Available online on 15.09.2022 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Research Article

Oral and Intraperitoneal Acute Toxicity Studies of *Sesamum radiatum* Aqueous Leaf Extract in Female Wistar Rats

Kouamé Amoin Flora Kouacou, Brou André Konan*, Koffi Bruno Koko

UPR-Nutrition and Pharmacology, Laboratory of Biology and Health, UFR-Biosciences, Félix Houphouët-Boigny University, P.O. Box 582 Abidjan 22, Côte d'Ivoire.

Article Info:

Article History:

Received 21 July 2022
Reviewed 27 August 2022
Accepted 05 Sep 2022
Published 15 Sep 2022

Cite this article as:

Kouacou KAF, Konan BA, Koko KB, Oral and Intraperitoneal Acute Toxicity Studies of *Sesamum radiatum* Aqueous Leaf Extract in Female Wistar Rats, Journal of Drug Delivery and Therapeutics. 2022; 12(5):87-93

DOI: http://dx.doi.org/10.22270/jddt.v12i5.5603

*Address for Correspondence:

Brou André Konan, Doctor in Animal Physiology and Pharmacology, Senior Lecturer, UPR-Nutrition and Pharmacology, Laboratory of Biology and Health, UFR-Biosciences, Félix Houphouët-Boigny University, P.O. Box 582 Abidjan 22, Ivory Coast

Abstract

Background and aims: *Sesamum radiatum* leaves are commonly used by African and Ivorian people in particular to treat various diseases. However, few studies have been done on the pharmacological properties and even less on the acute toxicity of this medicinal plant in Côte d'Ivoire. Also, the present work was carried out in order to contribute to correcting this through a comparative study of the acute oral and intraperitoneal toxicity of the aqueous extract of the leaves (ESera) in the female Wistar rat.

Méthodes: According to the modified OECD 423 method, 2 groups of 6 rats were treated with ESera at 50 mg/kg and 2000 mg/kg in a single dose respectively by intraperitoneal and oral administration in comparison with the control group (NaCl 0.9 %). Dice weighing at regular intervals of 2 days of body weight and the removal of some organs and blood samples at the end of the 14-day observation period allowed the measurement of biological parameters.

Results: Irrespective of the administration route, ESera did not cause clinical signs of suffering, behavior change and death in rats. The morphology and the relative weight of the organs (heart, kidneys, liver and lungs) were not modified. Treated animals exhibited weight growth kinetics similar to those of the controls. Greater weight gains ($p < 0.05$) were obtained with ESera. The study carried out on the blood samples showed statistically significant changes ($p < 0.05$) in certain hematological and serum biochemical parameters. The changes observed were greater with ESera 50 mg/kg intraperitoneal administration.

Conclusion: *Sesamum radiatum* aqueous extract did not cause death or organ changes in rats during the 14 days of observation. However, in order to better determine its toxicity, other studies must be carried out due to the disturbances observed in hematological parameters, transaminases and electrolytes.

Keywords: Acute toxicity, Hematological parameters, Biochemical parameters, Organ biometry

INTRODUCTION

For thousands of years, plants have been used for human and veterinary health care [1,2]. Even today, populations increasingly use these plants for primary health care throughout the world. Ito et al. (2012) report that 70-95 % of people in developing countries use plants to treat various diseases [3]. Plants have contributed enormously to the development of modern therapy. And this growing interest of populations for plants would be justified by poverty faced with the high costs of pharmaceutical products and hospital services and especially cultural beliefs in the therapeutic virtues of medicinal plants. This belief is reinforced by the strong contribution that these plants have made to modern therapeutics. Indeed, more than 25% of modern medicines are derived from medicinal plants [4,5].

However, empirical and/or uncontrolled use poses problems with real risks of poisoning, metabolic disorders, liver damage, kidney dysfunction, cardiovascular disorders and various other diseases [6-11]. Various scientific studies must therefore be made for a rational and efficient use of medicinal plants [12].It is in this context that scientific works have been undertaken on medicinal plants, including *Sesamum radiatum*.

Belonging to the Pedaliaceae family, *Sesamum radiatum* is a plant commonly used to treat various diseases [13-16] and to facilitate childbirth in parturient women [17,18]. Previous works have shown the therapeutic potential of this plant due to its richness in secondary metabolites and its pharmacological properties [19].

The effect of plants depending on several factors including soil, geography, climate, pharmacological and toxicological studies have been undertaken on *Sesamum radiatum* harvested in Côte d'Ivoire [20-24]. It is in this context that the present work has been carried out in order to study the acute toxicity of the aqueous extract of the leaves of this medicinal plant in the female Wistar rat.

MATERIALS AND METHODS

Plant material and extract

Fresh leaves of *Sesamum radiatum* (Pedaliaceae) were harvested in March 2018 in Koumassi (Abidjan, Côte d'Ivoire).

They have been identified and authenticated by an expert in Botany, Prof. Emma Aké-Assi at the National Floristic Center (CNF, UFR-Biosciences, Félix Houphouët-Boigny University). The authentication was made with reference to a specimen cataloged in this center under the number 8948 of June 17, 1966.

The extraction process was implemented according to the method described by some authors [25-28]. The fresh leaves were washed and dried at room temperature (28 ± 2 °C). Dried leaves were pulverized to powder using a laboratory blender (Mark RETSCH, type SM 100n Germany). The powder (100 g) was macerated 24 hours in 1 l water. The mixture was filtered (Whatman n°1) for 3 times until complete exhaustion. The filtrate was concentrated under reduce pressure using a rotary evaporator (Büchi R110, type MKE 6540/2) at a temperature of 60 °C and dried in a drying oven at 50 ± 5°C. The concentrated extract obtained (ESera: *Sesamum radiatum* aqueous leaf extract) was stored at 4°C until experiments. Concentrations of ESera to be tested were prepared extemporaneously by dilution in NaCl 0.9 % saline solution.

Animals and ethical consideration

Female Wistar rats (*Rattus norvegicus*) weighing 157-167 g and aged 8-10-week-old were used for the subacute oral toxicity study. They were obtained from the *Vivarium* (Animal house) at the Ecole Nationale Supérieure (ENS), Abidjan, Côte d'Ivoire. Animals housed in metabolic cages and maintained under standard laboratory conditions (temperature 25 ± 2 °C) with dark and light cycle (12/12 h). They were allowed free access to standard dry pellet diet and water *ad libitum*. Rats are fasted 18 hours before the experiment. Animals were treated according to good laboratory practices [29]. The experimental protocols were conducted in accordance with the protocols for the protection of experimental animals of the European Council on Legislation 2012/707 [30].

Chemicals used

Isoflurane (Forène®, Roche, France), Sodium chloride crystals (Delbet, France) and Commercials Kit (Spinreact, Spin) were used.

Study design

Three groups of six rats were used for the acute toxicity study conducted according to the OECD 423 protocol [31] modified by Ahmed et al. (2010) [32]. Thus, Group 1 (Control) received *per os* the saline solution NaCl 0.9 %, Group 2 received ESera 2000 mg/kg per os and Group 3 received ESera 50 mg/kg intraperitoneally. The drugs were administered in a single dose on D1 and the animals were observed until D14. Clinical signs and toxicity were observed immediately after administration, 3 h after administration of drugs daily in all animals. Rats were observed daily to record any apparent physiological and/or behavioral changes. Weighings were made on D1, D14 and at regular intervals of 2 days in order to assess the evolution of the animals' body weight. At D15 (D14 + 1), the 16 hr-fasted rats were anaesthetized with Isoflurane and blood was collected in test tubes from the retro-orbital sinus. All animals were sacrificed and organs (heart, kidney, liver, lungs) were sampled for biometric parameters measurement.

Measurement of biological parameters

Weight gain

Weight gain (WG) was determined according to the method used by Méité et al. (2016) [33]. It was calculated with the body weights measured at D1 and D15 and is given by the following equation:

$$WG\ (g/d) = (W_{J15} - W_{J1}) / Duration\ (14\ days)$$

Relative organ weights

Organs removed and freed of any adhesion were weighed for the calculation of the relative weights (RW) according to the formula below:

$$RW\ (\%) = [Organ\ Weight / Animal\ Final\ weight\ (J15)] \times 100$$

Hematological parameters

Blood samples were collected in Ethylene Diamine Tetra-Acetic acid (EDTA) coated bottles. Samples were analyzed for the assessment of the number of Red blood cells (RBCs), White blood cells (WBCs), platelets, lymphocytes, hemoglobin (Hb), hematocrit, Mean Corpuscular Volume (MCV), Mean Cellular Hemoglobin (MCH) and Mean Cellular Hemoglobin Concentration (MCHC) according to standard methods using the Sysmex XN-100 I Kobe auto-analyser (Japan).

Biochemical essays

Blood samples collected in non-heparinized tubes were allowed to clot for about 15 min and centrifuged at 3000 rpm for 5 min. Serum was separated from the clot with pasteur pipette and dispensed into clean tube for the measurement of the biochemical indices. Analysis of the selected serum biochemical indices were carried out on each sample using the Sysmex XN-100 I Kobe auto-analyser (Japan). Parameters measured were the Aspartate aminotransferase (AST) and Alanine transaminase (ALT) for liver profile and the Urea, Creatinine, Na^+, Cl^- and K^+ for the kidney profile.

Data analysis

The values were expressed as mean with standard error of the mean (m ± sem). The data were evaluated by analysis of variance followed by Tukey-Kramer with GraphPad Instat software (Microsoft, San Diego, California, USA) method. The graphical representations of data were performed by the GraphPad Prism 5 software (Microsoft, San Diego, California, USA). The difference between the averages is considered statistically significant when $p < 0.05$.

RESULTS

Mortality and clinical signs of toxicity

No signs of toxicity were observed in female rats after administration of ESera 50 mg/kg and 2000 mg/kg respectively by intrapreritoneal and oral roots. In terms of the acute toxicity, there was no change in the general appearance of rats (hair, skin, eyes, ears and mouth). The animals had no diarrhea, hematuria, uncoordinated movements, or respiratory distress during the study period. No symptoms of illness were observed during the 14 days of treatment. All animals survived after 14 days of observation.

Effects of *Sesamum radiatum* aqueous leaf extract on animals weight

Body weight evolution

L'administration intrapéritonéale de ESera 50 mg/kg et l'administration orale de ESera 2000 mg/kg n'ont pas entrainé de perte de poids chez les rattes. La croissance pondérale n'a pas été perturbée par les deux doses de ESera (Figue 1). Il a été une augmentation régulière du poids corporel avec une des cinétiques semblables à celle des témoins ayant reçu la solution saline NaCl 0,9 %. Le poids était passé de 167 ± 0,90 g (J1) à 186,5 ± 1,30 g (J14) contre 157,83 ± 1,83 g à 184,33 ± 2,78 g et 162 ± 0,40 g à 183,2 ± 2,50 g respectivement pour ESera 50 mg/kg administré par voie intrapéritoéale et ESera 2000 mg/kg par voie orale. La comparaison du poids corporel à J14 à celui mesuré à J1 a montré une augmentation significative à $p < 0.05$ pour chaque groupe d'animaux.

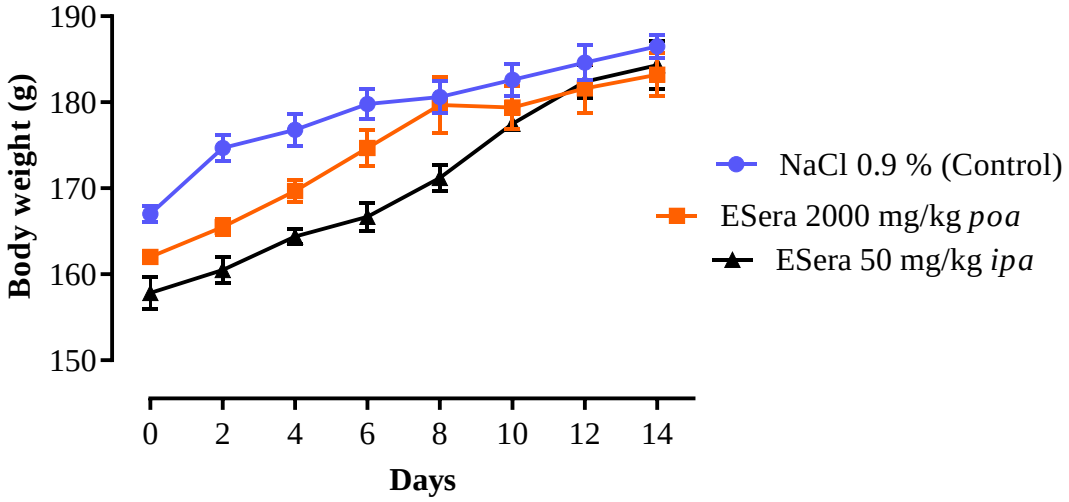

Figure 1: Evolution of the body weight of female rats 14 days after administration of a single dose of *Sesamum radiatum* aqueous leaf extract. m ± sem, *n* = 6, ESera: *Sesamum radiatum* aqueous leaf extract, *ipa* : intraperitoneal administration, *poa* : *per os* administration

Weight gain

L'extrait de plante (ESera) donné *per os* à 2000 mg/kg et à 50 mg/kg par voie intrapéritonéale a entrainé chez les rattes une augmentation significative du gain de poids en comparaison à celui des témoins ayant reçu la solution saline NaCl 0.9 % (Table 1). Les gains de poids obtenus étaient 1,40 ± 0,18 % pour les témoins contre 1,51 ± 0,19 % ($p < 0.05$) pour ESera 2000 mg/kg administré par voie orale. Le gain de poids le plus élevé à $p < 0.01$ a été enregistré suite à l'administration intrapéritonéale de ESera 50 mg/kg avec une valeur de 1,89 ± 0.24 %.

Table 1: Weight gain in female rats 14 days after administration of single doses of *Sesamum radiatum* aqueous extract

	NaCl 0.9 % (Control)	ESera 50 mg/kg *poa*	ESera 2000 mg/kg *ipa*
Weight gain (g/day)	1.40 ± 0.28	1.89 ± 0.31**	1.51 ± 0.42*

m ± esm, *n* = 6, *$p < 0.05$: significant, **$p < 0.01$: significant, ESera: *Sesamum radiatum* aqueous leaf extract, *ipa*: intraperitoneal administration, *poa*: *per os* administration

Effects of *Sesamum radiatum* aqueous leaf extract on biometric parameters of organs

Morphology of organs

Macroscopic examination did not reveal any modification of the removed organs (heart, liver, kidney, and lungs) in the rats. Organ shape and color were unaffected by the different doses of ESera given to the animals. No anomaly (hypertrophy, atrophy, presence of nodules) was observed.

Relative organ weights

Table 2 presents the relative organ weights of rats. Analysis of the data collected showed that the administration routes and the doses of *Sesamum radiatum* aqueous leaves extract did not significantly modify ($p > 0.05$) the relative weights of the regulating organs (heart, kidneys, liver and lungs) during the 14-day study period.

Table 2: Relative organ weights of rats 14 days after administration of single doses of *Sesamum radiatum* aqueous extract

Treatment groups	Relative organ weights (%)			
	Heart	Kidneys	Liver	Lungs
NaCl 0.9 % (Control)	0.37 ± 0.08	0.52 ± 0.06	3.93 ± 0.52	0.94 ± 0.12
ESera 50 mg/kg ipa	0.39 ± 0.04 ^{ns}	0.63 ± 0.11^{ns}	3.84 ± 0.23 ^{ns}	0.84 ± 0. 10 ^{ns}
ESera 2000 mg/kg *poa*	0.36 ± 0.09 ^{ns}	0.57 ± 0.08^{ns}	3.78 ± 0.34 ^{ns}	0.73 ± 0.08 ^{ns}

m ± sem, n = 3, $^{ns}p > 0.05$: no significant, ESera : *Sesamum radiatum* aqueous leaf extract, *ip* : intrapreritonael administration, *po* : *per os* (Oral) administration

Effects of *Sesamum radiatum* aqueous leaf extract on hematological parameters

Red cell lineage

Red cell parameter values were modified by ESera (Table 3). The changes recorded with ESera 2000 mg/kg *poa* were not statistically significant ($p > 0.05$) for all the parameters studied in comparison with those of the controls. Except the MCHC which increased from 31.57 ± 0.92 g/100 mL (controls) to 32.03 ± 0.075 g/100 mL, the other erythrocyte parameters decreased with the single dose of ESera 2000 mg/kg *poa* insignificantly. ESera 50 mg/kg *ipa* caused a significant increase at $p < 0.05$ of MCHC estimated at 33.03 ± 0.54 g/100 mL. On the other hand, decreases were observed for the other parameters in comparison with those of the controls. They were significant for MCH (17.45 ± 0.5 ρg; $p < 0.05$), Hb (11.87 ± 1.01 g/100 ml; $p < 0.001$), MCV (52.77 ± 0.72 fl; $p < 0.0001$) and Hematocrit (35.98 ± 1.92%; $p < 0.0001$). As for the red blood cell count, it decreased insignificantly ($p > 0.05$) with a value of 6.61 ± 06.7 x 10^6/mm^3 (ESera 50 mg/kg *ipa*) and 7.67 ± 0.53 x 10^6/mm^3 (ESera 2000 mg/kg *poa*) against 7.83 ± 0.48 x 10^6/mm^3 (Controls)

Leukocyte lineage

The measured leukocyte parameter values are reported in Table 3. The overall level of leukocytes (white blood cells) was not statistically modified ($p > 0.05$) by the treatment with the two doses of the plant extract. However, the levels of certain types of leukocytes experienced significant changes. Thus, ESera 50 mg/kg ipa induced a significant increase in the level of lymphocytes (82.25 ± 1.43 %; $p < 0.01$) and that of monocytes (8 ± 0.67 x 10^6/mm^3; $p < 0.001$) and an equally significant drop in eosinophils (1.33 ± 0.44 x 10^6/mm^3; $p < 0.01$). The respective values of these parameters were 78.67 ± 1.67 %, 3.33 ± 0.44 x 10^6/mm^3 and 2 x 10^6/mm^3 in controls. In rats treated with ESera 2000 mg/kg *poa*, only the lymphocyte level changed. A statistically significant increase at $p < 0.01$ was observed with a value of 82.33 ± 1.11 % against 78.67 ± 1.67 % in the control females.

Platelets

Blood platelet count was greatly reduced in the presence of doses of *Sesamum radiatum* aqueous extract (ESera). Indeed, the platelet count which was 1080.50 ± 1.44 x 10^3/µL (Controls) dropped significantly to a value of 929.17 ± 1.44 x 10^3/µL with ESera 2000 mg/kg poa ($p < 0.0001$) and 690 ± 1.67 x 10^3/µL ($p < 0.0001$) for ESera 50 mg/kg *ipa* (Table 3).

Table 3: Hematological parameters of female rats 14 days after administration of single doses of *Sesamum radiatum* aqueous extract

Hematological parameters	NaCl 0.9 % (Control)	ESera 50 mg/kg *ipa*	ESera 2000 mg/kg *poa*
Erythrocyte lineage			
RBCs (10^6/mm^3)	7.83 ± 0.48	6.61 ± 0.67^{ns}	7.67 ± 0.53^{ns}
Hb (g/100 mL)	14.56 ± 0.52	11.87 ± 1,01***	14.16 ± 0.62^{ns}
Hematocrit (%)	59.07 ± 1.64	35.98 ± 1.92****	57.70 ± 0.77^{ns}
VGM (fl)	56.32 ± 1.56	52.72 ± 0.72****	54.12 ± 0.66*
MCH (pg)	18.6 ± 0.5	17.45 ± 0.5*	18.47 ± 0.44^{ns}
MCHC (g/100 mL)	31.57 ± 0.92	33.03 ± 0.54*	32.03 ± 0.75^{ns}
Leukocyte lineage			
WBCs (10^6/mm^3)	17.73 ± 1.34	16.61 ± 0.55^{ns}	19.20 ± 0.70^{ns}
Eosinophile (10^6/mm^3)	2.00 ± 0.00	1.33 ± 0.44**	2.00 ± 0.00^{ns}
Lymphocytes (%)	78.67 ± 1.67	82,25 ± 1.43**	82,33 ± 1.11**
Monocytes (10^6/mm^3)	3.33 ± 0.44	8.00 ± 0.67****	3.33 ± 0.44^{ns}
Platelets (10^3/µL)	1080.50 ± 1.83	690 ± 1.67****	929.17 ± 1.44****

m ± sem, n = 6, $^{ns}p > 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, $^{****}p < 0.0001$, ESera: *Sesamum radiatum* aqueous leaf extract, *ipa*: intraperitoneal administration, *poa*: *per os* administration, WBCs: White blood cells, RBCs: Red blood cells, Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean Cellular Hemoglobin, MCHC: Mean Cellular Hemoglobin Concentration

Effects of *Sesamum radiatum* aqueous leaf extract on biochemical parameters

Biochemical markers of kidney

As shown in Table 4, the level of urea did not change significantly ($p > 0.05$) 14 after single doses of ESera were applied to rats. This observation was not made with creatinine. Indeed, variations of this biological marker have been recorded. Compared to the control value (6.67 ± 0.44 IU/L), ESera 50 mg/kg *ipa* caused a significant decrease ($p < 0.001$) in the creatinine level with a value of 3.33 ± 0.44 IU/L. On the contrary, a significant increase at $p < 0.01$ was obtained with ESera 2000 mg/kg *poa*. At this dose of 2000 mg/kg *poa*, ESera made it possible to record a creatinin value of 8.00 ± 0.44 IU/L in female rats *Rattus norvegicus*.

Regarding electrolytes (Table 4), statistically significant increases were observed. Na+ was estimated at 141.00 ± 1.33 mmol/L ($p < 0.01$) and 143.00 ± 1.33 mmol/L ($p < 0.001$) with ESera 2000 mg/kg *poa* and ESera 50 mg/kg *ipa* respectively against 138 ± 1.33 mmol/L in the control rats having received the saline solution NaCl 0.9 %. Cl^- concentration increased non-significantly ($p > 0.05$) with ESera 50 mg/kg *ipa* (98.17 ± 1.22 mmol/L) whereas a significant rise at $p < 0.05$ was recorded in animals treated with ESera 2000 mg/kg *poa* (99.17 ± 0.56 mmol/L). Its value was 97.00 ± 1.33 mmol/L in controls. As for the potassium ion (K+), its value of 4.69 ± 0.50 mmol/L (Controls) increased with the treatment of animals with *Sesamum radiatum* extract. It reached 5.17 ± 0.92 mmol/L, a statistically insignificant higher value ($p > 0.05$) for ESera 2000 mg/kg *poa* against a higher value (8.88 ± 0.45

mmol/L) and highly significant at $p < 0.0001$ for ESera 50 mg/kg *ipa*.

Biochemical markers of liver

Transaminases (ALT and AST) were modified differently by the plant extract (Table 4). ESera caused a statistically significant decrease at $p < 0.0001$ in ALT. Its value was measured at 46.17 ± 1.89 IU/L (Controls) against 34.00 ± 1.00 IU/L (ESera 50 mg/kg *ipa*) and 29.17 ± 0.89 UI/L (ESera 2000 mg/kg *poa*). At the AST level, its initial value of 153.83 ± 1.50 IU/L (Controls) increased significantly at $p < 0.0001$ for ESera 50 mg/kg *ipa* and reached 162.83 ± 0.89 IU/L. Conversely, ESera 2000 mg/kg *poa* with a value of 132.17 ± 0.56 IU/L induced a significant decrease ($p < 0.0001$) in AST transaminase.

Table 4: Serum biochemical parameters of female rats 14 days after administration of single doses of *Sesmum radiatum* aqueous extract

Biochemical parameters	NaCl 0.9 % (Control)	ESera 50 mg/kg *ipa*	ESera 2000 mg/kg *poa*
Kidney profile			
Urea (g/L)	0.23 ± 0.03	0.19 ± 0.02^{ns}	0.27 ± 0.02^{ns}
Creatinine (UI/L)	6.67 ± 0.44	3.33 ± 0.44***	8.00 ± 0.67**
Na^+ (mmol/L)	138 ± 1.00	143.00 ± 1.33***	141.00 ± 1.33*
Cl^- (mmol/L)	97.00 ± 1.33	98.17 ± 1.22^{ns}	99.17 ± 0.56*
K^+ (mmol/L)	4.69 ± 0.50	8.88 ± 0.45****	5.17 ± 0.92^{ns}
Liver profile			
ALT (UI/L)	46.17 ± 1.89	34.00 ± 1.00****	29.17 ± 0.89****
AST (UI/L)	153.83 ± 1.50	162.83 ± 0.89****	132.17 ± 0.56****

m ± sem, $n = 6$, $^{ns}p > 0.05$, $^{ns}p > 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, $^{****}p < 0.0001$,, ESera: *Sesamum radiatum* aqueous leaf extract, *ipa*: intraperitoneal administration, *poa*: *per os* administration, AST: Aspartate aminotransferase, ALT: Alanine transaminase

DISCUSSION

Sesamum radiatum aqueous leaves extract (ESera) administered at 50 mg/kg intraperitoneally did not cause any death in rats. This result differs from that of Konan et al. (2012) [24] which showed that this extract was toxic according to Diezi's scale [34]. This difference would be related to the low dose used in the present study. It is well below the lethal dose of between 169.7 and 142 mg/kg obtained by these authors. Indeed, several studies have all demonstrated that the toxicity of a plant extract depends on several factors including the dose, the administration route, the animal species and even the chemical composition of the plant [35,36]. Oral administration of ESera 2000 mg/kg also did not cause rat death. Esera administered orally would have a toxicity greater than 2000 mg/kg and would be classified in category 5 (non-toxic substances) according to the OECD globally harmonized classification system. Thus, the two doses of ESera administered by different routes do not appear to have had any toxic effect in rats.

This non-toxicity of ESera was also observed at the levels of certain biological parameters. No clinical sign of toxicity was recorded during the 14 days of the experiment. Underpinned by a positive weight gain, the treated rats had continuous growth with kinetics similar to those of the controls. At the macroscopic level, the morphology and the relative weights of the regulatory organs studied (heart, kidneys, liver and lungs) were not significantly modified. Similar results were observed by Allo et al. (2020) with *Lippia multiflora* [26].

Examination of hematological and serum biochemical parameters revealed that some of these parameters were highly modified by the doses of the plant extract. These effects were greater with intraperitoneal administration of ESEra 50 mg/kg. These modifications were not observed by Konan et al. (2012) who conducted their investigation over a 24-hour period [24]. The modification of hematological parameters, electrolytes, urea, creatinine, AST, ALT and other transaminases would testify to ionic imbalance, metabolic disturbances and organ dysfunctions [37]. Referring to this, ESera could have deleterious effects in the long term. This toxicity in the long term was evoked by Karharo and Adams (1974) [13]. According to these authors, Fulani herders avoid places where *Sesamum radiatum* grows abundantly. For them, its abundant/or regular consumption causes severe diarrhea and severe poisoning in livestock.

CONCLUSION

To summarize this work, the analysis of the results on toxicity, organ biometrics and weight growth has showed that *Sesamum radiatum* aqueous extract would not be toxic in rats. Indeed, this extract did not cause death, clinical signs of suffering and behavior change. The morphology and the relative weight of the regulating organs did not vary significantly in comparison with the controls. The animals had positive growth and weight gain. However, the observation of significant changes in certain hematological and serum biochemical parameters leads to other toxicological studies. Long-term repeated administration toxicity tests must be carried out in order to better assess the lethality of this plant. These works should include lipid profile, redox status and organ histopathology.

ACKNOWLEDGMENTS

The authors express their thanks to Prof. Emma Aké-Assi, botanist of the National Floristic Center of Felix Houphouët-Boigny.

FUNDING

This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed in the current study are available from the corresponding author on reasonable request.

DECLARATIONS

We confirm that this work is original and has not been published elsewhere, nor is it currently under consideration for publication elsewhere

AUTHORS' CONTRIBUTION

KAFK collected the data and carried out statistics analysis. The first draft was prepared by KBK, and BAK supervised the work.

CONSENT FOR PUBLICATION

This manuscript does not contain any individual person's data, and further consent for publication is not required.

COMPETING INTERESTS

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

REFERENCES

[1] Pousset JL. Plantes médicinales africaines. Utilisation pratique. A.C.C.T., Ed. Ellipses. 1989; P. 2-12.

[2] Sofowara A. Medicinal Plants and Traditional Medicine in Africa. Spectrum Books, Ltd, Ibadan, Nigeria. 1993; P. 157-161.

[3] Ito A, Munakata K, Imazu Y, Watanabe K. First nationwide attitude survey of japanese physicians on the use of traditional Japanese medicine (kampo) in cancer treatment. Evidence-Based Complementary and Alternative Medicine. 2012; 13:957082. https://doi.org/10.1155/2012/957082

[4] Sahoo N, Manchikanti P., Dey S. Herbal drugs: standards and regulation. Fitoterapia. 2010; 81(6):462-471. https://doi.org/10.1016/j.fitote.2010.02.001

[5] Newman DJ, Cragg GM. Natural products as sources of new drugs over 30 years from 1981 to 2010. Journal of Natural Products. 2012; 75(3):311-335. https://doi.org/10.1021/np200906s

[6] Gies J-P. Bases de pharmacologie moléculaire. Edition Marketing, Paris, France. 1993; P. 5- 6.

[7] Binlin-Dadié R, Soro S, N'Dri KD. Complications après usage de produits de la pharmacopée traditionnelle (Aspects cliniques). Médecine d'Afrique Noire. 1997: 44:128-130.

[8] Astin JA. Why patients use alternative medicine ? Results of a national study. Journal of the American Medical Association. 1998; 279(19):1548-1553. https://doi.org/10.1001/jama.279.19.1548

[9] Mashour NH, Lin GL, Frishman WH. Herbal medicine for the treatment of cardiovascular disease: Clinical considerations. Archives of Internal Medicine. 1998; 158(20):2225- 2234. https://doi.org/10.1001/archinte.158.20.2225

[10] Hilaly JE, Isaili ZH, Lyoussi H. Acute and chronic toxicological studies of *Ajuga iva* in experimental animals. Journal of Ethnopharmacology. 2004; 91(1):43-50. https://doi.org/10.1016/j.jep.2003.11.009

[11] Maïga A, Diallo D, Fane S, Sanogo R, Paulsen BS, Cissé B. A survey of toxic plants on the market in the District of Bamako, Mali. Traditional kwnoledge compared with a literature seach of modern pharmacology and toxicology. Journal of Ethnopharmacology. 2005; 96(1-2):183-193. https://doi.org/10.1016/j.jep.2004.09.005

[12] Lüllmann H, Mohr K, Ziegler A. Atlas de poche de pharmacologie. Ed Flammarion Médecine Sciences, Paris, France. 1998; P. 7-10.

[13] Kerharo J, Adams JG. La pharmacopée sénégalaise traditionnelle, plantes médicinales et toxiques. Vigot Frères Ed., Paris, France. 1974; P. 630-632.

[14] Gautier-Beguin D. Plantes de cueillette à utilisation alimentaire en Côte d'Ivoire Centrale. Boissiera 46. 1992; 341 p.

[15] Bellomaria B, Kacou P. Plantes et médecine populaire d'Agboville (Côte d'Ivoire). Fitoterapia. 1995; 66: 117-141.

[16] Bedigian D. Evolution of Sesame revisited: domestication, diversity and prospects. Genetic Resources and Crop Evolution. 2003; 50:779-787. http://dx.doi.org/10.1023/A:1025029903549

[17] N'Guessan K. La lutte contre la tragédie de l'accouchement par les plantes. Revue Internationale des Sciences de la Vie et de la Terre. 2000; 1:57-66.

[18] Malan DF, Neuba DFR. Traditional practices and medicinal plants use during pregnancy by AnyiNdenye women (Eastern Côte d'Ivoire). African Journal. Reproduction Health. 2011; 15(1):85-93. PMID: 21987942

[19] Konan BA, Amonkan KA, Bléyéré NM, Kouakou KL, Bouafou KGM, Datté YJ. *Sesamum radiatum* leaves can help childbirth. International Research Journal of Pharmaceutical and Applied Sciences. 2013; 3(4):69-73.

[20] Konan BA, Datté YJ, Offoumou AM. Action of the aqueous extract of *Sesamum radiatum* Schum. & Thonn. (Pedaliaceae) on the cardiovascular system of mammalians: Hypotensive effect. Current Bioactive Compdounds; 2006: 2(3):263-267. http://dx.doi.org/10.2174/1573407210602030263

[21] Konan BA, Datté YJ, Yapo AP. Nitric oxide pathway-mediated relaxant effect of aqueous sesame leaves extract (*Sesamum radiatum* Schum. & Thonn.) in the guinea-pig isolated aorta smooth muscle. BMC Complementary and Alternative Medicine. 2008; 8:23. https://doi.org/10.1186%2F1472-6882-8-23

[22] Konan BA, Amonkan KA, Ahui MLB, Bouafou KGM, Kouakou KL, Kpahé ZF, Datté YJ. Myostimulating effects of *Sesamum radiatum* aqueous leaf extract in isolated guinea-pig *Taenia caeci* contractile activity. African Journal of Traditional, Complementary and Alternative Medicine. 2011; 8(4):377-385. https://doi.org/10.4314%2Fajtcam.v8i4.6

[23] Konan BA. Bouafou KGM, Kouakou KL, Bléyéré NM, Amonkan KA, Zannou-Tchoko JV, Ahui MLB, Datté YJ. Effects of *Sesamum radiatum* aqueous leaf extract on rhythmic contractions of uterine smooth muscle bundles from pregnant rats. International Journal of Life Sciences and Medical Research. 2012; 2(4):82-89. https://doi.org/10.5963/LSMR0204005

[24] Konan BA, Bouafou KGM, Bléyéré NM, Zannou-Tchoko V, Amonkan KA, Datté YJ. Acute toxicity study and effects of sesame (*Sesamum radiatum*) aqueous leaf extract on rabbit's electrocardiogram. International Journal of Biomolecules & Biomedicine. 2012; 2(1):17-27. https://doi.org/10.6084/M9.FIGSHARE.1397421.V1

[25] Koko BK, Konan BA, Kouacou FKA, Djétouan JMK, Amonkan KA. Galactogogue effect of *Euphorbia hirta* (Euphorbiaceae) aqueous leaf extract on milk production in female Wistar rats. Journal of Biosciences and Medicines. 2019; 7(9):51-65. https://doi.org/10.4236/jbm.2019.79006

[26] Allo FY, Méïté S, Konan BA, Datté YJ. Acute and sub-acute toxicity studies of the aqueous leaf extract of *Lippia multiflora*. Asian Journal of Emerging Research. 2020; 2(1): 43-54. https://doi.org/10.3923/AJERPK.2020.43.53

[27] Konan BA, Kpahé ZF, Koko KB, Adepo YP. Diuretic activities of root bark aqueous and ethanolic extracts of *Parquetina nigrescens*. I-Effects on urinary excretion in Wistar rat. Journal of Drug Delivery and Therapeutics. 2022; 12(3):57-61. http://dx.doi.org/10.22270/jddt.v12i3.5318

[28] Amonkan KA, Konan BA, Djétouan KJM. Effects of *Ficus exasperata* root bark aqueous and ethanolic 70 % extracts on urinary excretion in Wistar rat. American Journal of Pharmacological Sciences. 2022; 10(1):20-25. http://dx.doi.org/10.12691/ajps-10-1-4

[29] OCDE. Série sur les principes de bonnes pratiques de laboratoire et vérification du respect de ces principes. ENV/MC/CHEM. 1998 ; 98: 17. https://doi.org/10.1787/20777868

[30] Europeen Union. Commission implementing decision of 14 november 2012 establishing a common format the submission of the information pursuant to Directive 2010/63/EU of the Europeen parliament and the council on the protection of animals used for scientific purposes (notified under document C (2012) 8064) text with EEA relevance. Special Education Croatian. 2012; 15(28):163- 180. http://data.europa.eu/eli/dec_impl/2012/707/oj

[31] OECD. Test guideline 423, OECD guideline for chemicals. Acute Oral Toxicity – Acute Toxic class Methods. 2001; 14 p.

[32] Ahmed FZB, Merzouk H, Bouanane S1 , Benkalfat NB, Sid Ahmed Merzouk SA, Mulengi JK, Narce M. Acute toxicity evaluation of 2-hydroxy-methyl-1 (N-phtaloyltryptophyl) aziridine in Wistar rat. Annales de Toxicologie Analytique. 2010; 22(3):115-121. https://doi.org/10.1051/ata/2010017

[33] Méïté A, Ouattara H, Dally T, Bouafou KGM, Kouamé KG, Kati-Coulibaly S. Wheat flour fortification with that of defatted seed of *Citrullus lanatus* (Cucurbitaceae): Effects on organs Biometry. International Journal of Environment, Agriculture and Biotechnology. 2016; 1(3):418-421. http://dx.doi.org/10.22161/ijeab/1.3.17.

[34] Diezi J. 1989. Toxicologie : principes de base et répercussions cliniques. In : Pharmacologie des concepts fondamentaux aux applications thérapeutiques. Ed. Slatkine-Genève. 1989; p. 33-44.

[35] Néné-Bi SA, Traoré F, Zahoui OS, Soro TY. Composition chimique d'un extrait aqueux de Bridelia furruginea Benth. (Euphorbiaceae) et études de ses effets toxicologique et pharmacologique chez les mammifères. Afrique Sciences. 2008; 4(2):287-305. https://doi.org/10.4314/afsci.v4i2.61690

[36] Onyebuchi C, Kavaz D. Effect of extraction temperature and solvent type on the bioactive potential of *Ocimum gratissimum* L. extracts. Scientific Reports. 2020; 10(1):21760. https://doi.org/10.1038/s41598-020-78847-5

[37] Kew MC. Serum aminotransferase concentration as evidence of hepatocellular damage. The Lancet. 2000; 355(9204):591-592. https://doi.org/10.1016/s0140-6736(99)00219-6