results for the anthropometric parameters and the quantitative aspect of the hematological parameters are presented as an average followed by the standard error on the mean (SEM). They are analyzed from the repeated two-way ANOVA followed by the Bonferroni post-hoc test. Differences are significant for $p<0.05$. Asterisk (*, **, ***) express significant decrease while the letters (a, b, c) indicate significant increases compared to the controls.

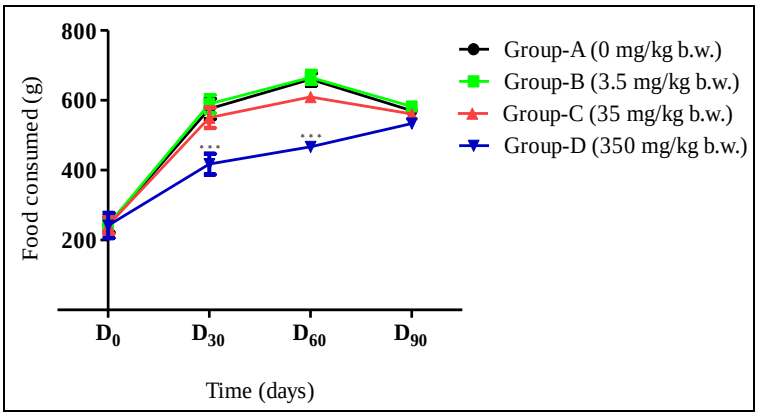
3. Results

3.1 Effect of the aqueous extract of *Sacoglottis gabonensis* stem bark on anthropometric parameters

3.1.1 Effect on food and water consumption

The results of the effects of the aqueous extract of *S. gabonensis* on feed and water consumption are recorded in Figures 1 and 2 respectively.

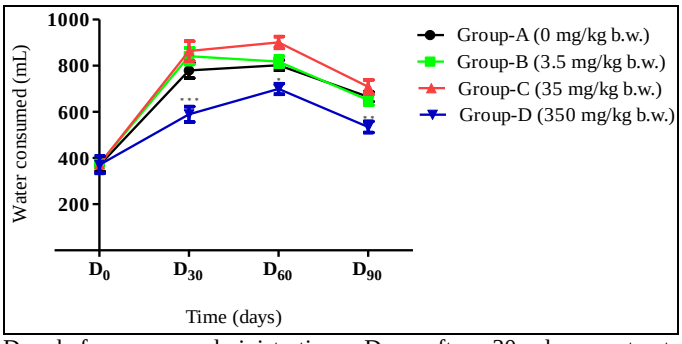
The amount of food consumed by rats receiving distilled water (Group A) increased from 242.8 ± 20.75 to 570.5 ± 5.42 during the 90 days of the study with peak consumption of 660 ± 17.76 at D_{60}. Extract doses of 3.5 and 35 mg/kg b.w. did not have significant effects ($p>0.05$) on food consumption. In contrast, this parameter was significantly decreased ($p<0.001$) in rats group daily administered with 350 mg/kg b.w. of *S. gabonensis* (Fig 1).



D_0: before any administration; D_{30}: after 30 days extract administration; D_{60}: after 60 days extract administration; D_{90}: after 90 days extract administration; n = 20; *** = $p<0.001$.

Fig 1: Effects of the aqueous extract of *Sacoglottis gabonensis* stem bark on food consumption

Concerning water consumption, control rats group increased their intake from 368.6 ± 27.4 mL (D_0) to 665.5 ± 20.73 mL (D_{90}) with a peak of 802.3 ± 22.06 mL at D_{60}. The doses of 3.5 and 35 mg/kg b.w. of *S. gabonensis* administered to rats do not influence water intake. As for the rats tested with the dose of 350 mg/kg b.w. of this extract, water consumption is decreased significantly (p<0.001) and reached only 699.3 ± 23.15 mL on day 60 (Fig 2).

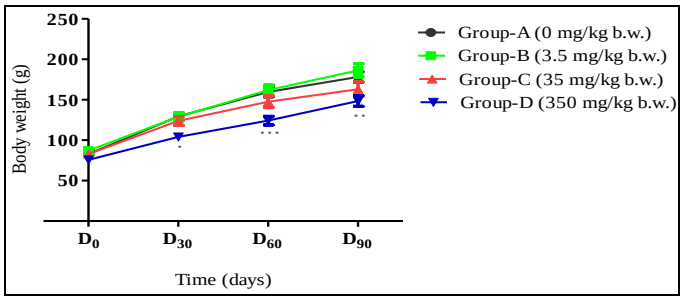


D_0: before any administration; D_{30}: after 30 days extract administration; D_{60}: after 60 days extract administration; D_{90}: after 90 days extract administration; n = 20; * = p<0.05; ** = p<0.01; *** = p<0.001

Fig 2: Effects of the aqueous extract of *Sacoglottis gabonensis* stem bark on rats' water consumption over time.

3.1.2 Effect on rats' body weight

The results of the effect of *S. gabonensis* aqueous extract on the increase of rats' body weight show that those administered with distilled water vary from 82.9 ± 4.98 g (D_0) to 178.3 ± 6.25 g (D_{90}). Except the dose of 350 mg/kg b.w. of *S. gabonensis* which significantly reduces (p<0.01) weight gain, those of 3.5 and 35 mg/kg b.w. have no significant effect (p>0.05) compared to the control group (Figure 3).



D_0: before any administration; D_{30}: after 30 days extract administration; D_{60}: after 60 days extract administration; D_{90}: 90 days extract administration; n = 20; * = p<0.05; ** = p<0.01; *** = p<0.001.

Fig 3: Effects of the aqueous extract of *Sacoglottis gabonensis* stem bark on rats' body weight.

3.2 Effect of aqueous extract on hematological parameters

3.2.1 Effect of aqueous extract on erythrocyte and erythrocyte parameters

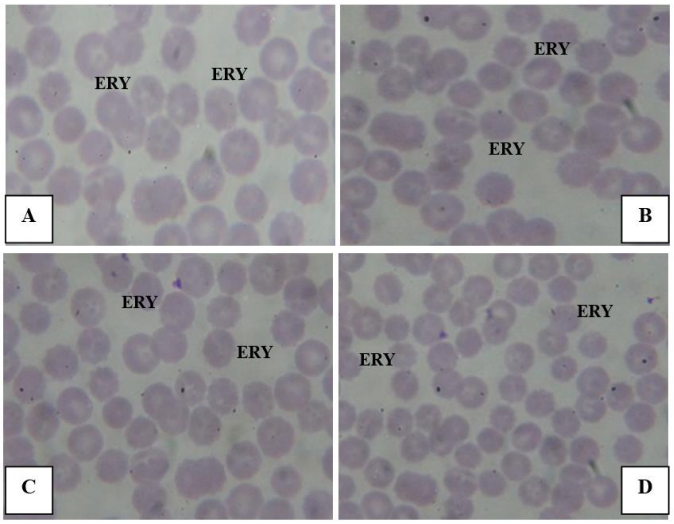
Administration of the aqueous extract of *S. gabonensis* stem barks had no significant effect on erythrocyte levels and the other erythrocyte parameters of the tested groups (3.5; 35 and 350 mg/kg b.w.) when compared to control groups after 30, 60 and 90 days of administration (Table 1). In fact changes in Hemoglobin (Hb), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC) values were generally insignificant compared to controls.

Regarding the reticulocytes, their rate has had the same evolution as controls, at all doses of the aqueous extract (Table 1). In terms of the qualitative aspect of the cells of the erythrocyte line, results didn't show any significant effect of the extract. In fact, the erythrocyte cells in blood samples of treated rats groups kept their size, their color and their shape to those of the control group (Fig 4).

Table 1: Effect of the aqueous extract of *Sacoglottis gabonensis* stem bark on rats' erythrocyte parameters

Erythrocyte parameters	Doses (mg/kg b.w.)	Administration time (Days)			
		D_0	D_{30}	D_{60}	D_{90}
Erythrocyte (10^6/mm^3) (NS)	0	7.63 ± 0.22	7.47 ± 0.11	8.08 ± 0.17	7.73 ± 0.15
	3.5	7.84 ± 0.33	7.88 ± 0.10	8.19 ± 0.15	7.88 ± 0.15
	35	7.38 ± 0.42	7.88 ± 0.11	7.92 ± 0.12	7.43 ± 0.29
	350	8.22 ± 0.24	7.72 ± 0.10	7.72 ± 0.12	7.74 ± 0.12
Reticulocytes (%) (NS)	0	2.58 ± 0.07	3.45 ± 0.17	4.61 ± 0.49	5.18 ± 0.55
	3.5	2.55 ± 0.07	3.10 ± 0.16	4.49 ± 0.42	5.06 ± 0.55
	35	2.86 ± 0.15	2.92 ± 0.16	4.39 ± 0.45	4.96 ± 0.45
	350	2.80 ± 0.14	2.83 ± 0.14	4.38 ± 0.49	4.96 ± 0.37
Hemoglobin (g/dL) (NS)	0	12.53 ± 0.34	12.91 ± 0.20	13.95 ± 0.16	13.38 ± 0.16
	3.5	12.72 ± 0.44	13.50 ± 0.16	13.80 ± 0.23	13.53 ± 0.17
	35	11.90 ± 0.68	13.48 ± 0.12	13.19 ± 0.23	12.74 ± 0.18
	350	13.28 ± 0.34	12.83 ± 0.15	13.24 ± 0.21	13.15 ± 0.20
Hematocrit (%) (NS)	0	40.49 ± 1.14	40.79 ± 0.56	44.93 ± 0.79	41.42 ± 0.46
	3.5	40.70 ± 1.59	42.02 ± 0.47	44.29 ± 0.66	41.21 ± 0.50
	35	38.21 ± 2.11	42.62 ± 0.41	44.07 ± 0.67	38.96 ± 1.17
	350	41.93 ± 0.86	40.84 ± 0.40	42.79 ± 0.59	39.72 ± 0.47
MCV (fL) (NS)	0	53.17 ± 0.58	54.66 ± 0.45	55.71 ± 0.55	53.68 ± 0.65
	3.5	52.25 ± 0.55	53.37 ± 0.42	54.16 ± 0.55	52.47 ± 0.62
	35	52.62 ± 0.91	54.70 ± 0.51	55.69 ± 0.41	53.36 ± 1.37
	350	51.26 ± 0.64	53.01 ± 0.62	55.55 ± 0.77	51.43 ± 0.60
MCH (Pg) (NS)	0	16.47 ± 0.17	17.29 ± 0.15	17.38 ± 0.38	17.32 ± 0.19
	3.5	16.61 ± 0.51	17.14 ± 0.12	16.86 ± 0.17	17.22 ± 0.20
	35	15.75 ± 0.42	17.38 ± 0.14	17.43 ± 0.15	18.43 ± 1.33
	350	16.19 ± 0.20	16.63 ± 0.19	17.18 ± 0.21	17.02 ± 0.20
MCHC (g/dL) (NS)	0	31.00 ± 0.25	31.63 ± 0.15	31.21 ± 0.55	32.30 ± 0.16
	3.5	31.70 ± 0.69	32.13 ± 0.12	31.14 ± 0.13	32.82 ± 0.15
	35	30.21 ± 0.96	31.79 ± 0.14	31.32 ± 0.23	33.07 ± 0.34
	350	31.63 ± 0.24	31.39 ± 0.12	30.92 ± 0.16	33.13 ± 0.20

The values are expressed as means ± standard error on the mean; n = 20; NS: Not significant (p>0.05); D_0: before any administration; D_{30}: after 30 days extract administration; D_{60}: after 60 days extract administration; D_{90}: after 90 days administration; MCV: Mean Corpuscular Volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration.



ERY: Erythrocytes; **A:** Erytrocytes of group-A (0 mg/kg b.w.); **B**: Erythrocytes of group-B (3.5 mg/kg b.w.); **C**: Erythrocytes of group-C (35 mg/kg b.w.); **D**: Erythrocytes of group-D (350 mg/kg b.w.). Magnification × 100.

Fig 4: Effects of the aqueous extract of *Sacoglottis gabonensis* stem bark on rats' red blood cells

3.2.2 Effect of the aqueous extract of *Sacoglottis gabonensis* stem bark on leukocyte and thrombocyte count

The aqueous extract did not cause any significant (p>0.05) changes in the leukocyte, eosinophils, basophils, lymphocyte and monocyte levels of treated rats groups compared to the control. However, neutrophil count decreased significantly (p<0.05) in rats treated with 35 mg/kg b.w. of the extract compared to value of rats in control group (Table 2).

The thrombocyte level significantly increased (p<0.05) at day 30 and day 60 before normalizing at day 90 at all doses compared to controls (Table 3).

3.3 Reversible and delayed effects of the aqueous extract of *Sacoglottis gabonensis* stem bark

At the high dose of 350 mg/kg b. w., after stopping the administration of the aqueous extract, some hematological parameters which were not disturbed compared with those of the controls, were modified. Thus, a significant decrease in hemoglobin (p<0.05) and hematocrit (p<0.01) levels, followed by a significant increase in leukocyte (p<0.01), lymphocyte (p<0.001) and monocytes (p<0.05) were found (Table 4). However, erythrocytes observed on blood smears after discontinuation of administration retained their size, staining, and shape relative to controls

Table 2: Effect of the aqueous extract of *Sacoglottis gabonensis* stem bark on leukocytes

parameters	Doses (mg/kg b. w.)	Administration time (Days)			
		D_0	D_{30}	D_{60}	D_{90}
LEU (10^3/mm^3) (NS)	0	17.97 ± 1.14	18.22 ± 1.16	19.84 ± 1.03	19.00 ± 0.74
	3.5	19.72 ± 1.16	19.24 ± 1.19	19.10 ± 1.08	17.03 ± 0.62
	35	19.79 ± 1.70	20.13 ± 1.34	20.57 ± 1.48	19.04 ± 0.66
	350	20.43 ± 1.38	17.14 ± 1.43	17.57 ± 1.02	19.24 ± 1.60
PNN (10^3/mm^3) (S)	0	3.41 ± 0.40	3.46 ± 0.60	4.69 ± 0.62	4.30 ± 0.56
	3.5	4.32 ± 0.48	4.37 ± 0.65	4.57 ± 0.69	3.31 ± 0.44
	35	4.51 ± 0.51	5.50 ± 0.65	4.81 ± 0.74	3.39 ± 0.41
	350	3.52 ± 0.53	2.52 ± 0.70	2.47 ± 0.56*	4.24 ± 0.60
PNE (10^3/mm^3) (NS)	0	0.34 ± 0.06	0.63 ± 0.10	0.53 ± 0.06	0.55 ± 0.06
	3.5	0.45 ± 0.11	0.64 ± 0.09	0.59 ± 0.05	0.50 ± 0.06
	35	0.57 ± 0.11	0.58± 0.07	0.61 ± 0.08	0.53 ± 0.08
	350	0.59 ± 0.08	0.54 ± 0.06	0.53 ± 0.06	0.68 ± 0.16
PNB (10^3/mm^3) (NS)	0	0.12 ± 0.02	0.17 ± 0.05	0.14 ± 0.01	0.46 ± 0.08
	3.5	0.16 ± 0.03	0.20 ± 0.05	0.20 ± 0.02	0.30 ± 0.06
	35	0.12 ± 0.03	0.16 ± 0.02	0.31 ± 0.16	0.58 ± 0.07
	350	0.23 ± 0.06	0.17 ± 0.01	0.17 ± 0.02	0.56 ± 0.18
LYM (10^3/mm^3) (NS)	0	12.24 ± 0.48	12.46 ± 0.65	12.55 ± 0.66	12.15 ± 0.80
	3.5	12.86 ± 0.82	12.10 ± 0.89	12.21 ± 0.68	11.22 ± 0.57
	35	12.09 ± 1.22	12.46 ± 0.91	13.25 ± 1.03	12.80 ± 0.76
	350	12.41 ± 1.91	12.90 ± 1.02	11.68 ± 0.89	12.07 ± 0.94
MONO (10^3/mm^3) (NS)	0	1.87 ± 0.29	1.41 ± 0.17	1.93 ± 0.30	1.54 ± 0.20
	3.5	1.55 ± 0.31	1.36 ± 0.16	1.54 ± 0.11	1.54 ± 0.24
	35	2.51 ± 0.27	1.43 ± 0.18	1.93 ± 0.28	1.58 ± 0.19
	350	3.52 ± 0.52	2.07 ± 0.29	2.53 ± 0.34	1.96 ± 0.27

The values are expressed as means ± standard error on the mean; n = 20; NS: Not significant (p<0.05) compared to the control group; NS = Not significant (p>0.05); D_0: day before any administration; D_{30}: after 30 days extract administration; D_{60}: after 60 days extract administration; D_{90}: after 90 days extract administration; LEU: Leukocytes; PNN: neutrophils; PNE: eosinophils; PNB: basophils; LYM: Lymphocytes; MONO: Monocytes

Table 3: Effects of the aqueous extract of *Sacoglottis gabonensis* stem bark on rats' thrombocytes

Parameters	Doses (mg/kg b.w.)	Administration time (Days)			
		D_0	D_{30}	D_{60}	D_{90}
THR (10^3/mm^3)	**0**	554.4 ± 50.65	576.4 ± 47.80	556.6 ± 12.73	622.2 ± 24.60
	3.5	555.2 ± 38.66	774.9 ± 56.11^b	778.0 ± 24.58^c	555.1 ± 49.38
	35	470.8 ± 49.35	784.2 ± 37.00^b	796.9 ± 17.16^c	537.0 ± 48.53
	350	488.1 ± 38.19	748.2 ± 40.61^a	935.4 ± 25.58^c	515.0 ± 45.18

The values are expressed as means ± standard error on the mean; n = 20 rats; a = p<0.05; b = p<0.01; c = p<0.001; D_0: day before any administration; D_{30}: after 30 days extract administration; D_{60}: after 60 days extract administration; D_{90}: after 90 days extract administration; THR: Thrombocytes

Table 4: Hematological parameters of satellite rats 30 days after stopping the administration of the aqueous extract of *Sacoglottis gabonensis* stem bark

Hematological parameters	Doses (mg/kg b.w.)	Time	
		D_{90}	D_{120}
ERY (10^6/mm^3)	0	7.73 ± 0.15	9.01 ± 1.15
	350	7.74 ± 0.12	7.56 ± 0.13
Hemoglobin (g/dL)	0	13.38 ± 0.16	13.40 ± 0.28
	350	13.15 ± 0.20	12.57 ± 0.23*
Hematocrit (%)	0	41.42 ± 0.46	40.36 ± 0.65
	350	39.72 ± 0.47	37.79 ± 0.57**
MCV (fL)	0	53.68 ± 0.65	50.59 ± 0.87
	350	51.43 ± 0.60	50.05 ± 0.51
MCH (Pg)	0	17.32 ± 0.19	16.79 ± 0.22
	350	17.02 ± 0.20	16.63 ± 0.19
MCHC (g/dL)	0	32.30 ± 0.16	33.19 ± 0.24
	350	33.13 ± 0.20	33.25 ± 0.17
Reticulocytes (%)	0	5.18 ± 0.55	2.59 ± 0.11
	350	4.96 ± 0.37	2.59 ± 0.11
LEU (10^3/mm^3)	0	19.00 ± 0.74	20.46 ± 1.88
	350	19.24 ± 1.60	26.90 ± 1.56^b
PNN (10^3/mm^3)	0	43.00 ± 0.56	2.61 ± 0.24
	350	4.24 ± 0.60	2.66 ± 0.62
PNE (10^3/mm^3)	0	0.55 ± 0.06	0.73 ± 0.13
	350	0.68 ± 0.16	0.65 ± 0.13
PNB (10^3/mm^3)	0	0.46 ± 0.08	0.15 ± 0.02
	350	0.56 ± 0.18	0.25 ± 0.08
LYM (10^3/mm^3)	0	12.15 ± 0.80	16.27 ± 1.73
	350	12.07 ± 0.94	20.95 ± 1.67^c
MONO (10^3/mm^3)	0	1.54 ± 0.20	1.30 ± 0.27
	350	1.96 ± 0.27	2.38 ± 0.37^a
THR (10^3/mm^3)	0	622.2 ± 24.60	671.3 ± 41.21
	350	515.0 ± 45.18	669.3 ± 50.66

The values are expressed as means ± standard error on the mean; n = 20 rats; * = p<0,05; ** = p<0,01; a = p<0,05; b = p<0,01; c = p<0,001; D_{90}: after 90 days extract administration; D_{120}: after 120 days administration; ERY: Erythrocyte; MCV: Mean Corpuscular Volume; MCH: Mean corpuscular hemoglobin; MCHC: Means Corpuscular Hemoglobin Concentration; LEU: Leukocytes; PNN: neutrophils; PNE: eosinophils; PNB: basophils; LYM: Lymphocytes; MONO: Monocytes; THR: Thrombocytes.

4. Discussion

Anthropometric parameters results showed that the amount of food consumed by rats treated with 3.5 and 35 mg/kg b.w. of *Sacoglottis gabonensis* was closer to controls. However, a decrease in food consumption is observed in the rats treated with 350 mg/kg b.w. of the extract. This result indicates that at higher dose, the aqueous extract would inhibit the intake of food by the rats. Our results are similar to those obtained by Gatsing [5], which showed a decrease in food consumption in rats when they are fed with 300 mg/kg b.w. of the aqueous extract of *Allium sativum* Linn (Liliaceae). Administration of the extract did not influence water consumption by rats administered with S. *gabonensis* except those treated with 350 mg/kg b.w. which reduced their food intake. These results are similar to those of Salawu [21], who recorded a difference in water consumption in rats with the ethanolic extract of *Crossopteryx febrifuga* (Afzel.) (Rubiaceae) bark at 500 and 1000 mg/kg b.w. A Change in rats' body-weight is an indicator of the general health of animals. They reflect the good functioning or dysfunction of animals body [3]. The doses of 3.5 and 35 mg/kg b.w. of the aqueous extract of *S. gabonensis* stem barks had no influence on the rats' body weight during the study. These results partially confirm those reported by Koné [11], who showed that repeated administration of the total aqueous extract of *S. gabonensis* stem bark with the same doses to rats for 28 days doesn't affect their body weight. In contrast, the dose of 350 mg/kg b.w. of *S. gabonensis* stem bark lowered rats' body weight gain. Our results are similar to those of Gbogbo [6], which showed that daily administration of the aqueous extract of *Spondias mombin* L. (Anacardiaceae) stem bark for 28 days induced a decrease of rats.

Regarding the repeated administration of the aqueous extract of *S. gabonensis* stem bark on the hematological parameters for 90 days, no significant variation was observed in the erythrocyte and leukocyte cells. These results show that the aqueous extract of *S. gabonensis* stem bark would not disturb these cells. Our results are similar to those of Kouassi [12]. In fact, these authors revealed that the administration of the ethyl acetate extract of the leaves of *Holarrhena floribunda* (G. DON) Durand and Schinz (Apocynaceae) did not modify these parameters in the rats treated with 1000 mg/kg b.w. of the extract mentioned above for 28 days.

The probable toxicity of the extract were also assessed through rats' blood smear. Results revealed no abnormalities in size, shape and color of erythrocyte cells. Our results corroborate those of Agbaje [1], who showed a non-interfere with erythrocyte indices in a subchronic toxicity study of the aqueous extract of *Syzigium aromaticum* (L.) Merr. & Perry (Myrtaceae) in rats.

However, a significant decrease in neutrophils levels in rats treated with 350 mg/kg b.w. of *S. gabonensis*, is noted on the second month before normalizing on the third month of experimentation. Neutrophils reduction is an indicator of the

failure of the immune system predisposing to infections [15]. Thus, higher dose of the extract may act on the immune system function. This result differs from that of Maduka [14] who showed that the administration of this aqueous extract does not modify the neutrophils level in rats during their study on the influence of the aqueous extract of *S. gabonensis* stem bark on the side effects of 2.4-dinitrophenylhydrazine in blood and cellular metabolism.

Thrombocytes are the first cells which intervene in primary hemostasis in order to stop bleeding due to vascular injury [8]. This lesion leads to secretion of substances by platelets which promote their aggregation to stop bleeding [22]. Therefore, any significant change in thrombocytes levels would be responsible for hemostasis disorders. Administration of the aqueous extract of *S. gabonensis* stem bark days led to a significant increase in thrombocytes on the first two months. These results suggest that the aqueous extract could cause thrombocytosis in normal rats treated with this extract. They are similar to those obtained by Koné [11] who reported that daily administration of the aqueous extract of the stem bark of *S. gabonensis* for 28 days at doses of 3.5; 35 and 350 mg/kg b.w. induced thrombocytosis in rats. The absence of thrombocytosis observed at 90 days extract administration, shows that the action of the aqueous extract on the platelets is reversible. Debelo [4] also showed an absence of thrombocytosis with the aqueous extract of *Thymus schimperi* (Lamiaceae) leaves in rats tested at doses of 200 and 600 mg/kg b.w. for 90 days. After stopping the administration of 350 mg/kg b.w. *S. gabonensis* aqueous extract, some abnormalities such as anemia, leukocytosis, lymphocytosis and monocytosis persited. The effect of the aqueous extract of the stem bark of *Sacoglottis gabonensis* at this dose would therefore be late unlike some work done by Yao [25]. This author showed that after administration of the hydro-ethanolic and dichloromethanic extract of *Piliostigma reticulatum* stem barks at the dose of 500 mg/kg b. w., the effects were transient and vanished with time.

5. Conclusion

Oral administration of the extract of *Sacoglottis gabonensis* stem barks is nontoxic on anthropometric and hematological parameters in rats treated with the therapeutic dose of 3.5 mg/kg b.w. during 90 days administration. This plant is used in the treatment of Buruli ulcer, a chronic pathology. Hence, biochemical and histopathological studies should be supplemented in order to confirm its safety. These tests will be helpful in improved traditional drug manufactured against Buruli ulcer.

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7. References

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