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## Acute and sub-acute toxicity study of aqueous extract of *Pericopsis (Afrormosia) laxiflora* (Benth.) on white albino rats

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**Abstract**

Many plants investigated elsewhere were found to contain toxic substances. The objective of this study is to evaluate acute and sub-acute toxicity of aqueous extract of *Pericopsis laxiflora*, plant traditionally used to treat different diseases in Côte d'Ivoire. Acute toxicity of aqueous extract was assessed at a dose of 5000 mg/kg bw. For sub-chronic toxicity testing, Wistar rats were orally administered with different dose of the plant extract for 28 days. There was no mortality reported or any toxicity signs including autonomic effects in animals administered orally. The weights of the rats of the different batches increased over the 28 days after oral administration of the aqueous extract. Aqueous extract of *Pericopsis laxiflora* is not likely to produce any severe toxic effects. However, prolonged oral administration at high dose may cause observable changes in biochemical parameters, in particular Red blood cell and Platelets.

**Keywords:** *Pericopsis laxiflora*, Biochemical, hematological, toxicity

**Introduction**

The use of plants for the treatment of diseases dates back to the history of human life. In all parts of the world and more precisely in Africa and other least developed countries from Asia, plants are used in traditional medicine to treat different communicable and non-communicable diseases [1, 2]. It is estimated that more than 80% of people living in developing countries frequently use traditional practices for their primary health care needs [1-3]. This situation has given rise to inquietude among health professionals and consumers on the issue of safety. Indeed, many plants investigated elsewhere were found to contain toxic substances like certain secondary metabolites [4]. Among them are tannins, saponins, terpenoid, cyanogenic, toxic amino acids, glycosides, alkaloids, coumarins, flavonoids [5, 6].

*Pericopsis laxiflora* (Benth.) is traditionally used to treat different diseases. In Côte d'Ivoire, a decoction of the leaves and bark or roots of *Pericopsis laxiflora* is taken to treat headache, stomach ulcers, stomach aches, upset stomach, gastritis, enteritis, heart pain, abdominal pain [7, 8]. It is also used throughout the dry forests and savannas of Africa. For example, in Guinea, it is used against shigellosis and colibacillosis [9]. In Ghana, this plant is used in the treatment of malaria [10] and as antiulcer ancestral area Benoue in Nigeria [11]. Many studies reported the biological activities of extracts of this medicinal plant [12, 13]. Despite their biological properties the toxicological profile has not been clearly established. Therefore, the evaluation of the toxicity remains a priority in order to bring more confidence to their use. Thus, the acute and sub-acute toxicity of aqueous extract of *Pericopsis laxiflora* was evaluated in rat models.

**Materials and methods****Plant collection**

The plant, *Pericopsis laxiflora*, (Benth.) was obtained from Lataha village in Korhogo Department of Northern Côte d'Ivoire in December 2019. The plant's identity was confirmed at the herbarium of the Department of Agroforestry, Jean Lorougnon GUEDE University, Côte d'Ivoire.

**Preparation of aqueous extract of *Pericopsis laxiflora***

Fresh stem bark samples were cut into small pieces and then dried under shade for a week. 100 g of plant powder were macerated in 1 L of distilled water and homogenized under magnetic stirring for 24 hours at 25°C using a magnetic stirrer RCT-type IKAMAG. The homogenate obtained was filtered successively twice cotton wool and once on Whatman paper No 2.

The volume of the filtrate obtained is first reduced by means of a rotary evaporator Büchi type with the temperature of 60 °C. Then the rest of the filtrate is evaporated using an oven type Med Center Venticell at 50 °C to give a brown powder which is the total aqueous extract <sup>[14]</sup>.

### Experimental animals

Fifty six white male albino rats (Wistar stock) were obtained from the Department of Biochemistry and Microbiology, Jean Lorougnon GUEDE University, Côte d'Ivoire. The animals were fed on diet specially prepared from chick Grower's mash and were given water *ad libitum* throughout the study period. Animals' weights ranged from 143 g to 158 g just before the commencement of the experiment.

### Experimental design for acute toxicity study

The study was conducted in two phases using a total of sixteen male rats. In the first phase, nine rats were divided into 3 groups of 3 rats each. Groups 1, 2 and 3 animals were given 10, 100 and 1000 mg/kg body weight (b.w.) of the extract, respectively, to possibly establish the range of doses producing any toxic effect. Each rat was given a single dose after at least 5 days of adaptation. In addition, a fourth group of three rats was set up as control group and animals in the group were not given the extract.

In the second phase, further specific doses (1600, 2900 and 5000 mg/kg b.w.) of the extract were administered to three rats (one rat per dose) to further determine the correct LD<sub>50</sub> value. The extract was dissolved in Phosphate buffered saline (PBS) solution and given via intraperitoneal route. All animals were observed frequently on the day of treatment and for 2 weeks for signs of acute toxicity. Experiment was conducted in two phases; each dose group of phase-1 made up of 3 rats while those in phase 2 have 1 rat per group <sup>[15, 16]</sup>.

### Sub-acute toxicity study

For sub-chronic toxicity testing, twenty Wistar rats were used. They were divided into four (4) groups of five (5) male Wistar rats in each group. Group 1 was the control group, which was orally given 1% Dimethyl Sulfoxide (DMSO) daily, for 28 days. Wistar rats in group 2, 3 and 4 were orally administered with 100 mg/kg, 300 mg/kg, and 1000 mg/kg

body weight respectively, of the plant extract dissolved in 1% DMSO daily for 28 days. All the groups received standard pellet diet and water *ad libitum*.

During the entire dosing period, the animals were observed daily for clinical toxicity signs and mortality. The rats were weighed prior to dosing, after every 7 days. After administration of the plant extract for twenty-eight days, the animals were anaesthetized with ether and the blood of the rats was taken from the tail by amputation of the tip of the tail (5 mm of the tip) previously disinfected with ethanol 96°C then distributed in a dry tube and a tube containing anticoagulant ethylene diamine tetra-acetic acid (EDTA) <sup>[17]</sup>. Haematological assay parameters including white blood cells differential counts (WBC) and red blood cells (RBC) counts, haemoglobin concentration (HB), mean corpuscular haemoglobin concentration (MCHC), mean cell volume (MCV), platelets. The biochemical parameters included alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea, creatinine, and electrolytes. These parameters were determined for all groups using an autoanalyzer (ErbaChem 7, Germany) according to the manufacturer's prescribed protocol.

### Statistical Analysis

Using the graph pad software version 5.0.1 (USA), the results have been statistically processed. The test results are expressed as Mean ± SEM. The results of biochemical and hematological tests were analyzed by the one-way ANOVA, the Dunnett/ Neuman-keuls test for multiple comparisons and determination of significance levels. Values of  $P \leq 0.05$  are considered statistically significant.

### Results

#### Acute toxicity test

There was no mortality reported or any toxicity signs including autonomic effects (perspiration, defecation, inconstancy in urination, salivation and pilo-erection) in animals administered orally with of 5000 mg/kg body weight (b.w) of aqueous extracts of *P. laxiflora*. In addition, there was no sign of central nervous system intoxication (gait, lethargy, drowsiness, restlessness, convulsions and coma) reported (Table 1).

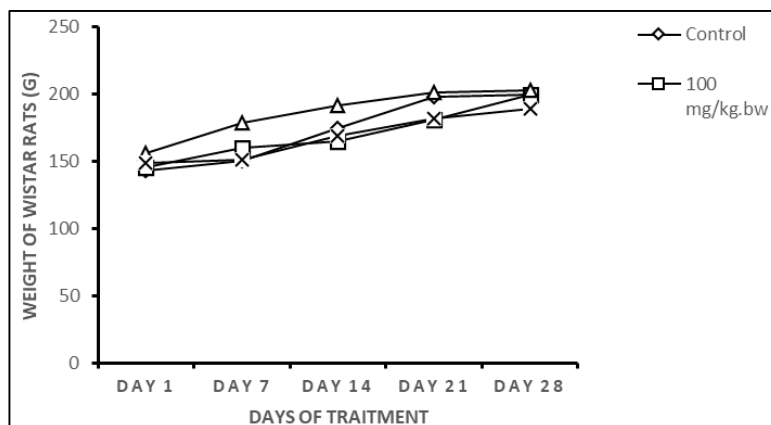
**Table 1:** Acute lethal effect of aqueous stem bark extract of *P. laxiflora* administered to white albino rats.

Experiment	Dose (mg/kg b.w)	No Dead rats after 24 hours	Observation
Phase-1 *	10	0/3	No sign of central nervous system intoxication (gait, lethargy, drowsiness, restlessness, convulsions and coma). No mortality reported or any toxicity signs including autonomic effects.
	100	0/3	
	1000	0/3	
Control	0	0/3	
Phase 2	1600	0/1	
	2900	0/1	
	5000	0/1	

\*Experiment was conducted in two phases; each dose group of phase-1 made up of 3 rats while those in phase 2 have 1 rat per group

In general, the weights of the rats of the different batches increased over the 28 days after oral administration of the aqueous extract of *P. laxiflora*. The rats in the control group recorded weight gains of between 6.94 g (day 7) and 56.35 g (day 28). The rats which received the dose of 100 mg/kg of bw had weight gains which varied between 14.44 g (day 7) and 54.44 g (day 28). At the concentration of 300 mg/kg bw,

the weight gains of the rats were ranged between 22.3 g (day 7) and 46.91 g (day 28). The rats which consumed the dose of 1000 mg/kg bw had their weight increased from 2.3 g (day 7) to 40.45 g (day 28). However, the concentration of 300 mg/kg b.w was that which increased the weight of the rats compared to the control batch (Figure 1).



**Fig 1:** Effect of oral administration of aqueous stem bark extract of *P. laxiflora* on body weight in Wistar rats.

Table 2 presents the biochemical parameters of the rats having received different doses of the aqueous extract of *P. laxiflora*. At the concentration of 100 mg/kg b.w, the aqueous extract studied did not modify the biochemical parameters of the rats compared to the rats in the control batch. The rats which absorbed the aqueous extract at the concentration of

300 mg/kg b.w had their sodium level ( $141.58 \pm 6.31$  mmol) modified compared to the control batch ( $p < 0.05$ ). Furthermore, the rats which received the dose of 1000 mg/kg b.w also had some of their biochemical parameters significantly modified ( $p < 0.05$ ) in particular Na ( $141.87 \pm 3.49$  mmol) and K ( $7.96 \pm 0.29$  mmol).

**Table 2:** Effects of of aqueous stem bark extract of *P. laxiflora* on biochemical parameters in Wistar rats.

Biochemical parameters	Control	Dose of <i>P. laxiflora</i> (mg/kg b.w)		
		100	300	1000
ALT (IU/L)	$135.97 \pm 2.8$	$136.2 \pm 3.13^{ns}$	$136.14 \pm 4.00^{ns}$	$136.33 \pm 5.3^{ns}$
AST (IU/L)	$223.96 \pm 4.81$	$224.01 \pm 3.39^{ns}$	$223.7 \pm 4.34^{ns}$	$224.92 \pm 3.59^{ns}$
CREAT (mg/dL)	$0.45 \pm 0.15$	$0.46 \pm 0.13^{ns}$	$0.45 \pm 0.19^{ns}$	$0.46 \pm 0.14^{ns}$
UREA (mmol)	$10.34 \pm 0.44$	$10.53 \pm 0.64^{ns}$	$10.38 \pm 0.54^{ns}$	$10.51 \pm 0.75^{ns}$
Na (mmol)	$140.01 \pm 5.4$	$140.05 \pm 5.99^{ns}$	$141.58 \pm 6.31^*$	$141.87 \pm 3.49^*$
K (mmol)	$6.28 \pm 1.67$	$6.32 \pm 0.98^{ns}$	$6.30 \pm 0.22^{ns}$	$7.96 \pm 0.29^*$

\*, significant ( $p < 0.05$ ), ns: Not significant, Values are expressed as Mean  $\pm$  SEM. CREAT: Creatinine; UREA: Urea; Na: Sodium; K: Potassium; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; mmol: Millimoles; IU/L: International units per litre;  $\mu$ m: Micromoles; g/l: Grams per litre.

No hematological parameter of the rats having received the dose of 100 mg/kg b.w was modified compared to the control lot. At 300 mg/kg b.w and 1000 mg/kg b.w, the red blood cell numbers (RBC) of the rats increased slightly and were  $9.33.10^6/\mu$ L and  $9.37.10^6/\mu$ L respectively. At these same concentrations (300-1000 mg/kg b.w), the number of Platelets

in rats was significantly different ( $p < 0.05$ ) from those in the control and were respectively  $8.39. 10^5/\text{mm}^3$  and  $8.02.10^5/\text{mm}^3$ . Also, the rats which received the dose of 300 mg/kg b.w had a different lymphocyte level (68.30%) from the control rats (Table 3).

**Table 3:** Effects of of aqueous stem bark extract of *P. laxiflora* on haematological parameters in Wistar rats.

haematological parameters	Control	Dose of <i>P. laxiflora</i> (mg/kg b.w)		
		100	300	1000
RBC ( $10^6/\mu$ L)	$8.20 \pm 0.13$	$8.22 \pm 0.20^{ns}$	$9.33 \pm 0.15^*$	$9.37 \pm 0.19^*$
Hb (g/dl)	$13.66 \pm 0.80$	$13.40 \pm 0.61^{ns}$	$13.56 \pm 0.65^{ns}$	$13.68 \pm 0.64^{ns}$
Hct (%)	$41.71 \pm 1.2$	$41.84 \pm 1.31^{ns}$	$42.01 \pm 1.45^{ns}$	$41.98 \pm 1.35^{ns}$
MCV (fL)	$66.18 \pm 1.23$	$65.92 \pm 1.80^{ns}$	$66.12 \pm 1.60^{ns}$	$66.23 \pm 1.55^{ns}$
MCH (pg)	$18.22 \pm 1.23$	$18.10 \pm 1.15^{ns}$	$18.15 \pm 1.76^{ns}$	$18.20 \pm 1.30^{ns}$
MCHC (%)	$34.10 \pm 0.40$	$34.14 \pm 0.51^{ns}$	$33.70 \pm 0.58^{ns}$	$33.84 \pm 0.65^{ns}$
WBC ( $10^3/\mu$ L)	$8.15 \pm 1.71$	$8.21 \pm 1.10^{ns}$	$8.36 \pm 1.30^{ns}$	$9.16 \pm 1.29^*$
Neutrophils (%)	$21.78 \pm 4.10$	$22.02 \pm 4.33^{ns}$	$21.98 \pm 4.65^{ns}$	$21.85 \pm 2.33^{ns}$
Lymphocyte (%)	$71.20 \pm 5.22$	$71.48 \pm 4.50^{ns}$	$68.30 \pm 3.87^*$	$70.98 \pm 3.60^{ns}$
Platelets ( $10^5/\text{mm}^3$ )	$7.85 \pm 0.7$	$7.81 \pm 0.19^{ns}$	$8.02 \pm 0.54^*$	$8.60 \pm 0.48^*$

\*, significant ( $p < 0.05$ ), ns: Not significant, Values are expressed as Mean  $\pm$  SEM, RBC: Red blood cell, Hb: Haemoglobin, Hct: haematocrit, MCV: Mean cell volume, MCH: Mean corpuscular haemoglobin, MCHC: Mean corpuscular haemoglobin concentration, WBC: White blood cells.

## Discussion

The first part of this study should determine the lethal dose ( $LD_{50}$ ) of extract, based on the observation of clinical signs and mortality in rats. Any clinical toxic effect was observed after oral administration of extract. No sign of central nervous system intoxication (gait, lethargy, drowsiness, restlessness,

convulsions and coma). No changes in behavior and no deaths were recorded during the experiment. Our results showed that the  $LD_{50}$  of aqueous extract of *P. laxiflora* were higher than 5000 mg/kg. Therefore, this extract could be considered non-toxic [18].

The body weight of treated rats gradually increased. This

could be due to body fat accumulation <sup>[19, 20]</sup>.

No differences was observed on most biochemical parameters of rats administrated with aqueous extract of *P. laxiflora*. The serum level of the transaminases ALT and AST did not undergo any significant variation and this good availability of transaminases in the blood of the experimental rats would be due to the presence of betulin resulting from the aqueous extract administered. These results showed in other words that the liver and muscles to a lesser degree have not been reached. Indeed, the liver is the first target of toxicity and the first organ exposed to all that is absorbed in the small intestine. In addition, the liver works in combination with the kidneys to remove toxic substances from the blood <sup>[21]</sup>. In the present study, no significant difference in creatinine and urea concentrations was observed in rats administered with the aqueous extract of *P. laxiflora*. These results also mean that the extract studied has no toxic effect on the kidney.

A slight significant difference of Na and K was observed in rats treated with this extract at 300 and 1000 mg/kg. The decrease of Na and K could be explained by a failure or blockage of the Na<sup>+</sup>/K<sup>+</sup> ATPase pump, thus causing a massive diffusion of K<sup>+</sup> ions in the extracellular medium <sup>[22]</sup>.

Evaluations of haematological parameters provide useful information on the adverse effects of extracts on blood elements <sup>[23]</sup>. In our study, the non-significant changes of several haematological parameters observed indicated that *P. laxiflora* extract does not affect these parameters.

## Conclusion

The LD<sub>50</sub> of aqueous extract of *P. laxiflora* is higher than 5000 mg/kg body weight. This extract could be considered non-toxic to rats. Aqueous extract of *P. laxiflora* is not likely to produce any severe toxic effects. However, prolonged oral administration at high dose may cause observable changes in biochemical parameters, in particular RBC and Platelets. Further studies on sub-chronic toxicity will allow to definitively confirm the toxicity profile of this medicinal plant. Therefore, caution and safety measures should be taken before oral ingestion of *P. laxiflora* for therapeutic purposes or for other uses; and prolonged use should be discouraged and lower doses encouraged. The histopathology study is needed to reveal extensive effects of *P. laxiflora* in the body.

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