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Acute toxicity study and effects of sesame (*Sesamum radiatum*) aqueous leaf extract on rabbit's electrocardiogram

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Abstract

Our studies examined the acute toxicity, the natural bioactive compounds contained in the aqueous leaf extract (ESera) and its actions on the electrocardiogram. They were therefore aimed to confirm the use in traditional medicine for the treatment of cardiovascular diseases and childbirth complications. After the revelation of the phytochemical compounds in *S. radiatum* leaves by general reactions, the determination of LD_{50} of acute toxicity in mice was achieved after treatment with the aqueous leaf extract (ESera). ESera was administrated intraveinously to the animal via the saphenous vein for ECG registration. The phytochemical analysis revealed the presence of quinones, tannins, alkaloids, sterols, terpens, polyphenols, saponosides and reducing compounds. Short treatments (24 hours) of mice with the leaves aqueous extract gave LD_{50} values of 169.7 ± 15 mg/kg of b.w. and of 184.2 ± 21 mg/kg of b.w., respectively by the method of Miller and Tainter and the method of Dragstedt and Lang. ESera induced negative inotrope and chronotrope actions on the global electric activity of rabbit. In Conclusion: 1. The aqueous leaf extract has a low toxicity which permits its uses by populations. 2. As shown by the electrocardiac investigation and the phytochemical study of the leaves, *S. radiatum* could have many pharmacological properties justifying its traditional use to treat many diseases including cardiovascular diseases and childbirth complications.

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Introduction

Traditional medicine plays an important role in primary health care in Africa (Pousset, 1989). However, this medicine which remains relatively empirical causes concerns (Astin, 1998; Mashour *et al.*, 1998). For Lüllmann *et al.* (1998), the treatment of a disease by a plant extract implies the administration of various molecules. The molecule can exert therapeutic action but also toxic effects. Intoxications following the use of traditional drugs are severe (Binlin-Dadié *et al.,* 1997). Therefore, the rational evaluation and scientific studies of drugs commonly used in traditional medicine would guarantee a best use, reduce the risks of accidents and permit the establishment of specific treatments of these intoxications (Gies, 1993).

So we carry our interest on *Sesamum radiatum* (Pedaliaceae). Commonly named "Semame noir" in French and "Black semame" in English, *S. radiatum* is a plant of the african pharmacopoeia. This plant has several medicinal and cosmetic uses (Thompson *et al.*, 1991; Neuwinger, 2000). In Côte d'Ivoire, this plant species grows on the whole territory and even on the lands and around habitations (Adjanohoun and Aké-Assi, 1979). The plant is often used by populations to facilitate childbirth and to treat cardiovascular diseases (Bellomaria and Kacou, 1995; N'Guessan, 2000).

However, there is no information on the nutritional composition of *S. radiatum*, but it is probably comparable to that of black sesame (*S. indicum*) (Bedigian, 2003; Kanu, 2011). The seed contains 32.3 % oil. The oil is similar in composition to sesame oil (Jeng and Hou, 2005; Ono *et al.*, 2006). The pharmacological properties of the leaves of *S. radiatum* are not yet well-known.

The present study was carried out to evaluate the acute toxicity of an aqueous extract of *S. radiatum*, to examine its effects on the global electric activity and to determine the natural bioactive compounds which could justify its traditional use for treatment of many diseases such as cardiovascular disease and childbirth complications.

Material and methods

Ethics

Experimental procedures and protocols used in this study were approved by ethical committee of Health Sciences, University of Cocody-Abidjan. These guidelines were in accordance with the internationally accepted principles for laboratory use and care (Mosihuzzaman and Choudhary, 2008).

Animals

Mices *Mus musculus* (12-20 weeks old) and rabbits *Oryctologus cuniculus* weighing 30 ± 5 g and 2 ± 0.4 kg respectively were used in our experiments. These animals were obtained from the Animal House of the Laboratory of Nutrition and Pharmacology of UFR-Biosciences at Cocody University in Abidjan (Côte d'Ivoire). They were housed in a constant temperature rooms with a light/dark cycle of 14/10 hours. All animals were fed and given water *ad libitum* until use.

Plant material

Fresh leaves of *S. radiatum* were collected in October 2005 in a forest of the Southern region of Côte d'Ivoire (Region des Lagunes). The leaves of *S. radiatum* were certified to be an identical sample at the specimen herbarium of National Plant Centre (Centre National Floristique) of Côte d'Ivoire at Cocody University in Abidjan. Voucher specimen were preserved and catalogued in the same herbarium (Voucher specimen n° 8948, *Sesamum radiatum* L. of 17 June 1966 and *Sesamum radiatum* voucher n° 11616 of June 1974 in Dabou). This pantropical plant was authenticated by a Botany expert, Prof. Aké-Assi Laurent of National Plant Centre, UFR-Biosciences, University of Cocody, Abidjan, Côte d'Ivoire.

Preparation of S. radiatum aqueous leaf extract

The methods were previously described (Konan *et al.*, 2006). The sun-dried leaves of *S. radiatum* leaves (at

room temperature: 27 ± 3°C) were cut into small pieces, using a micro-crusher (Retsch SK 100 Confort Geissen, Germany). The fine powder obtained was firstly (100 g) macerated for 24 hours in *n*-hexane using magnetic stirrer to remove oils and chlorophylls. Solvent was removed and the solid remainder was collected and dried at room temperature. It was macerated again in bi-distilled water (800 ml) for 24 hours. The supernatant was filtered with Wattman paper and it was evaporated (50 ± 5°C) using Rotavapor (Laborota 4002-Control Heidolph, Germany). The extract of plant (ESera, 1.75 g) was obtained and was stored at 4°C until experiments.

Phytochemical analysis

The fine powders of leaves (25 g) were macerated for 24 hours in bi-distilled water, *n*-hexane and ethanol (90°) respectively. After filtration, crude, hexanic and ethanolic extracts were obtained. These three extracts and ESera were subjected to phytochemical screening for the presence of alkaloids, flavonoids, tannins, sterols, terpenes, saponins, quinones and saccharoses using standard procedures (Silver *et al.*, 1998; Musa *et al.*, 2008; Néné-Bi *et al.*, 2008).

Acute toxicity study

According to Özbek *et al.* (2004) and Néné-Bi *et al.* (2008), male and female mice were randomly gathered in 10 groups with 10 animals in each group. First group was treated with normal saline (NS) and considered as control and the other 9 groups were treated with *S. radiatum* aqueous leaf extract (ESera) given intraperitoneally (i.p.) in increasing dosages ranging from 24.6 mg/kg b.w. to 575.5 mg/kg b.w. Maximum volume of extract administered to mice was kept below 0.5 ml. To study behavioural changes, the nine treated groups were observed every 30 min for a period of 2 hours (Mandal *et al.*, 2001). The mortality rate raised for 24 hours of experimentation. The percentages of mortality were converted to probits. The methods of Miller and Tainter (1944) on the one hand and that of Dragstedt and Lang (1957) on the other hand were used to determine the LD_{50}.

Registration of the electrocardiogram of rabbit

The methods were previously described (Traoré *et al.*, 2004). To record the global electric activity of the rabbit, we used the technique of external electrodes used in the human practices. Traoré *et al.* (2004) have shown that this technique can be adapted to the rabbit. The apparatus used in this study is the CARDIOFAX 6851K (Nihon Kehden, Japan) commonly used to record the ECG in humans. It has the same characteristics as the CARDIETTE AUTORULER 12/1 used by Traoré *et al.* (2004). The recording of the ECG requires the pose of four electrodes.

The technique employed was based on the registration and measurement of bioelectric phenomena. The bioelectric phenomena obtained on the preparation with the help of external electrodes were amplified appropriately and recorded by the graphic register. These bioelectric phenomena were transcribed on recording paper unrolled at a speed of 25 mm/s. DIII-derivation was used (Traoré *et al.*, 2004). These authors showed that, in rabbit, the DIII-derivation corresponds to the derivation tongue-anus recommended by Ticoche (1968) for ECG registration in small mammalians. Before all manipulations, it is necessary to adjust the constant of time, the filter and the speed of progress of the recording paper. The studied parameters were the cardiac frequency, the amplitude of R-wave, the RT interval, lasted of the ventricular electric activity (ventricular depolarization) and the PQ interval, auriculo-ventricular conduction time. The pharmacodynamic substances studied were administrated intraveinously to the animal via the saphenous vein.

Chemical used

Atropine (ATR) was purchased from Sigma Chemical Company (St Louis, MO, USA).

Statistical analysis

Data were expressed as means ± SEM obtained from η separate experiments. Statistical analysis and graphics were carried out using the software GraphPad Instat and GraphPad Prism 4 (San Diego, California, USA), respectively. Statistical analysis of the results was determined by using the unpaired Student's *t*-test. $p < 0.05$ was considered as indicative of significance.

Results

Phytochemical analysis of S. radiatum leaves

As shown in table 1, the aqueous leaf extract of *S. radiatum* (ESera.) used in the experimentation were composed of quinones, catechic tannins, alkaloids, sterols, terpenes, polyphenols, reducing compounds, flavonoids and saponins.

Table 1. Classes of phytochemicals present in the *S. radiatum* leaves.

Phytochemical category		Leaves Extracts			
		ESera	Crude	Ethanolic	Hexanic
Quinones		+	+	+	-
Tannins	Gallic	-	-	+	-
	Catechic	+	+	+	-
Alkaloids		+	+	+	+
Sterols and terpenes		+	+	+	-
Polyphenols		+	+	+	-
Reducing compounds		+	+	-	-
Flavonoids		+	+	+	-
Saponins		+	+	-	-

+ presence; - absence; ESera: S. radiatum aqueous leaf extract.

Behaviour of animals in the presence of S. radiatum aqueous leaf extract

The effects of low doses of Esera ranging from 24.6 mg/kg b.w. to 114.2 mg/kg b.w. on the behaviour of the mice for the first ten hours were not perceptible. Beyond that, when the dose raised, some mice showed difficulties of movement.

Esera, at high doses from 176.6 mg/kg b.w. to 575.5 mg/kg b.w., induced a general modification of the behaviour of mice. Just after the administration of ESera at these doses, animals tended to gather and presented difficulties of movement with a light relaxation of the rear feet. They refused to feed. Then, after the second hour, the displacements were followed by torsion of the body and a light relaxation of the rear feet. Finally, the mice curled up in a corner and convulsed periodically. The first mice death was recorded seven hours after ESera's application at a dose of 575.5 mg/kg b.w.

Table 2. Result of acute toxicity study in mice of *S. radiatum* aqueous leaf extract.

Groups	Dose of ESera (mg/kg b.w.)	Effectif of mice	Mortality (%)	Mortality (Probits)
1	NS	10	0	1.9
2	24.552	10	0	1.9
3	71.846	10	10	3.71
4	114.181	10	20	4.15
5	176.580	10	40	4.75
6	191.832	10	60	5.25
7	290.333	10	60	5.25
8	371.121	10	80	5.84
9	391.558	10	90	6.28
10	575.453	10	100	8.71

Group 1 was treated with normal saline (NS) and considered as control and the other 9 groups (Group 2-10) were treated with *S. radiatum* aqueous leaf extract (ESera) given intraperitoneally (i.p.). The mortality rate raised in the 24 hours of experimentation. The percentages of mortality were converted to probits.

The mortality rate increased within 24 hours and the percentages of mortality were converted to probits (Table 2). The determination of lethal dose at 50 % of ESera was obtained by two methods:

- Graphic method of Miller and Tainter (1944): After

24 hours, the mortality rate was determined (Fig 1). The repetition of this experiment (n = 3) permitted to obtain a LD_{50} value of 169.7 ± 15 mg/kg b.w.

- Calculation method of Dragsted and Lang (1957): The repetition of this experiment (n = 3) permitted to determine a LD_{50} value of 184.2 ± 21 mg/kg b.w.

Effects of S. radiatum aqueous leaf extract on the global electric activity of rabbit

Dose-response effects of ESera on the rabbit ECG: The *S. radiatum* aqueous leaf extracts (ESera) induced negative inotrope and chronotrope actions on the global electric activity of the rabbit heart (Table 3). ESera at doses ranging from to 10 mg/kg b.w. to 30 mg/kg b.w. decreased the rabbit ECG in dose-dependent manner. The cardiac frequency was reduced from 225 ± 2.73 cycles/min (Control) to 210 ± 2.78 cycles/min ($p > 0.05$) and 135 ± 3.47 ($p < 0.001$) when ESera was employed at 10 mg/kg b.w. and 30 mg/kg b.w. respectively. These values correspond to respective reductions of 6.7 % and 40 %. This reduction of the cardiac frequency was accompanied by a depolarization of the QRS-complex, with a dercrease of the amplitude of the R-wave. The amplitude of this parameter decrease from 1 ± 0.05 mV to 0.95 ± 0.05 mV ($p > 0.05$) for 15 mg/kg b.w. and 0.7 ± 0.06 mV ($p < 0.05$) for 30 mg/kg b.w.. The decreases recorded were respectively 5 % and 30 % in comparison with the control value. The application of ESera at 30 mg/kg b.w. showed and elongation of the intervals RT and PQ of the rabbit ECG. The length of the RT interval increased from 120 ± 3.75 ms (Control) to 136.7 ± 2.54 ms ($p < 0.001$) giving an elevation de 13.9 % while the PQ interval progressed from 40 ± 2.13 ms to 78 ± 3.22 ms ($p < 0.001$) corresponding to an increase of 95 %.

Reversible action of ESera on the rabbit ECG: The values of the parameters indicated in table 4 showed that the action of ESera (30 mg/kg b.w.) on the rabbit ECG was reversible. The control cardiac frequency and the amplitude of the R-wave were 225 ± 2.73 cycles/min and 1 ± 0.06 mV respectively. After 1 min of ESera treatment, the cardiac frequency was decreased to 180 ± 4.26 cycles/min ($p < 0.001$) and the R-wave amplitude was 0.7 ± 0.05 mV ($p < 0.05$). These two parameters undergo a decrease of 20 % for the cardiac frequency and 30 % for the R-Wave amplitude. When the recording of the ECG was performed 10 min after administration of ESera, the cardiac frequency was 218 ± 5.4 cycles/min ($p>0.05$) corresponding to a decrease of 3.3 %. As for the R-Wave amplitude is estimated at 1 ± 0.1 mV ($p > 0.05$). This reversible effect of ESera was observed with other parameters studied. The length of the RT interval progressed from 120 ± 3.75 ms (Control) to 136.7 ± 2.54 ms ($p < 0.01$) and 120.5 ± 2.7 ms ($p > 0.05$) when the ECG was recorded respectively 1 min and 10 min after the injection of ESera to the anesthetized rabbit. Thus we pass to a rise of 13.9 % to 0.4 %. The length of the PQ interval, in the absence of ESera was 40 ± 2.13 ms was estimated at 78 ± 3.22 ms ($p < 0.001$) giving an increase of 95 % in the second minute of the ESera treatment. At the tenth minute, the length of PQ interval was evaluated to 41.5 ± 2.12 ms ($p > 0.05$) corresponding to an increase of 3.75 %.

Cholinergic effects of ESera on the rabbit ECG: Atropine, antagonist of the muscarinic receptors, suppressed the bradycardisant effects of ESera in dose-dependent manner (Table 5). ESera (30 mg/kg b.w.) used alone reduced the R-wave amplitude of 30 ± 2.35 %. In the presence of low dose of ATR (10^{-7} mg/kg b.w.), ESera caused a decrease of 25 ± 2.82 % ($p > 0.05$). In the presence of the high dose of ATR (10^{-3} mg/kg b.w.), ESera decreased the R-wave amplitude of 4.2 ± 0.91 % ($p<0.001$). This inhibition of the negative inotrope action of ESera by ATR was accompanied by that of the negative chronotrope effect our plant extract. Indeed, ESera used only caused a reduction of 40 ± 1.93 % of the cardiac frequency. This cardiac frequency was reduced to 33 ± 1.92 % ($p < 0.05$) and 8.9 ± 1.7 % ($p < 0.001$) when the rabbit was pretreated with the respective ATR doses of 10^{-7} mg/kg b.w. and 10^{-3} mg/kg b.w.

Discussion

The LD_{50} value of the aqueous leaf extract of *S. radiatum* (ESera), determined with the method of Miller and Tainter (1944) and that of Dragsted and Lang (1957) were 169.9 ± 15 mg/kg b.w. and 184.2 ± 21 mg/kg b.w., respectively. The values were statistically very close. According to the classification of Diezi (1989), ESera has a low toxicity. The toxicity of ESera was nearly equal to those of *Caesalpinia bonduc* (Caeasalpiniaceae), a uterotonic plant, and *Bridelia furruginea* (Euphorbiaceae) which had a LD_{50} of 166.66 mg/kg b.w. and 167 mg/kg b.w. , respectively (Datté and Offoumou, 2001; Néné-Bi *et al.,* 2008). The toxicity of ESera was higher than that of *Erythrina senegalensis* (Fabaceae) which LD_{50}-value was 1663 mg/kg b.w. (Traoré *et al.*, 2002). On the other hand, the toxicity caused by ESera was less important than those of other medicinal plants such as *Securidaca longepedunculata* (Polygalaceae) and *Swartzia madagascariesis* (Ceasalpiniceae) having LD_{50}-values respectively equal to 64 mg/kg b.w. and 5.99 mg/kg b.w. (Traoré *et al.*, 2002).

Table 3. Dose-response effects of *S. radiatum* aqueous leaf extract on the rabbit ECG.

ESera (mg/kg b.w.)	Heart rhythm (Cycles/min)	R-wave Amplitude (mV)	Length of PQ interval (ms)	Length of RT interval (ms)
0 (Control)	225 ± 2.73	1 ± 0.06	40 ± 2.13	120 ± 3.75
10	210 ± 3.8^{ns}	1 ± 0.05^{ns}	44 ± 2^{ns}	123 ± 4.6^{ns}
15	188 ± 5.1***	0.95 ± 0.05^{ns}	51 ± 3.7^{ns}	125 ± 5.1^{ns}
20	175 ± 2.4***	0.9± 0.09^{ns}	62 ± 2.65***	127 ± 2.7^{ns}
25	152 ± 2.6***	0.8± 0.05^{ns}	72 ± 4.8***	132 ± 2.3***
30	135 ± 3.47***	0.7 ± 0.5*	78 ± 3.22***	136.7± 2.54***

S. radiatum aqueous leaf extract (ESera) induced negative inotrope and chronotrope effects on the global electric activity of the rabbit heart. Data shown are mean ± S.E.M. (n = 6). *ns*, $p > 0.05$ vs. control; *, $p < 0.05$ vs. control; **, $p < 0.01$ vs. control; ***, $p < 0.001$ vs. control.

Table 4. Reversible action of *S. radiatum* aqueous leaf extract on the rabbit ECG.

Periods of registration (min)	Heart rhythm (Cycles/min)	R-wave Amplitude (mV)	Length of PQ interval (ms)	Length of RT interval (ms)
0 (Control)	225 ± 2.73	1 ± 0.06	40 ± 2.13	120 ± 3.75
0.5	210 ± 2.78^{ns}	0.8 ± 0.05^{ns}	56.7 ± 3.1**	133.3 ± 2.87*
1	180 ± 4.26***	0.7 ± 0.05*	76.7 ± 3.12***	136.7 ± 2.54**
2	135 ± 3.47***	0.8± 0.07^{ns}	78 ± 3.22***	126.7 ± 2.91^{ns}
5	165 ± 3.48***	0.9± 0.06^{ns}	53.3 ± 2.6*	123.3 ± 2.69^{ns}
10	230.5 ± 5.4^{ns}	1 ± 0.1^{ns}	41.5 ± 2.12^{ns}	120.5± 2.7^{ns}

The values of the parameters showed that the action of ESera (30 mg/kg b.w.) on the rabbit ECG was reversible. Data shown are mean ± S.E.M. (n = 6). *ns*, $p > 0.05$ vs. control; *, $p < 0.05$ vs. control; **, $p < 0.01$ vs. control; ***, $p < 0.001$ vs. control.

Table 5. Effects of ESera on the rabbit ECG after atropine pretreatment.

Drugs (mg/kg.b.w.)	Decrease of Heart rhythm (%)	Decrease of R-wave Amplitude (%)	Increase of PQ interval (%)	Increase of RT interval (%)
ESera (30)	40 ± 1.93	30 ± 2.35	95 ± 1.76	13.9 ± 2
ATR (10^{-7}) + ESera	33 ± 1.91*	25 ± 2.82^{ns}	76.7 ± 3.82***	8 ± 1.73*
ATR (10^{-3}) + ESera	8.9 ± 1.7***	4.2 ± 0.91***	12 ± 2.28***	1.2 ± 0.16***

Atropine, antagonist of the muscarinic receptors, suppressed the bradycardisant effects of ESera in dose-dependent manner. Data shown are mean ± S.E.M. (n = 6). *ns*, $p > 0.05$ vs. ESera value; *, $p < 0.05$ vs. ESera value; **, $p < 0.01$ vs. ESera value; ***, $p < 0.001$ vs. ESera value.

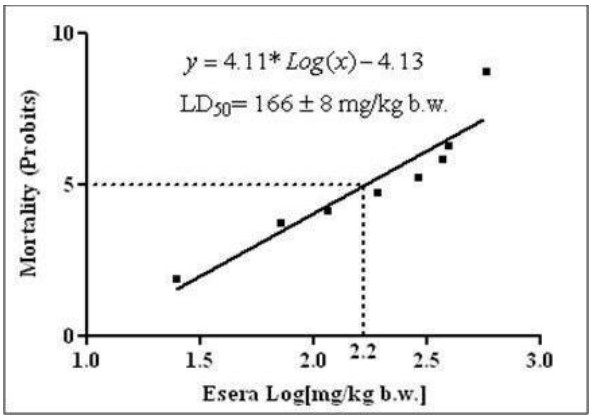

Fig 1. Curve of acute toxicity of *S. radiatum* aqueous leaf extract (ESera). The animals were treated by intraperitoneal (i.p.) administration of ESera. Horizontal scale: ESera log [mg/kg b.w.], vertical scale: mortality (Probits).

The toxicity of *S. radiatum* was observed in sheep but not in humans because the quantities used by humans for their needs (food and therapeutic) were lower than those swallowed by sheep (Kerharo and Adams, 1974). According to the route of administration, the toxicity of a same extract can change. Different values of toxicity were observed by Diouf and Diallo (2000) with *Pilostigma reticulatum* (Caesalpiniaceae) and Néné-Bi *et al.* (2008) with *Bridelia furruginea* (Euphorbiceae). This corroborates what Lüllmann *et al.* (1998) wrote highlighting the relation between the dose and the route of administration. *S. radiatum* is lightly toxic. However, this toxicity could not be a barrier to its use because all pharmacodynamic substances are toxic when the administered doses are supraliminal (Lüllmann *et al.*, 1998).

The *S. radiatum* aqueous leaf extract reduced the global electric activity of rabbit. This reduction results in a change of the rhythm and the amplitude of the different cardiac waves. These changes were well illustrated with the application of high dose of 30 mg/kg b.w. ESera increased the auriculo-ventricular conduction time. It could change the pacemaker reactivity center. This means lowering the threshold of excitability center of automatism of the right atrium. ESera caused a negative chronotrope effect. This bradycardisant effect could result from a slowing of intracardiac conduction (auriculo-ventricular conduction). It could also affect the negative bathmotrope properties reducing the automatism of heart (Vogt *et al.*, 1993). ESera reduced the amplitude of the QRS-complex with an increase of the RR interval. The negative chronotrope and inotrope effects of Esera were similar to those of *Caesalpinia bonduc* (Datté, 1996). The effects of ESera indicated that ESera exerts an inhibitory action on the rabbit heart. This action was comparable to those of misoprostol and oxytocin, two pharmacodynamic substances commonly used in obstetrical practice to augment labor (Ciccutti et *al.*, 1999; Gutkwoska *et al.*, 2000, Baskett *et al.*, 2007).

Our results revealed that a pre-treatment of the rabbits with ATR, a muscarinic cholinoceptor antagonist, revoked the negative chronotrope and inotrope effects of ESera. These effects observed with ESera and suppressed in the presence of a cholinoceptor blocker showed that our plant extract could contain some cholinergic substances. It is known that acetylcholine (ACh) is a cardioinhibitory substance. It dercrease the cardiac activity acting on the membrane permeability at the sinoatrial node (node of Keith and Flack). ACh has muscarinic receptors in the cardiac muscle (Field *et al.*, 1978). The binding of ACh on its muscarinic recpetors increase the potassium conductance (Sojima and Noma, 1984) and reduces the low calcium current (Hino and Ochi, 1980).

The effects of ESera obtained on the ECG were in accordance with previous studies. These studies showed that the administration of sesame (*S. radiatum*) aqueous leaf extract to rabbits induced hypotension, which could result from both cardiodepression mechanism and vasorelaxation (Konan *et al.*, 2006). The hypotension caused by ESera was comparable to those observed with pharmacodynamic substances used in gynaeco-obstetric cares (Konan *et al.*, 2006). The hypotension induced by these substances (oxytocin and misoprostol) could contribute to facilitate childbirth (Zingg, 2001; Baskett *et al.*, 2007).

The hypotensive action of ESera could be due to the tannins, the flavonoids and the alkaloids found in the extract. The aqueous leaf extract of *S. radiatum*, as indicated with the phytochemical analysis, contained quinones, catechic tannins, flavonoids and alkaloids. These compounds were also found in *Tabernaemontana pandaqui* (Taesotikul *et al.*, 1998), *Arbustus unedo* (Ziyyat and Boussairi, 1998), *Lippia alba*, *Melissa officinalis*, *Cymbopogon citratus* and in the majority of plants used traditionally in the treatment of arterial hypertension (Gazola *et al.*, 2004).

The cardiovascular actions of the plants could be due to the presence of the tannins, the flavonoids, and the alkaloids. The tannins and the flavonoids could relax the vascular endothelium whereas the alkaloids could cause a bradycardia (Ziyyat and Boussairi, 1998; Slowing *et al.*, 2001). The alkaloids could act either by the stimulation of the cardiac muscarinic receptors or by blocking the calcium channel attributed, or the two mechanisms at the same time (Vasquez and Mefeiros, 1998; Udoh and Lot, 1998).

In conclusion, the study of *S. radiatum* aqueous leaf extract revealed that it has a low toxicity by intraperitoneal administration. This low toxicity permits its uses by populations. According to the phytochemical study of the leaves, *S. radiatum* leaves could have many pharmacological properties justifying its traditional use to treat many diseases including cardiovascular diseases and childbirth complications. Chemical and pharmacological studies are now in progress to isolate and characterize the constituents responsible for such effects, and also to investigate in more detail the mechanism underlying these actions of *S. radiatum* leaves.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors contributed equally in the study. They made substantial contributions to the design of the study, the collection of the data as well as the preparation and analysis of the data. They also drafted the manuscript and gave final approval for its submission to the journal for consideration of publication.

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