

BEHAVIORAL EVIDENCE OF ANTIDEPRESSANT-LIKE ACTIVITY OF *CASSIA SIEBERIANA* EXTRACT IN MICE**Bakou Niangoran François¹, B. A. Abdoulaye², Diabate D.² and Atayi E.³**¹Unit of Animal Physiology, Jean Lorougnon GUEDE University, Daloa, (Côte d'Ivoire)²Laboratory of Neuroscience, UFR Biosciences, Felix HOUPHOUET-BOIGNY University, Abidjan, (Côte d'Ivoire)³Neurology Service, Functional Exploration Unit of the Nervous System, C.H.U. from Cocody-Abidjan, (Côte d'Ivoire).***Corresponding Author: Bakou Niangoran François**

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ABSTRACT

Objective: The present study was designed to evaluate the acute and chronic behavioral and antidepressant effects of hydro alcohol extract of stem bark of *Cassia sieberiana* in standardized mice models of depression. Materials and Methods: hydro ethanolic extract of stem bark from *Cassia sieberiana* were prepared, and phytoconstituents were determined using appropriate chemical analytical methods. Animals were divided into five groups (n=5/group): The control group received vehicle (saline water 0,1ml/mouse). Amitriptyline (20mg/kg b.w., IP) was used as the positive control or standard group while the treated mice received CS (100, 200, and 400mg/kg body weight i.p). In the acute treatment study, a single dose was administered 30 min prior to testing. For the chronic treatment study, a single dose was administered daily for 14 days. In the chronic dose study, the behaviors of all groups were assessed for antidepressant activity 30 min after the last treatment dose on the 14th day. Different standardized depression models were used for behavioral tests to evaluate the antidepressant activity, such as forced swim test (FST), and tail suspension test (TST) test. Results: the preliminary pharmacological screening with acute dosing exhibited the antidepressant activity of CS, but its antidepressant activity was more enhanced after repeated dosing. In comparison with the acute studies, chronic dose studies displayed a significant antidepressant manifestation in the behavioral patterns when compared to the vehicle controls. Conclusion: The results obtained in this work suggest that the hydro ethanolic extract of stem bark from *Cassia sieberiana* may possess an antidepressant activity.

KEYWORDS: *Cassia Sieberiana*, antidepressant activity, mice.**INTRODUCTION**

Depression is a widespread chronic psychiatric complaint which interferes with social life and work performance. Today, millions of people of all ages suffer from this disease.^[1] According to figures from the World Health Organization, by the year 2020, depression is estimated to be the second known cause of world disability,^[2] and through 2030, it will probably make the greatest contribution to the burden of disease.^[3] In last few decades, several drugs have been discovered to treat depression such as tricyclic antidepressants, monoamine oxidase inhibitors,^[4] and selective serotonin reuptake inhibitors (SSRI). But unfortunately, all of the drugs have serious side effects including insomnia, anxiety, weight gain etc. It is well known that nature is the best and safe source for all medicine. So it becomes worth to search for a new antidepressant drug from natural source with less side effects and complications.^[5] *Cassia sieberiana*, (*Cassia kotschyana* Oliv.; Fam. Caesalpinaceae), is a savannah tree that grows to about

15 m tall and is commonly fairly cultivated because of its attractive blossom and curious fruits commonly referred to as the African laburnum. *C. sieberiana* has a very wide range of phytotherapeutic application in Ghana including the use of its roots in the management of hernia, leprosy, indigestion and gastric ulcer.^[6] At the Centre for Scientific Research into Plant Medicine (CSRPM) in Ghana, an aqueous suspension of the powdered roots bark is used to manage abdominal colic and pains associated with the joints. Earlier studies we conducted indicated that the aqueous roots bark extract of *Cassia sieberiana* possesses anti-ulcerogenic properties against gastric ulcers induced by various methods.^[7] In traditional medicine, the plant is used as antimicrobial, antiviral, antibacterial, anti-inflammatory, antitrypanosomal and antioxidant agent, as a strong purgative, diuretic, abortifacient, anti-schistosomiasis, anti-dysentery and antihemorrhoid.^[8, 9] No scientific report regarding the in vivo antidepressant activity of *Cassia sieberiana* extract has been published. That's

why, the present study was undertaken to assess the possible antidepressant effects following single administration of hydro ethanolic extract of stem bark from *Cassia sieberiana* (CS) in mice. For this purpose, we used the forced swim test (FST) and the tail suspension test (TST).

MATERIALS AND METHODS

Plant material

Cassia sieberiana stems bark were harvested in October, 2019 at the Jean Lorougnon GUEDE university from Daloa, (Cote d'Ivoire). The plant was identified and verified by botanist Professor from Jean Lorougnon GUEDE university of Daloa (Cote d'Ivoire).

Extract preparation

The stems bark of *Cassia sieberiana* were dried for four weeks. The drying process of the stems barks of *Cassia sieberiana* was done in the absence of light to avoid the principle of the clear phase of photosynthesis which is for the plant (*Cassia sieberiana*) to capture the light energy Photons and to transmit it by way of the electrons charged with this energy, to a chain of electron acceptors (molecules with variable oxidoreduction potentials). Then the dried stem bark of *Cassia sieberiana* a made powder using an electric grinder IKAMAG RCT®. 100 grams of powder of *Cassia sieberiana* were macerated for 24 hours in 1 liter of ethanol (ethanol and distilled water mixture: 70/30). The macerated obtained was then filtered twice on white cotton and once on Whatman filter paper N°4. The filtrate obtained in 70% ethanol was evaporated to dryness at reduced pressure at temperature of 40°C using a rotary evaporator type Buchi 161 Water Bath.

Animals

25 healthy adult male Swiss albino mice weighing (20–30 g) were obtained from the animal house of Jean Lorougnon GUEDE University, Daloa. These animals were housed under standard environmental conditions. The rats were fed with FACI® (Fabrication d'Aliments de Côte d'Ivoire) pellets, groundnuts and dried fish. They had free access to drinking water ad libitum.

Drugs and chemicals

The standard drugs amitriptyline and saline water were collected from Square Pharmaceuticals Ltd., Cote d'Ivoire. Distilled water which was used for dilution purpose was prepared was obtained from Jean Lorougnon GUEDE university of Daloa (Cote d'Ivoire).

Behavioral parameters used to test antidepressant activity

Forced swim test

The procedures for the FST, a widely used behavioral test for the detection of antidepressant-like effects, were similar to those described earlier.^[10,11] Animals were initially placed individually to swim in plastic cylinders (30 cm of diameter by 40 cm in height containing 25 cm of water at $24 \pm 1^\circ\text{C}$ ^[10] for 15 min (pretest). They were

then removed and allowed to dry in a separate cage before returning to their home cages. Twenty-four hours later the animals were submitted to a 5 min session of forced swimming session (test). During this session the total amount of time in which animals remained immobile (except for small limb movements necessary for floating) were recorded by an observer that was blind to the treatments. The water was changed after each trial to avoid the influence of alarm substances.

Tail suspension test

TST was carried out according to the method described by Porsolt *et al.*^[11,12] Briefly, rats were suspended by their tails using an elastic band attached to the tails by adhesive tape, and the elastic band was hooked onto a horizontal rod. The distance between the tip of the nose of the rat and the floor was approximately 20 cm. The mice were suspended for a period of 5 min, and the time spent immobile during the last 4 min of the 5 min was recorded for each individual, by an observer blinded to the genotype.

Experimental study design

Twenty-five mice were randomly divided into five groups (5 mice/group). The control group received vehicle (saline water 0,1mL/mouse). Amitriptyline (20mg/kg b.w., IP) was used as the positive control or standard group while the treated mice received CS (100, 200, and 400mg/kg body weight i.p). In the acute treatment study, a single dose was administered 30 min prior to testing. For the chronic treatment study, a single dose was administered daily for 14 days. In the chronic dose study, the behaviors of all groups were assessed for antidepressant activity 30 min after the last treatment dose on the 14th day. Different standardized depression models were used for behavioral tests to evaluate the antidepressant activity, such as forced swim test (FST), and tail suspension test (TST) test. The groups assigned for acute and chronic dose study were as follows: Group 1: Control group (saline water); Group 2: amitriptyline (20mg/kg); Group 3: CS-1 (100mg/kg); Group 4: CS-2 (200mg/kg); Group 5: CS-3 (400mg/kg).

Statistical analysis

The differences between experimental and control groups were determined using the statistica 10.0 software for windows. Comparisons among different groups were performed by analysis of variance test. Statistically significant differences between control and experimental groups were assessed by Student's *t*-test. All data are expressed as mean \pm standard error of mean. $P < 0.05$ was considered to be significant.

RESULTS

Acute treatment study

Forced swim test

The results indicated that after 30 min administration of hydro ethanolic extract of stem bark from *Cassia sieberiana* CS 100mg/kg, there was no significant decrease in the immobility time, but both amitriptyline

and test substance treated animals (CS 200mg/kg and CS 400mg/kg) showed slight reductions in immobility time compared to the vehicle controls (Figure 1).

Tail suspension test

No decrease in the immobility time was observed after administering 100 mg/kg of hydro ethanolic extract of stem bark from *Cassia sieberiana* CS, whereas the immobility time was markedly shortened in 200 mg/kg CS treated animals. Significant reductions in the immobility time were also noted in 400 mg/kg CS treated animals in comparison with the vehicle control (Figure 2).

Chronic treatment study

Forced swim test

In the chronic investigation, results summarized in (Figure 3) show that intraperitoneal administration of

hydro ethanolic extract of stem bark from CS at 100 mg/kg, 200mg/kg, and 400mg/kg caused reductions in FST immobility time in mice. Standard amitriptyline dose of 20 mg/kg displayed a significant decrease in the immobility time.

Tail suspension test

Results of the 14 days chronic study revealed that there was an inverse relationship between the dose of the extract and the immobility time, that is, an increase in the CS dose produced a corresponding reduction in the immobility time in comparison with the control group (Figure 4). In addition, repeated administration of standard amitriptyline (20 mg/kg/day) showed a profound decrease in the mean immobility period. Overall, 14 days repeated administration of CS showed a significant decrease in the immobility activity in both FST and TST animal models.

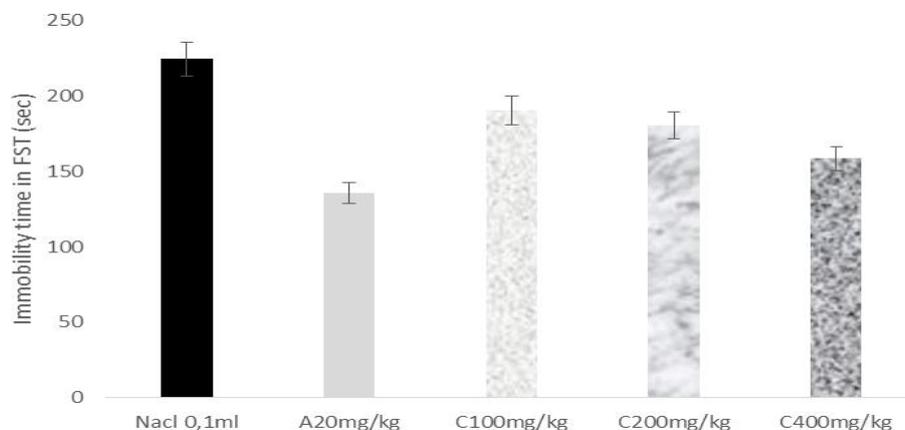


Figure 1: effet of *Cassia sieberiana* extract on duration of immobility forced swim test. Group 1: Control group (saline water); **Group 2: amitriptyline (20mg/kg); Group 3: CS-1 (100mg/kg); Group 4: *CS-2 (200mg/kg); Group 5: *CS-3 (400mg/kg). Results are represented as mean \pm standard error of mean significantly different at *P<0.05 and **P<0.01 compared to vehicle control.

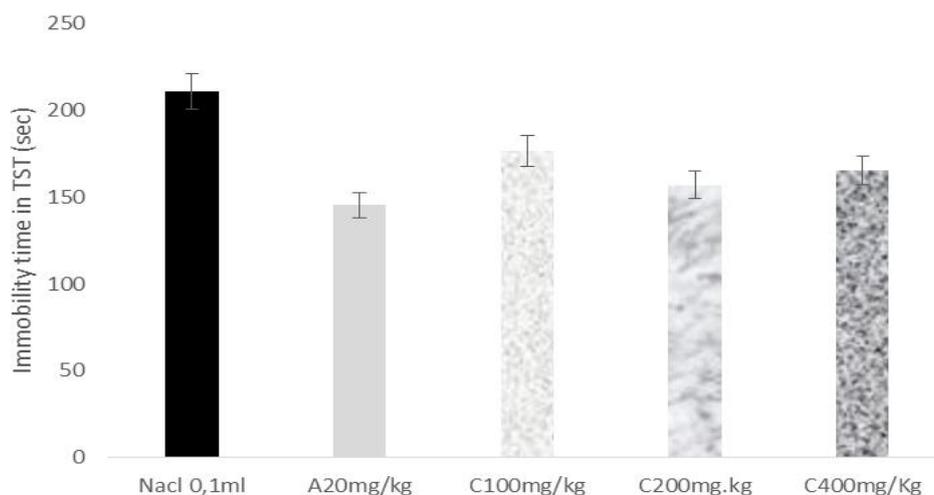


Figure 2: effet of *Cassia sieberiana* extract on duration of immobility in tail suspension test. Group 1: Control group (saline water); **Group 2: amitriptyline (20mg/kg); Group 3: CS-1 (100mg/kg); *Group 4: CS-2 (200mg/kg); *Group 5: CS-3 (400mg/kg). Results are represented as mean \pm standard error of mean significantly different at *P<0.05 and **P<0.01 compared to vehicle control.

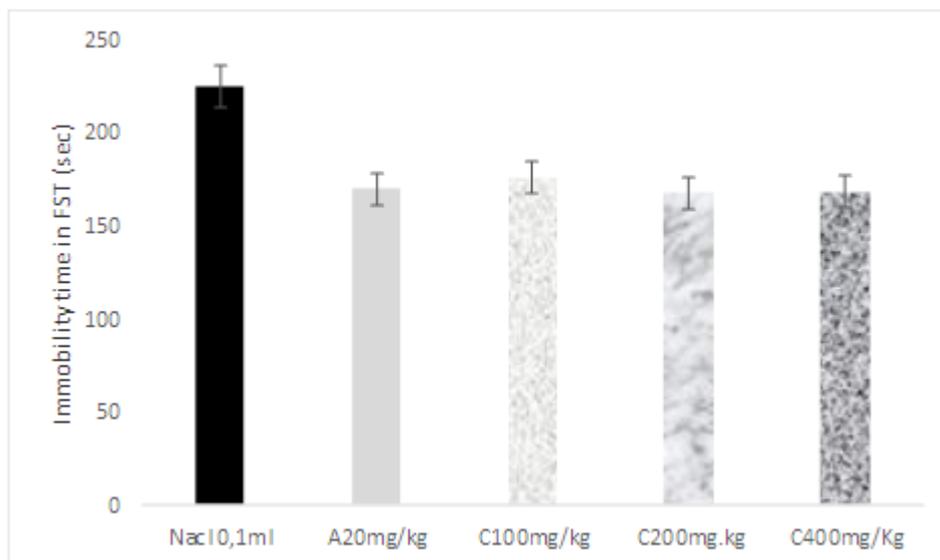


Figure 3: effet of chronic administration of *Cassia sieberiana* extract on duration of immobility forced swim test. Group 1: Control group (saline water); **Group 2: amitriptyline (20mg/kg); *Group 3: GS-1 (100mg/kg); **Group 4: GS-2 (200mg/kg); *Group 5: GS-3 (400mg/kg). Results are represented as mean \pm standard error of mean significantly different at * $P < 0.05$ and ** $P < 0.01$ compared to vehicle control.

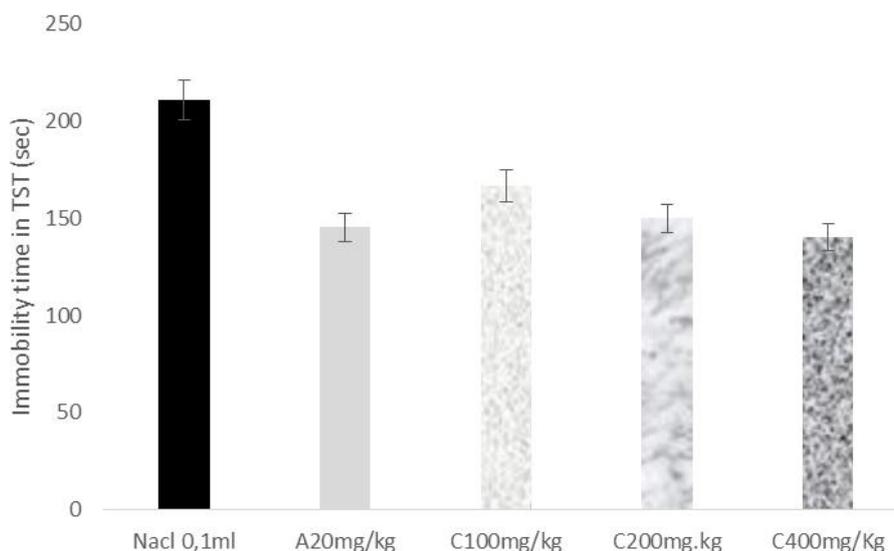


Figure 4: effet of chronic administration of *Cassia sieberiana* extract on duration of immobility in tail suspension test. Group 1: Control group (saline water); **Group 2: amitriptyline (20mg/kg); **Group 3: CS-1 (100mg/kg); **Group 4: **CS-2 (200mg/kg); **Group 5: CS-3 (400mg/kg). Results are represented as mean \pm standard error of mean significantly different at * $P < 0.05$ and ** $P < 0.01$ compared to vehicle control.

DISCUSSION

In our study, the significant reduction in the immobility time observed in the FST following the acute and chronic administration of hydro ethanolic extract of stem bark from *Cassia sieberiana* CS 200 mg/kg and 400 mg/kg suggests the antidepressant action of CS. The results also showed a significant reduction in the immobility time in the TST following the acute and chronic administration of hydro ethanolic extract of stem bark from *Cassia sieberiana* CS 100, 200 and 400 mg/kg/day. This tendency for the extract to reduce the immobility time as a function of the increase in the dose may be due to a

reduction in the synthesis of corticosteroid hormone since the active molecules exert a predominant noradrenergic effect by increasing the climbing time, and a serotonergic effect by increasing swimming time.^[13] In addition,^[14] (Connon, 1999) have demonstrated that FST or TST causes corticosterone activation, increases serotonergic activity at the level of the circuit involved (tonsil, frontal cortex and hippocampus) and increases dopamine turnover. Dopamine which is involved in functions such as energy, motivation, appetite, libido, aggression, initiative, euphoria, pleasure, mood, emotions and higher functions could also potentiate its

antidepressant effects.^[15] In our present study, antidepressant-like effect of *Cassia sieberiana* in all the classic models of depressants, where it was found to possess antidepressant-like activity comparable to the standard drug Amitriptyline. Amitriptyline acts by inhibiting norepinephrine (NE) reuptake and has been used as a standard drug in majority studies. The beneficial effect of Amitriptyline in the forced swimming test model seems to be due to increased availability of these neurotransmitters (NE) and serotonin (5HT) at the post synaptic site following reuptake inhibition.^[16] Our results are to be compared with the work of Kaur, who in a similar study showed the antidepressant activity of *Moringa oleifera*.^[17]

Initial hypothesis of depression has been formulated about 40 years ago, proposing that the main symptoms of depression due to functional deficiency of cerebral monoaminergic transmitters such as (NE), 5HT, and dopamine (DA) located at synapses.^[18] Some studies have also shown the adaptogenic effect of the plant extract via normalization of the various stress parameters and monoaminergic levels which may provide a clue that the extract is bringing their possible antidepressant-like effect through restoration of normal monoaminergic neurotransmitters.^[19] The phytochemical screening of the hydro ethanolic extract of stem bark from *Cassia sieberiana* revealed the presence of active chemical compounds (phenols, anthraquinones, tanins saponins, anthocyanes and flavonoids),^[20] Moreover, the results obtained by Evenamede, showed that stem bark of *Cassia sieberiana* extract contain an important amount of total phenol responsible for its remarkable antioxidant activity exhibited.^[20] Recently, oxidative stress was linked with the pathophysiology of major depression, with significant correlations being found between the severity of depression and erythrocyte superoxide dismutase/lipoperoxidation levels.^[21] Meanwhile, treatment with antidepressants reduces the oxidative stress related to depressive disorder.^[22,23] Additionally, some species such as *Bacopa monneira*, *Withania somnifera* and *Asparagus racemosus*, all of which are reported to have antidepressant-like properties, also possess antioxidant activity.^[23,24] Therefore, it is possible that the antioxidant activity of the hydro alcohol extract from *Cassia sieberiana* may contribute to its antidepressant-like effect.

CONCLUSION

The results obtained in this study suggest that extracts of hydro ethanolic of stem bark from *Cassia sieberiana* CS may possess an antidepressant activity. The preliminary pharmacological screening with acute dosing exhibited the antidepressant activity of hydro ethanolic extract of stem bark from *Cassia sieberiana* CS, but its antidepressant activity was more enhanced after repeated dosing. In comparison with the acute studies, chronic dose studies displayed a significant antidepressant manifestation in the behavioral patterns when compared to the vehicle controls. This effect was far more

significantly pronounced in animals treated with hydro ethanolic extract of stem bark from *Cassia sieberiana* CS at a dose of 200 and 400mg/kg/day.

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