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Original Article

Neuropharmacological effects of the ethanolic extract of *Sida acuta*

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ABSTRACT

Sida acuta Burm. f., Malvaceae, is regarded as astringent, tonic and useful in treating urinary diseases and blood disorders, bile, liver and as treatment for nervous diseases. Different methods were developed: sodium pentobarbital-induced sleeping time, anxiolytic activity, test for muscle-effects, pentylenetetrazole (PTZ)-induced seizures, effect on normal body temperature. All experiments were performed in an isolated room with 12/12 h light/dark cycles at 22 ± 1 °C. The effects described in this work for *Sida acuta* are according to what is known in traditional medicine, where is used as sedative agent. At the higher doses used in this work (500 and 1000 mg/kg), the *Sida acuta* extract reduced the latency time (T1) and increased the sleeping time (T2) induced by pentobarbital, indicating a sedative and hypnotic effect of the plant's extract. The extract of *Sida acuta* shows an increase in open arm exploration (anxiolytic activity). Results obtained in the rota-rod test showed that only the elevated dose (750 mg/kg) of *Sida acuta* extract, acutely administered, promotes significant changes, at 60 and 120 min post-administration, in the time of permanence in the rod. The ethanolic extract from the leaves and stems of *Sida acuta*, causes effects on the central nervous system in experimental animals.

Introduction

Malvaceae is a family of flowering plants containing over 200 genera with close to 2300 species. The main economic use of Malvaceae plants is as a source of natural fibers, the family is also used for food, beverages, timber, in traditional medicine and in horticulture. The largest genera are *Hibiscus* (300 species), *Streculia* (250 species), *Dombeya* (225 species), *Pavonia* (200 species) and *Sida* (200 species) (Rizk and Soliman, 2014). *Sida acuta* Burm. f., locally known as "escobabosa" and "kuala" in Cuna, "samampiisa" in Burkina Faso (Nadembega et al., 2011), "arbre à balai" in French and "zon-raaga" in Mooré, is a perennial shrub widely distributed in the subtropical regions, found in bushes, in farms, around habitations. Grows abundantly on cultivated fields, waste areas, roadsides and highways, in damp or dry, between 0 and 1800 masl (Mejía et al., 1994; Karou et al., 2007).

In Colombia, the whole plant of *S. acuta* is widely used in traditional medicine of the Indigenous Tribes *Embera*, *Wounaan*, *Cunas* and *Katíos*, and in others regions of Antioquia, prepared as drinks, ointements and external baths against snakebite (Otero et al., 2000a,b,c; Vásquez et al., 2015). It is also used as stomachic, diaphoretic and antipyretic. It is regarded as astringent, tonic, useful in urinary diseases treatment (diuretic) and also blood disorders (stops bleeding), bile and liver and nervous diseases treatment (sedative) in Indian traditional medicine (Sreedevi et al., 2009; Govindarajan, 2010); in Mexico, smoked as marihuana substitute, and it is also used to treat asthma, renal inflammation, colds, gonorrhea, fever, bronchitis, malaria, diarrhea, headache, dysentery, abortion, breast cancer, skin diseases, hemorrhoids, insects' bites, erectile dysfunction, elephantiasis, rheumatism and ulcers (Napralert database, Bhardwaj et al., 2011; Kumar et al., 2012). It is claimed to have aphrodisiac properties (Govindarajan, 2010). The root's juice is applied to wounds and the barks are used for measles (Adetutu et al., 2011; Allabi et al., 2011). In Nigeria, *S. acuta* is one of the plants most commonly used for the treatment of hypertension, using its leaves, seeds and stems in different preparations (Gbolade, 2012).

The phytochemical screening of *S. acuta* species revealed the presence of alkaloids such as vasicine, ephedrine and cryptolepine (the main alkaloid in the plant) (Prakash et al., 1981; Karou et al., 2005), saponosides (unspecified type or hemolytic), coumarins,

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steroids (ecdysterone, β-sistosterol, stigmaterol, ampesterol), tannins, phenolic compounds (evofolin-A, and B, scopoletin, loliolid and 4-ketopinoresinol, polyphenol, sesquiterpene and flavonoids (Konaté et al., 2010; Napralert database).

The tested pharmacological activities of the *S. acuta* involve stimulating smooth muscle, abortifacient, antiulcer, antiyeast, diuretic, antiplasmodial, antimicrobial, antiophidian, antioxidant, hepatoprotective, insecticidal, larvicidal-repellent and cytotoxic activities (Otero et al., 2000a; Karou et al., 2003; Banzouzi et al., 2004; Ekpo and Etim, 2009; Akilandeswari et al., 2010; Pieme et al., 2010; Upadhyay et al., 2010; Adeniyi et al., 2010; Ahmed et al., 2011; Koudouvo et al., 2011). Meanwhile, *S. acuta* extracts impact in the cardiovascular system function in zebrafish embryos (Kannan and Prakash, 2012). Additionally, it has been proved that the aqueous-acetone and ethanolic extracts of *S. acuta* leaves have analgesic activity and antidepressant-like properties tested in different animal models, proving that the plant contains psychoactive substances (Konaté et al., 2012; Ibironke et al., 2014).

Sida cordifolia (L.) extract has been reported to have central nervous system activity in experimental animals (Franco et al., 2005) and *Sida tiagii* Bhandari has been reported to have anxiolytic and anticonvulsant activity (Datusalia et al., 2008). In the present study, assesses the neuropharmacological properties of *S. acuta* leaves and stems, including sedative, anticonvulsant and anxiolytic activities.

Materials and methods

Plant material

Sida acuta Burm. f., Malvaceae, was collected from Medellín, in a University of Antioquia (Colombia), at 1525 m altitude above sea level, in February 2012. It was identified by Dr. Fernando Alzate Guarín, Institute of Biology, University of Antioquia (Medellín, Colombia), where voucher specimens have been deposited with the number 5111 in the collection.

Preparation of Sida acuta *extracts*

Leaves and stems (60:40) of *S. acuta* were air-dried in an oven at 40 °C for 4 days, then the dry plant was cut and ground to powder by mechanical milling. The dried powdered plant material was submitted to a continuous extraction in a Soxhlet extractor for 5 days using 100% ethanol as solvent. The solvent was then eliminated by vacuum distillation in a rotary vacuum evaporator (Büchi R – 124, Flawil, Switzerland), and it was lyophilized, representing an extraction yield of 3.1% of the dry material.

Animals

Male CD1 albino Swiss mice (weighing 22 ± 2 g) were obtained from the Central Animal House (University of Santiago de Compostela) and housed in groups of four, eight or twelve in standard Makrolon® cages (215 mm × 465 mm × 145 mm). The animals received standard laboratory chow (Scientific Animal Food and Engineering (SAFE), Augy, France) and tap water ad lib until the beginning of the experiments. Three days after laboratory arrival, both the housing and handling during experimentation were carried out according with the standards established in the directive 2010/63UE of the European Parliament and the Council and the Galician (Decreto 296/2008, DOGA number 11, January 16, 2009) and Spanish (Real Decreto 53/2013, BOE number 34, February 8, 2013) legislation on animal experimentation.

Drugs

All drugs were bought from Sigma–Aldrich (USA) or Merck (Germany). Drugs or the crude extract of *Sida acuta* were prepared immediately before use and orally administered (*per os*) in a total volume of 0.1 ml/10 g body weight (b.w.). Diazepam (DZP), sodium pentobarbital (PTB) and Pentylenetetrazole (PTZ) were dissolved in saline solution (NaCl 0.9%). The crude extract of *S. acuta* was suspended in a 1% (weight/volume) sodium carboxymethylcellulose (NaCMC) dispersion at doses of 50, 100, 300, 500 and 1000 mg/kg.

Pharmacological evaluation

All experiments were performed in an isolated room with 12/12 h light/dark cycles at 22 ± 1 °C, at the same time of day, in order to avoid potential variations caused by circadian rhythms.

The evaluation of time in open arms, number of entries, traveled distance, velocity, and another evaluated parameter in elevated plus maze (EPM) test and the open field test (OFT) were made with the video computerized animal observation system EthoVision V. 3.16 (Noldus Information Technology, Wageningen, The Netherlands).

All the procedures follow the guidelines of the research ethics committee at the University of Santiago de Compostela, according with the guidelines of the European Community Council Directive 86/609.

Sodium pentobarbital-induced sleeping time

The effect of *S. acuta* extract on pentobarbital sleeping time was performed in six groups of mice ($n = 4$). Four groups received graded doses of the extract (100, 300, 500 and 1000 mg/kg *p.o.*). One group received diazepam (5 mg/kg *i.p.*), while animals in the control group were administered NaCMC (0.1 ml/10 g *p.o.*). Thirty minutes post-treatment, sodium pentobarbital (40 mg/kg *i.p.*) was administered to each mouse. The elapsed time between the administration of pentobarbital until the loss of the righting reflex was recorded as the sleep latency (T1), and the time elapsed between the loss and recovery of the righting reflex (T2) was recorded as the sleep time (Carlini and Burgos, 1979; Ramírez et al., 1998; Wambebe, 1985).

Anxiolytic activity

Elevated plus maze (*EPM*): The EPM test was introduced in the research of new drugs with potential anxiolytic activity (Hanledy and Mithani, 1984). Experimental groups of four mice were treated with vehicle (NaCMC 1%, 0.1 ml/10 g *p.o.*), *Sida acuta* (50, 100, 300 and 500 mg/kg *p.o.*) or diazepam (1 mg/kg *i.p.*).

The elevated plus maze (EPM) is made of wood painted black. It has two arms 60 cm × 10 cm, arranged opposite to each other, and enclosed by walls 35 cm height. It also has two open arms of the same size and without flanges. The four arms are interconnected by a central square of 10 cm × 10 cm, forming a cross, and elevated to a distance of 75 cm from the ground. The device is illuminated by four independent tubes, arranged in a cross, located in the ceiling of the room, and the animal behavior was observed with a video camera disposed on the center.

Sixty minutes after the treatment, animals were placed individually at the center of the elevated plus maze with their nose facing the direction of one of the enclosed arms, and observed for 5 min (Pellow et al., 1985; Lister, 1987; Yemitan and Adeyemi, 2003). The maze platforms and walls were thoroughly cleaned with 70% ethanol between sessions and allowed to dry. Total residence time in open or closed arms, time ratio spent in open arms, and the number of entries (frequency) in the open or closed arms were recorded.

Open field test (*OFT*): This method is used to evaluate possible sedative or stimulating activities of animals (Carlini et al., 1986),

through the evaluation of ambulatory behavior in mice; also useful to detect both anxiolytic and anxiogenic agents. 30 min after the treatment ($n = 4$) with vehicle (1% NaCMC 0.1 ml/10 g, *p.o.*), *S. acuta* at doses of 50, 100, 300 and 500 mg/kg *p.o.* or diazepam 1 and 5 mg/kg *i.p.*, the animals were placed at the center of an open field arena. The apparatus consisted of four identical arenas measuring each arena 50 cm (width) × 50 cm (length) 30 cm (height). Traveled distance (cm), velocity (cm/s) and number of rearing behaviors were recorded and analyzed with EthoVision in a 30 min session (Siegel, 1946; Archer, 1973; Carlini et al., 1986). After each trial, the open-field apparatus was wiped clean with ethanol (10%) solution.

Test for muscle-effects

Rota-rod test (*RRT*): It is the classic method used for the assessment of motor coordination in mice or rats (Dunham and Miya, 1957; Ozturk et al., 1996; Pérez et al., 1998). Animals were trained previously (72 h before experiment) based on their capacity to maintain their balance (for 3 min) on the rotating bar (16 rpm) with a 3 cm diameter axis. A rota-rod treadmill device (Rotamex 4/8, Columbus Instruments, OH, USA) was used for this purpose.

At time 0 (0 min) the pre-trained animals were placed on a horizontal rotating rod set at a speed of 16 revolutions per min. Mice that were able to remain on the rod longer than 180 s were selected and classified into six groups of four mice per group. Four groups of the selected animals received graded doses of the *S. acuta* extract (100, 300, 500 and 750 mg/kg, *p.o.*), while the remaining groups received NaCMC (0.1 ml/10 g b.w *p.o.*) or diazepam (5 mg/kg *i.p.*). Sixty minutes later, each mouse was placed on the rota-rod, for evaluation of motor-coordination (cut-off time was 180s). Two complementary measurements were made 60 min apart (120 and 180 min).

Traction test (*TT*): The mouse's fore paws were placed on a small twisted wire rigidly supported above (20 cm high) a laboratory bench top. Normal mice grasped the wire with the fore paws, and when allowed to hang free, placed at least one hind foot on the wire within 5 s. Inability to place at least one hind foot marked failure in the traction test – low muscular strength (Rudzik et al., 1973). Groups of four male mice were used for the test at 0 and 60, 120 and 180 min after the administration of *Sida acuta* (500, 750 and 1000 mg/kg, *p.o.*), diazepam (5 mg/kg, *i.p.*) or NaCMC (0.1 ml/10 g, *p.o.*) to five different groups.

Chimney test (*ChT*): The chimney test measures the animals' motor coordination and muscle dysfunction and it was performed according to a method described by Boissier et al. (1960). A mouse was introduced at one end and allowed to move to the other end of a Pyrex glass tube (30 cm long × 3.0 cm diameter), marked at 20 cm from base. When the animal reached the end of the tube, the tube was moved to the vertical position and immediately, the mouse tried to climb the tube with a backward movement. The mice that cross the mark in 30 s or less are "normal" unless are "affected". The test was repeated at 0, 60, 120 and 180 min after the administration of *S. acuta* extract (500, 750 and 1000 mg/kg, *p.o.*), diazepam (5 mg/kg, *i.p.*) or NaCMC (10 ml/kg, *p.o.*) to different groups ($n = 4$). Motor/muscle impairment was expressed as the percentage of animals unable to perform this test within 30 s. The average time necessary to climb backwards up the chimney was also counted for each experimental group.

Pentylenetetrazole (PTZ)-induced seizures

The capacity of *S. acuta* to provide protection was measured in chemical seizure tests by determining modulation of characteristics of the seizures induced by the *i.p.* injection of PTZ. In agreement with Swinyard et al. (1952), this dose (75 mg/kg) was given intraperitonealy 30 min after *S. acuta* extract administration (50, 100, 300 and 500 mg/kg *p.o.*) or diazepam (1 mg/kg *i.p.*) to groups of eight mice. Another group of eight mice serves as control (NaCMC 1% *p.o.*). After PTZ injection mice were placed separately into circular and transparent plexiglass devices, measuring 25 cm (diameter) × 14 cm (height) and observed for 30 min for the occurrence of seizures, and were taken as the maximum time of onset of seizures (Tmax) (Vogel and Vogel, 2002). The time taken before the onset of clonic convulsions and the percentage of seizure protection were individually recorded.

Effect on normal body temperature

The rectal temperature of each mouse was measured 30 min after administration of each dose of *Sida actua* (SA) (100, 300 and 500 mg/kg, *p.o.*) using a thermometer model 0331 (PanLab Instruments, Barcelona, Spain).

Results presentation, plotting and statistical analysis

Results are expressed as mean ± standard error of the mean (SEM). All data were analyzed using one-tailed test analysis of variance (ANOVA) followed by Dunnet's test post hoc. The graphical representation and statistical analysis were performed using GraphPad Prism (V 4.3) (San Diego, USA). Statistically significant differences were determined by one-way ANOVA (treatment) followed by the Dunnet's test or by two-way ANOVA (treatment–time) followed by Boferroni test. Statistically significant differences were determined with $p < 0.05$.

Results

Sodium pentobarbital-induced sleeping time

Treatment with SA at high doses (500 and 1000 mg/kg) increased the sleeping time (T2) and decreased the sleeping latency (T1); the effect was significantly different from the control group ($p < 0.05$). Diazepam 5 mg/kg increased the sleeping time (T2) and decreased the sleeping latency (T1) (Fig. 1). The effects of graded doses of SA showed a dose dependent effect.

Anxiolytic activity

Elevated plus maze (EPM)

Administration of SA (at dose of 500 mg/kg) significantly increased the amount of time spent and the percentage of entries in the open arms of the EPM ($p < 0.05$), compared to vehicle administration. Similarly, animals treated with diazepam (1 mg/kg, *i.p.*) demonstrated a significantly increased number of entries and increased time in the open arms, as compared with controls ($p < 0.01$) (Fig. 2).

The higher the percentages of entries and time in open arms means, rodents have lower levels of anxiety (Park et al., 2005; Primeaux et al., 2006).

Open field test

In the OFT, SA at doses of 50, 100, 300 and 500 mg/kg decreased the distance moved (cm), velocity (cm/s) and rearings (*f*) as compared to control (NaCMC 1%) ($p < 0.01$). Diazepam, as expected, showed no effect at the dose used (1 mg/kg, *i.p.*), but at dose of 5 mg/kg shows diminution of these parameters (Table 1).

Tests for muscle effects

The rota-rod, chimney and traction tests were used to assess motor activity coordination, muscle relaxant and muscle strength in experimental animals under stimulants or depressants central nervous system drugs. SA shows no decrease in motor coordination at all used doses, except 750 mg/kg at 60 and 120 min ($p < 0.05$ vs. control group) (Fig. 3).

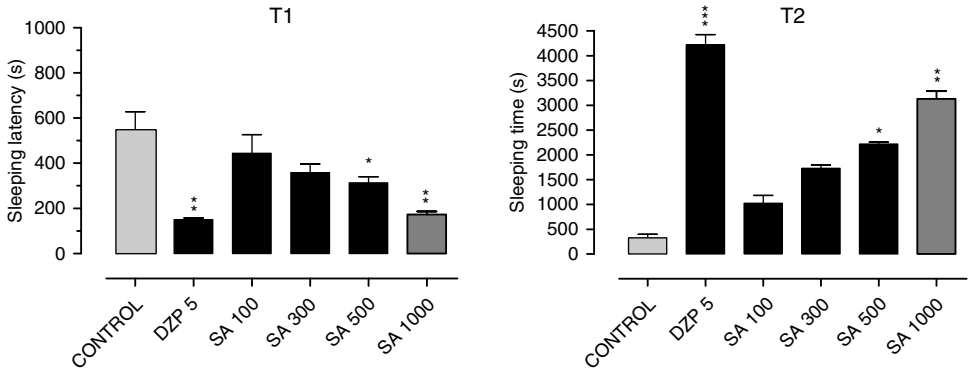

Fig. 1. Effects of the ethanolic extract of *Sida acuta* (SA) at doses of 100, 300, 500 and 1000 mg/kg, diazepam 5 mg/kg and control (vehicle) on pentobarbital (40 mg/kg *i.p.*) induced sleeping time in mice. T1 = time of latency and T2 = time of duration of sleep, $n = 4$. Values are expressed as mean ± SEM. $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$, as compared to normal control. ANOVA and Dunnet's as the post hoc test were performed.

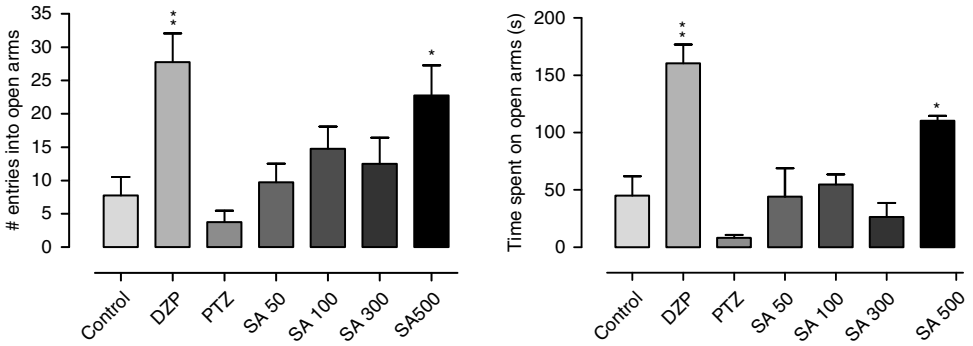

Fig. 2. Influence of the ethanolic extract of *Sida acuta* (SA) at doses of 50, 100, 300 and 500 mg/kg, diazepam 1 mg/kg and control (vehicle), expressed by percentage of entries in open arm (a) and the time spent in open arms (b) in the elevated plus maze. Results are expressed as mean ± SEM, $n = 4$ each group; $^{*}p < 0.05$ vs. control; $^{**}p < 0.01$ vs. control; ANOVA with Student–Dunnet's post hoc test.

Table 1
Effects of *Sida acuta* (SA) on the open field test in mice at doses of 50, 100, 300 and 500 mg/kg, and diazepam at 1 and 5 mg/kg. Values represent the mean ± SEM of distance moved (cm), velocity (cm/s) and rearing (*f*). Values represent the mean ± SEM, medium ± E.S. of distance moved (cm), velocity (cm/s) and rearing (*f*). ANOVA and Dunnet's as the post hoc test were performed.

Group	Distance moved (cm)	Velocity (cm/s)	Rearing (*f*)
Control	11,268 ± 466.4	6.26 ± 0.26	350.5 ± 28.9
Diazepam 1 mg/kg	14,862 ± 2334.0	8.26 ± 1.30	312.3 ± 38.6
Diazepam 5 mg/kg	980 ± 11.7**	0.77 ± 0.16**	22.5 ± 3.8**
SA 50 mg/kg	2901 ± 938.7**	1.61 ± 0.52**	26.5 ± 8.7**
SA 100 mg/kg	2726 ± 385.0**	1.52 ± 0.21**	14.8 ± 5.4**
SA 300 mg/kg	1513 ± 146.3**	0.84 ± 0.08**	11.8 ± 4.6**
SA 500 mg/kg	1614 ± 254.4**	0.89 ± 0.14**	20.0 ± 14.4**

** $p < 0.01$ compared with control group (CMC 1%).

In the traction test (TT) *S. acuta* (500, 750 and 1000 mg/kg) did not impair the ability to place at least one hind foot on the wire within 5 s, unlike diazepam (Table 2).

In the chimney test (ChT) no significant effect was observed in mice pretreated with *S. acuta* extract (500, 750 and 1000 mg/kg) in the time taken to climb backward in the Pyrex glass tube. However, mice pretreated with diazepam could not climb backwards in the Pyrex glass tube (Table 3).

Pentylenetetrazole (PTZ)-induced seizures

SA extract at 50 mg/kg doses shows a diminution of the number of mice that present seizures (0%), at doses of 100 mg/kg shows de 50% of the number of mice that present seizures. At doses of 300 mg/kg just demonstrated a 25% of protection the seizure induced PTZ. Meanwhile, doses of 500 mg/kg do not show protection against the PTZ induced seizure (Table 4).

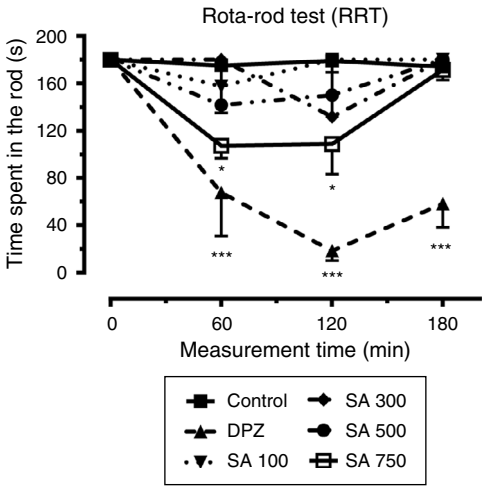

Fig. 3. Effects on rota-rod in mice at 0, 60, 120 and 180 after administration of *Sida acuta* (SA), at doses of 100, 300, 500 and 750 mg/kg or diazepam (DZP) at 5 mg/kg, $n = 4$. Values are expressed as mean ± SEM. $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$, as compared to normal control (NaCMC 1%). Two ways ANOVA and Bonferroni as the post hoc test were performed.

Body temperature

S. acuta at doses of 100 mg/kg ($p < 0.05$) and 300 mg/kg ($p < 0.01$) caused a significant hypothermia relative to control group, over the 30 min after injection (Fig. 4).

Table 2
Effect of *Sida acuta* (SA) on the muscle strength in the traction test. The muscle strength in mice was measured at 60, 120 and 180 min. Each value represents the mean ± SEM, $n = 4$. For diazepam all values > 5 s – cutoff time. ANOVA and Dunnet's as the post hoc test were performed.

Treatment	Dose (mg/kg)	Mean time it takes to put one foot back on the wire (±SEM) [s]		
Time		60	120	180
Control	–	2.1 ± 0.6	3.9 ± 0.7	3.6 ± 0.6
Diazepam	5	>5.0**	5 ± 0.0**	>5**
SA	500	3.1 ± 0.7	2.9 ± 0.5	3.5 ± 0.8
SA	750	4.0 ± 0.6	5.0 ± 0.0	4.1 ± 0.9
SA	1000	3.4 ± 0.9	4.3 ± 0.8	4.0 ± 0.6

** $p < 0.01$ compared with the control group.

Table 3
Muscle relaxant activity of *Sida acuta* (SA) in the chimney test. The muscle relaxation in mice was measured at 60, 120 and 180 min. Each value represents the mean ± SEM, $n = 4$. For diazepam all values > 30 s – cutoff time. ANOVA and Dunnet's as the post hoc test were performed.

Treatment	Dose (mg/kg)	Mean time to climb up the chimney (±SEM) [s]		
Time		60	120	180
Control	–	12.5 ± 31	11.7 ± 2.7	11.8 ± 2.3
Diazepam	5	>30.0**	>30.0**	>30.0**
SA	500	11.3 ± 3.2	20.7 ± 5.5	22.0 ± 2.8
SA	750	17.6 ± 5.4	22.0 ± 5.2	17.8 ± 5.8
SA	1000	17.1 ± 4.4	21.2 ± 3.3	20.0 ± 2.0

** $p < 0.01$ compared with the control group.

Table 4
Effect of *Sida acuta* (SA) on pentylenetetrazole (PTZ) induced seizures in mice. Values are expressed as mean ± SEM of time of onset seizures. η = number of mice that have seizures, % of protection against PTZ (75 mg/kg), t conv = time of onset of seizures. $N = 8$. ANOVA and Dunnet's as the post hoc test were performed. The maximum time of onset of seizures was 1800 s (Tmax).

Group	η	% protection	t conv (s) X ± SEM	% mortality
Control	8/8	0.0	151.5 ± 10.7	0
Diazepam 1 mg/kg	0/8	100.0	1800.0 ± 0.0**	0
SA 50 mg/kg	0/8	100.0	1800.0 ± 0.0**	0
SA 100 mg/kg	4/8	50.0	986.0 ± 310*	0
SA 300 mg/kg	2/8	75.0	1009.0 ± 259.8**	0
SA 500 mg/kg	7/8	12.5	405.5 ± 200.9	12.5

* $p < 0.05$ as compared to normal control.
** $p < 0.01$ compared with the control group.

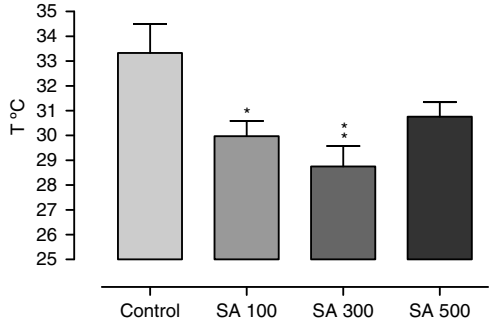

Fig. 4. Effects on corporal temperature in mice of *Sida acuta* (SA) at doses of 100, 300 and 500 mg/kg, 30 min after administration, $n = 4$. Values are expressed as mean ± SEM. *$p < 0.01$ and **$p < 0.01$, as compared to normal control (NaCMC 1%).

Discussion

This work represents the first step toward the understanding of the effects in the central nervous system of the crude extract obtained from the leaves and stems of *S. acuta*, on rodents. The plant showed depressive, anxiolytic and anticonvulsant effects; in addition, a potentiation of hypnosis induced by pentobarbital. The effects described in this work for *S. acuta* are according to what is known in traditional medicine, where is used as sedative agent (Otero et al., 2000a; Sreedevi et al., 2009; Govindarajan, 2010), also for plants within the same species *S. tiagii* and *Sida cordifolia* (Datusalia et al., 2008; Franco et al., 2005).

At the higher doses used in this work, the *S. acuta* extract indicated a sedative and hypnotic effect of the plant. This effect is probably caused by vasicine or cryptolepine, which are alkaloids isolated from this plant (Ahmed et al., 2011); even though, the effects of these compounds on the central nervous system have not been studied. The sedative effect was also evident with *S. tiagii* (Datusalia et al., 2008).

Anxiolytic compounds reduce the natural animal aversion to the open arms and promote the exploration thereof in the elevated-plus maze test. On the other hand, the forced or voluntary passages of animals into the closed arms of the EPM are associated with hormonal and behavioral changes indicative of increased anxiety (Adebesin et al., 2015). Avoidance of the open arm portrays a manifestation of fear and anxiety. Based on these assertions, the elevated plus-maze test is a reliable mean for identifying selective anxiolytic effect of drugs (Adebesin et al., 2015). The extract of *S. acuta* shows an increase in open arm exploration (anxiolytic activity), reflected by an increase in the percentage of entries into and time spent on the open arms. But, all doses of the extract of SA decreased the distance moved, velocity and rearing measured in the open field, similarly to DZP. This suggests anxiolytic effect of the extract at the dose of 500 mg/kg, giving credence to the indication in the hole-board test.

Results obtained in the rota-rod test (RRT) showed that treatment with *S. acuta*, at 100, 300 and 500 mg/kg, did not modify the spontaneous activity of the mice, none signs that denote depressant effects were observed, with comparison to the mice treated with DZ, a classic benzodiazepine with anxiolytic effects that produced a decrease of locomotor activity in comparison with the control group. Thus, these results suggest that this plant did not produce myorelaxation, neither alters the motor coordination of mice experimental, which are undesirable sedative side effects of some benzodiazepines.

In the present study, results showed that *S. acuta* leaves and stems extract has anticonvulsant effects on PTZ model of epilepsy in mice. *S. acuta* at the dose of 50 mg/kg was most effective against PTZ induced seizure (100% protection), followed by the dose of 300 mg/kg with a 75% of protection. The anti-epileptic effects of drugs such as benzodiazepines are accompanied by decreased motor activity and sedation (Gupta et al., 2012). Therefore, *S. acuta* might possibly be producing anti-epileptic action by increasing the effect of GABA, the principal inhibitory transmitter in the central nervous system. This is in accordance with the pharmacological effects of benzodiazepine and highlights the relevance of the putative anti-epileptic effects of *S. acuta* (Gupta et al., 2012). However, further studies on neurotransmitter or neuromodulators involvements are necessary for complete understanding of anticonvulsant effects of *S. acuta*.

Conclusion

In conclusion, these data showed that mice treated with crude extract of the leaves and stems of *S. acuta* presented sedative effect. Also, the extract protects against seizures induced by PTZ and it shows anxiolytic effect. Therefore, it is important to further research of this plant species.

Authors' contributions

The identification and collection of plant material were made by FAG in company of JV and IC. G-B prepared the extracts. The pharmacological evaluation was performed by DMB, AG-S and JAF The manuscript was elaborated by DMB All the authors have read the final manuscript and agreed to its submission for appraisal.

Conflicts of interest

The authors declare no conflicts of interest.

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