Evaluation of the Antidepressant Activity of *Griffonia simplicifolia* Aqueous Extracts

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**Abstract**

**Objective:** The present study was designed to evaluate the acute and chronic behavioral and antidepressant effects of aqueous extracts of *GS* leaves in standardized rats models of depression. Materials and Methods: Aqueous extracts of *GS* leaves were prepared, and phytoconstituents were determined using appropriate chemical analytical methods. Animals were divided into five groups: The control group received vehicle (saline water 10ml/rat). Amitriptyline (20mg/kg b.w., IP) was used as the positive control or standard group while the treated rats received *GS* (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 *GS*, 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 study suggest that aqueous extracts of *GS* may possess an antidepressant activity.

**Keywords:** *Griffonia simplicifolia*, leaves, antidepressant activity.

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extract has been published. That’s why, the present study was undertaken to assess the possible antidepressant effects following single administration of seed extract from *G. simplifolia* in rat. For this purpose, we used the forced swim test (FST) and the tail suspension test (TST).

**MATERIALS AND METHODS**

**Plant Material**

Seeds from *G. simplifolia* plant were collected from Daloa, (Cote d’Ivoire) in October, 2019. The plant was identified and verified by botanist Professor from Jean Lorougnon GUEDE university of Daloa (Cote d’ivoire). The collected seeds were dried under a shade during two weeks and pulvForced 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 [14, 15]. 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 ± 1°C [14] for 15 min

**RESULTS**

**Acute treatment study**

Forced Swim Test

The results indicated that after 30 min administration of GS 100mg/kg, there was no

**Tail suspension test**

TST was carried out according to the method described by Porsolt et al., [16, 17]. 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 rats were randomly divided into five groups (5 rats/group). The control group received vehicle (saline water 10mL/rat). Amitriptyline (20mg/kg b.w., IP) was used as the positive control or standard group while the treated rats received GS (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: GS-1 (100mg/kg); Group 4: GS-2 (200mg/kg); Group 5: GS-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 ± standard error of mean. *P* < 0.05 was considered to be significant.

Forced Swim Test

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**Extract Preparation**

The powder of Seeds from *G. simplifolia* was used to prepare the various extracts. Fifty (50) grams of the powder were extracted in 1 L of distilled water. The mixture obtained was then homogenized using a Mixor during 24 hours. The homogenate obtained is filtered successively twice on absorbent cotton then once on Wattman N˚1 filter paper. The filtrate was carried thereafter to evaporation in a drying oven with 50˚C during 48 hours. We obtained this way

**Animals**

25 males Wistar rats aged 8-10 weeks weighing (145 - 250 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 [14, 15]. 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 ± 1°C [14] for 15 min

| Experimental Study Design | 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) |
|----------------------------|-------------------------------|-------------------------------|------------------------|------------------------|------------------------|
| Statistical Analysis       |                               |                               |                        |                        |                        |
| RESULTS                    |                               |                               |                        |                        |                        |
| Acute treatment study      |                               |                               |                        |                        |                        |
| Forced Swim Test           |                               |                               |                        |                        |                        |

**RESULTS**

**Acute treatment study**

Forced Swim Test

The results indicated that after 30 min administration of GS 100mg/kg, there was no
significant decrease in the immobility time, but both Amitriptyline and test substance treated animals (GS 200mg/kg and GS 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 GS, whereas the immobility time was markedly shortened in 200 mg/kg GS treated animals. Significant reductions in the immobility time were also noted in 400 mg/kg GS 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 aqueous extracts of GS at 100 mg/kg, 200mg/kg, and 400mg/kg caused reductions in FST immobility time in rats. 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 GS dose produced a corresponding reduction in the immobility time in comparison with the control group (Figure-4). In addition, repeated administration of standard fluoxetine (20 mg/kg/day) showed a profound decrease in the mean immobility period. Overall, 14 days repeated administration of GS showed a significant decrease in the immobility activity in both FST and TST animal models.

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**Fig-1: Effet of G. simplicifolia 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 ±standard error of mean significantly different at *P<0.05 and **P<0.01 compared to vehicle control.

**Fig-2: Effet of G. simplicifolia extract on duration of immobility in tail suspension 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 ± 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 GS 200 mg/kg and 400 mg/kg suggests the antidepressant action of GS. The results also showed a significant reduction in the immobility time in the TST following the acute and chronic administration of GS 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 [18]. In addition [19, 20] 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 [20]. In the case of aqueous GS extracts, it could therefore initially be an increase in the synthesis and production of serotonin induced by 5-HTP and potentiating its effects at the level of the organism because as indicated above serotonin is involved in several brain functions. In addition, neuropsychiatric disorders such as depression, dementia and anxiety are associated with functional abnormalities of serotonergic neurons [21]. The increase in the synthesis of serotonin could influence the synthesis of corticosterone by potentiating the negative feedback control exerted by corticosterone on the HPA axis which would thus cause a decrease in its secretion [22]. Indeed 5-HTP being the direct precursor of serotonin its administration induces an increase in synthesis of serotonin which in return acts by reducing the synthesis of corticosterone. It should be noted that it is rather plausible to refer to the reduction of immobility to the inhibition of corticosterone [23]. Indeed, it has been shown that during forced swimming, corticosteroid hormones regulate the time of immobility what Baèz and Volosin in 1994, confirm in their work by showing that an increase corticosterone was accompanied by increased immobility time during forced swimming in rats [24]. Our results are to be compared with the work of Kaur [25], who in a similar study showed the antidepressant activity of Moringa oleifera.

The results of the preliminary phytochemical analysis of G.S. seeds carried out by John Addotey [26] revealed the presence of phenolic compounds such as tannins, and flavonoids. Extracts rich in phenolic compounds have complex actions which include: inhibition of MAO-A and MAO-B, inhibition of synaptosomes of reuptake of serotonin, dopamine and norepinephrine, downregulation of receptors βadrenergics, the positive regulation of the 5-HT2 receptor and the regulation of genes that control the function of the hypothalamic-pituitary-adrenal axis [27]. Catechins, as flavonoids found in the plant, inhibit the absorption of serotonin, dopamine and norepinephrine by synaptosomes from different regions of the brain [28]. Several investigations suggest that some minor and major depressive disorders can be ameliorated with flavonoids [29]. It has been reported that flavonoids act through their antioxidant mechanism as well as through neurogenesis.

CONCLUSION

The results obtained in this study suggest that aqueous extracts of GS may possess an antidepressant activity. The preliminary pharmacological screening with acute dosing exhibited the antidepressant activity of GS, 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 GS at a dose of 200 and 400mg/kg/day.

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