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Assessment of Anxiolytic and Antidepressant Effects of *Crossopteryxfebrifuga* in Mice

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Abstract: ***This study is based on the psychopharmacological properties of Crossopteryxfebrifuga that is aplant of the traditional pharmacopoeia in the Republic of Congo. The anxiolytic and antidepressant effects of the extracts were evaluated. Two methods were used for each test, respectively stress-induced hyperthermia and elevated cross labyrinth test, forced swimming test, and catalepsy test. The decoction of C. febrifugashowed a significant decrease in stress-induced hyperthermia (HIS) of 1.3 ° C to 0.6 ° C for treated animals. This decoction has carried away a significant increase of the entrances number and the timespent in the open arms of the labyrinth respectively, from 1.83 ± 0.55 for the control to 45.33 ± 3.33 for treated mouse and 41.5 ± 3.5 sec in the control at 195.83 ± 10.11 for treated mouse, as well as the percentage of entries into the open arms of the labyrinth. C. febrifuga, however, provoked a decrease of the entries number, the time spent and the percentage of labyrinth closed arms in the mice. Regarding the antidepressant activity, the decoction of C. febrifugaprovoked a significant increase of the climbs and swimming duration as well as a significant decrease of the immobility duration in both mice subjected to forced swimming and those subjected catalepsy test.***

Keywords: *C. febrifuga*, anxiolytic, antidepressant, catalepsy, mice

1. Introduction

Generally in Africa and in Congo as well as, medicinal plants are widely used for the prevention and treatment of various diseases. They are now sources of natural substances used to treat many diseases. *Crossopteryxfebrifuga* is a medicinal plant of the Congolese pharmacopoeia where it is widely used in various African localities to treat several diseases including: gastric ulcers [11, 1], dry cough, respiratory infections, fever, dysentery, pain, hypoglycemia[12,], trypanosomiasis, staphylococcal aureus infections [9,], stomachaches, connective tissue worms eyes, headache, gonorrhea, heart aches, wounds and epilepsies [3], malaria [6], epilepsy [2]. *Crossopteryxfebrifuga* also has effects on the central nervous system. This present study is carried out in order to assess the anxiolytic and antidepressant properties of *C. febrifuga* leaves extracts.

2. Material and Method

2.1 Plant material

Crossopteryxfebrifuga leaves were used for different tests. They were dried at ambient temperature and then pulverized for extracts preparation.

2.2 Preparation of the extract

20 g of powder of *C. febrifuga* leaves were boiled in 250 ml of distilled water for 30 minutes. After cooling and then filtering, the filtrate was dried in an oven for 48 hours. The dry residue is dissolved in the water before its administration.

2.3 Animal material

Mus musculus swiss mice(20 - 30 g) were used. They are placed in an environment with an ambient temperature of about 25°C, and a cycle of 12 hours of light and 12 hours of darkness, with free access to food and drinking water.

Pharmacological tests

3. Assessment of anxiolyotic properties

3.1 Test of hyperthermia induced by stress

Miceare brought to the laboratory 72 hours before the test performance for acclimation [4]. They are distributed homogeneously in batches of 10 mouse each and treated as follows: the negative control group received 10 ml/kg of distilled water. The positive control group is treated with 20 mg/kg (i.p.) of phenobarbital and the test lots are treated with the decoction of *C. febrifuga* respectively at doses of 60, 80, 100 and 120 mg/kg. After administration of the different products, the mice are put back into their cages to reduce the neophobic responses carrier away by experimental environment [4]. One hour after the various treatments, the mice are removed from their cage at the rate of one mouse per minute. The rectal temperature of each mouse is measured by introducing a probe (2 mm in diameter and 2 cm in length) into the rectum. The probe remains inserted into the anus of the animal until the temperature read on the dial of the thermometer is stabilized. Before each temperature measurement, the probe is maintained in 0.9% NaCl. Stress-induced hyperthermia (HIS) is determined by making the difference between the rectal temperature of the last three mice and those of the first three mice [7].

3.2 Labyrinth test on a raised cross

The raised cross labyrinth is an experimental device consisting of two open (opposing) arms of 15 × 5 cm and two closed (opposing) arms of 15 × 5 × 10 cm, including a platform in the center and it is 50 cm of the ground. The test was performed in a quiet room lit by daylight. The mice are

brought 72 hours before the test to acclimatize them. They are classified homogeneously in 6 lots of 6 animals each and treated as follows: 10 ml/kg of distilled water for the negative control and3 mg/kg; i.p. of diazepam for the positive control and the different doses of the decoction of *C. febrifuga* for the tested lots are 60, 80,100 and 120 mg/kg per-os. After administration of the different substances, the mice are again put back into their cages to reduce the neophobic responses due to the experimental environment [4]. An hour later, the mice are placed one after the other in the center of the labyrinth platform. The behavior of each mouse is observed for 5 minutes: the number of entries and the time spent in the different arms of the labyrinth are noted.

4. Evaluation of Antidepressant Properties

4.1. Forced swimming test

24 hours before the actual experimental session, the mice are individually pre-tested for 15 minutes. The mice are treated 1 hour before carrying out the experiment, with distilled water for the negative control batch, the different doses of the decoction of *C. febrifuga* (80, 100, and120 mg / kg) for the test lots, and clomipramine (25 mg / kg) for the positive control group. One hour after all treatments, the mice are subjected to forced swimming for 6 minutes. The duration of swimming, the time of immobility and the time of the climbing are noted for each animal.

4.2. Haloperidol-induced catalepsy test

The test is to swing the mouse on a wire stretched between two metal bars and placed at a height of 10 cm from the ground. Lots of six mice each were constituted and treated as follows: the negative control group received 10 ml / kg of distilled water; the positive control group is treated with 25 mg / kg ofClomipramine (Anafranil *). The test lots are treated with the decoction at doses of 80, 100 and 120 mg/kg). The catalepsy is induced by administration of 5 mg/kg of haloperidol one hour after all treatments. The mice are then placed in turn on the wire. The time of immobility is then measured.

Statistical analysis

Parameters measured in pharmacological tests are expressed as mean ± standard error on mean (E.S.M.) and standard deviation. The values were compared using the analysis of variance test (ANOVA). From p <0.05, the values were considered significant.

5. Results and discussion

The results of the anxiolytic activity of *C. febrifuga* are shown in the figures 1, 2, 3, 4, 5, 6 and 7. The decoction of *C. Febrifuga* at doses of 80 and 100 mg/kg resulted in a significant decrease in stress-induced hyperthermia (HIS) of 0.6°C in treated mice, such as the 20 mg/kg of Phenobarbital (fig.1). Stress-induced hyperthermia is antagonized by anxiolytic substances [3,8]. The decoction of *C. febrifuga*at doses to 100 and 120 mg/kg caused a significant increase the entries number and the spent time in the labyrinth open arms respectively of 1.83 ± 0.55 to the mice of the negative control group. at 43.83 ± 1.83; 45.33 ± 3.33 in the treated mice and from 41.5 ± 3.5 sec to 186.5 ± 9.5 sec; 195.83 ± 10.11 sec, as well as the percentage of entries in these arms of 7.5% in controls to 68.5%, 88.8% and 90.6% in those treated at doses of 80 , 100 and 120 mg / kg (Figures 2, 3, 4). However, *C. Febrifuga* at doses of 80, 100 and 120 mg/kg resulted in a decrease of the number of entries and the spent time as well as the percentage of entries in the labyrinth closed arms respectively of 22 ± 2.33 for negative controls at 7.16 ± 66, 5.5 ± 1; 5.16 ± 1.22 for the treated mice and 185.83 ± 8.83 sec for the negative controls at 89.16 ± 2.83 sec; 67.16 ± 5.44 sec and 52.66 ± 4.33 sec, the percentage of entrances from 92.4% in the negative controls to 31.4% and 10% in the treated mice (Figures 5, 6, and 7). Decreased activity in the closed arms indicates a reduction in stress [9,14] whereas, the increase in activity in the open arms of the labyrinth reflects a decrease in anxiety in the labyrinth [6, 7 ,8]. These results suggest that *C. febrifuga* has anxiolytic properties [2, 9].

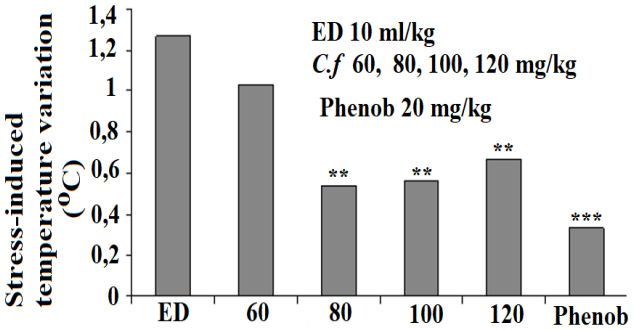

Figure 1: Effect of decoction of *C. febrifuga* on stress-induced temperature variation; n = 6. ** p ≤ 0.01; *** p ≤ 0.001, significant difference from the negative control group; ED: distilled water; Phenob: Phenobarbital (20 mg / kg).

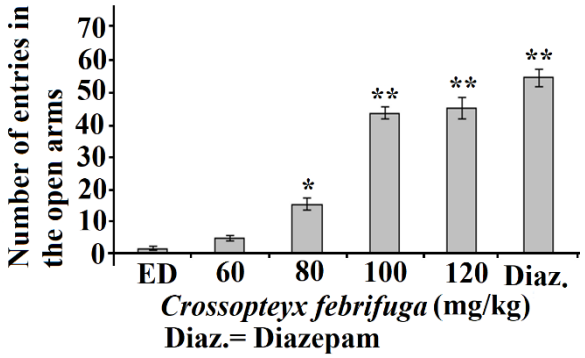

Figure 2: Effect of *C. febrifuga* on the number of entries in the open arms; n = 6; * p ≤ 0.05, ** p ≤ 0.01, significant difference compared to the negative control group; ED: distilled water; diazepam 3mg / kg.

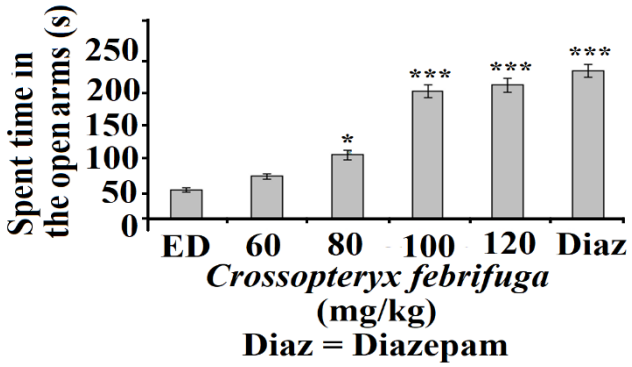

Figure 3: Effect of *C. febrifuga* on the spent time in the open arms; n = 6, * $p \leq 0.05$, *** $p \leq 0.001$, significant difference compared to the negative control group; ED: distilled water; diazepam 3mg / kg.

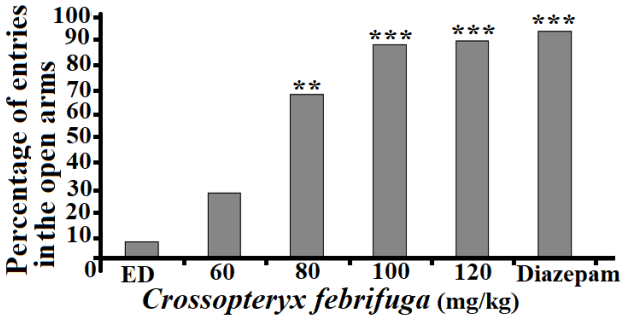

Figure 4: Effect of *C. febrifuga* on the percentage of entries in the open arms; n = 6; ** $p \leq 0.01$ *** $p \leq 0.001$, significant difference compared to the negative control group; ED: distilled water; diazepam 3 mg / kg

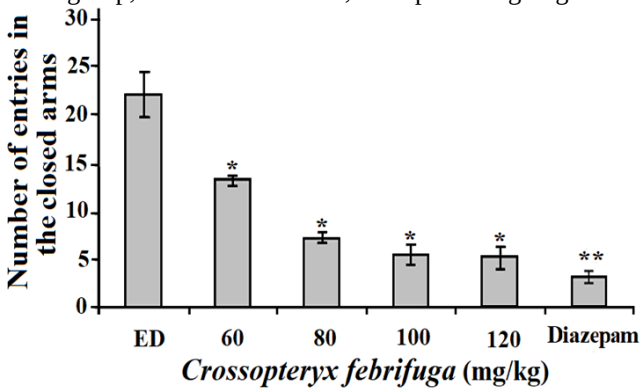

Figure 5: Effect of *C. febrifuga* on the number of entries in the closed arms; n = 6, * $p \leq 0.05$, ** $p \leq 0.01$, significant difference from the negative control group; ED: distilled water; diazepam 3 mg / kg.

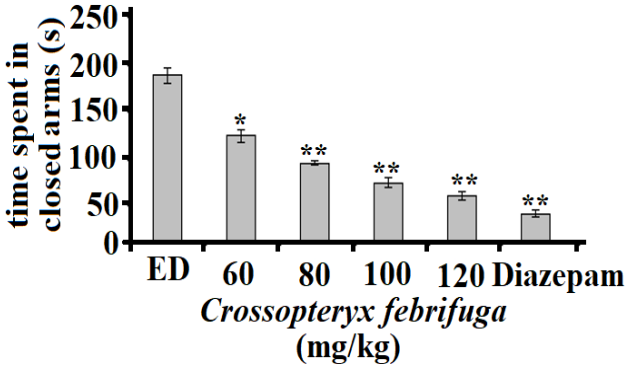

Figure 6: Effect of *C. febrifuga* on time spent in closed arms; n = 6; ** $p \leq 0.01$ *** $p \leq 0.001$, significant difference compared to the negative control group; ED: distilled water, diazepam 3 mg / kg.

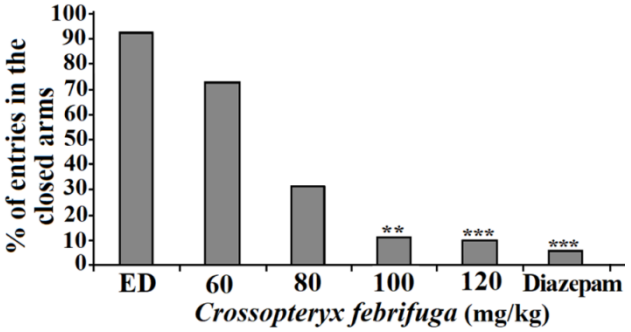

Figure 7: Effect of *C. febrifuga* on the percentage of entries in the closed arms; n = 6; ** $p \leq 0.01$ *** $p \leq 0.001$, significant difference compared to the negative control group; ED: distilled water; diazepam 3 mg / kg.

The results of the antidepressant activity are shown in Figures 8 and 9. It can be seen that the decoction of *C. febrifuga*at doses of 80, 100 and 120 mg/kg resulted in an increase in the forced swimming mice. Significant rise duration and significant reduction in immobility duration, respectively from 98 ± 2 (sec) in negative controls to 130 ± 05 (sec); 151 ± 01 (sec) and 120 ± 5 (sec) in the treated mice; 100 ± 3 (sec) in the controls at 150 ± 4 (sec) and 200 ± 3 (sec) in the mice treated at doses of 100 and 120 mg / kg, respectively. The immobility time decreased from 250 ± 5 (sec) in controls to 98 ± 2.3 (sec) in treated mice (Figure 8). These results suggest an antidepressant activity of the decoction of this plant by stimulating the mice to continue to make efforts to leave the closed environment [5, 8, 10]. *C. febrifuga* resulted in a significant decrease in the immobility time in the mice suspended on the wire after induction of catalepsy such as anafranil. This effect could confirm the observed antidepressant properties of the decoction.

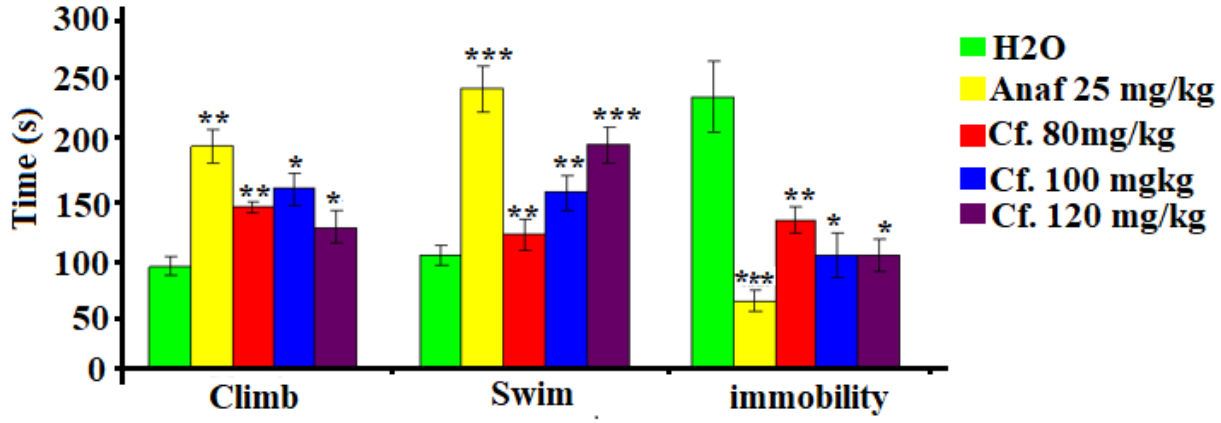

Figure 8: Effect of *C.febrifuga* on forced swimming; n = 6. * p ≤ 0.05; ** p ≤ 0.01; *** p ≤ 0.001, significant difference compared to the negative control group; Anaf: Anafranil 25 mg / kg; H20: distilled water,C.f: *Crossopteryxfebrifuga*

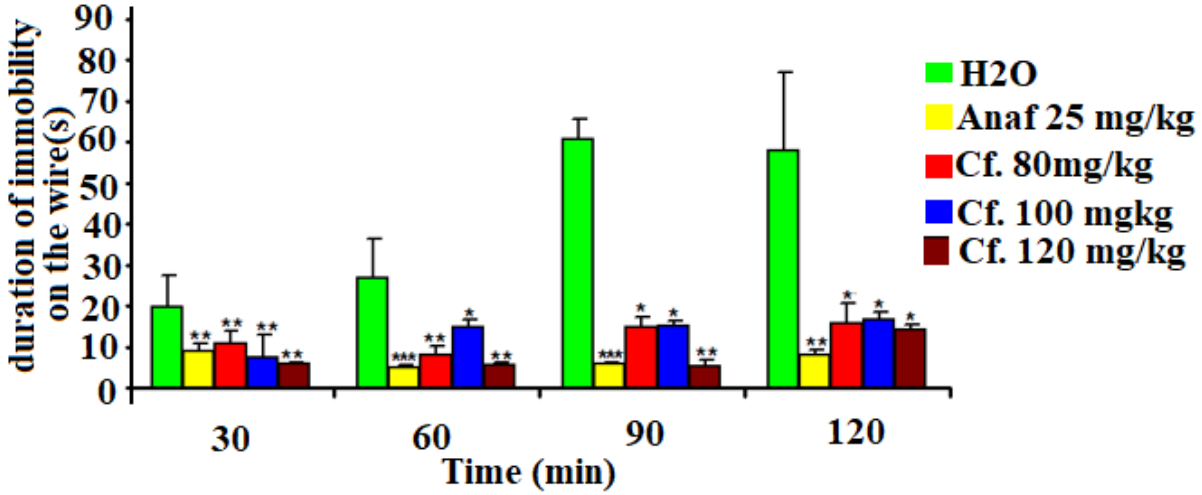

Figure 9: Effect of *C. febrifuga* on the duration of immobility in the mice suspended on the wire; n = 6. ** p ≤ 0.01; *** p ≤ 0.001 significant difference compared to the negative control group; Anaf: Anafranil 25 mg / kg;; H20: distilled water, C. f: *Crossopteryxfebrifuga*

6. Conclusion

The present study has done in order to assess the anxiolytic and anti-depressive properties of the *leaves* decoction *of C. febrifuga*. The decoction *of C. Febrifuga* showed anxiolytic activity decreasing stress-induced hyperthermiato mice and increasing the entries nombre and the spent time in the open arms of the labyrinth.It sowed as wel as an antidepress if effect by increasing the time of swimming and climbing tomice subjected to forced swimming and decreasing the immobity time of mice suspended on the wire. This results confirmed the traditional use of this plant for the l' anxiety and depression treatment.

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