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# Antidepressant Effect of*Calliandra portoricensis* on Mice

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**Abstract:** The problem of depression in the world today is very high. Consequently, there is a growing need to address this problem and find an effective remedy. *Calliandra portoricensis* has several therapeutic applications in folk medicine curing a wide range of diseases. This present study was undertaken to investigate the antidepressant effects of *C. portoricensis.* Antidepressant activity of ethanol extract of *C. portoricensis* (EECP) was investigated using forced swim test (FST) and tail suspension test (TST) models in mice. Acute toxicity studies were performed using fluoxetine (10 mg/kg) as a reference standard throughout the studies. Ethanolic extracts were administered 60minutes prior to the test. It was observed that that EECP showed significant ($p > 0.05$) decrease in immobility in suspension and forced swim models of depression at increasing doses comparable to fluoxetine. The phytochemicals analysis revealed that the main constituents of *C.portoricensis* were flavonoids, phenol, tannins and alkaloids.

**Key words:** Antidepressant · *Calliandraportoricensis* · Phytochemistry · Forced Swimming Test · Tail Suspension Test

## INTRODUCTION

Depression can be described as a common mental disorder which is always accompanied with depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite and poor concentration which often comes with symptoms of anxiety [1]. It isreported as the most common psychiatric disorder and one of the causes of disability in adults under the age of 50. It is estimated that between 2–7 % of adults with major depression cases die by suicide, while up to 60 percent of suicidal deaths records are connected to depression or other mood disorders [1]. There are several symptoms of depression which could be said to be all mood based [2]. However, most often among the elderly, depression has been observed to coexist with physical disorders like stroke, cardiovascular diseases, Parkinson's disease, chronic obstructive pulmonary disease etc [3].

However, it is surprising to know that the etiology of most prevalent of all mental disorders remains largely unknown [4]. For instance, no single region of the brain or neurotransmitter pathway has been specifically identified as a single root cause.Although the cause of major depressive disorder is unknown, the preexisting vulnerability can be either genetic or schematic [4]. It is believed that 30–40 % of depression cases are related to genetics, although no specific genes have been implicated [5, 6].Testing for depression should therefore be aimed at ruling out physical conditions that can cause similar symptoms [7].

Presently, more than 300 million people are living with depression and an increase of more than 18 % between 2005 and 2016 was recorded, yet the number of them that are receiving basic treatment is negligible [8].

Several classes of antidepressant are currently being used for the treatment of depression but these are mainly associated with adverse effects such as problematic interaction and relatively low response due to clinical limitations and adverse effects.There is a critical interest in the development of efficient and safe drugs for the treatment of depression [9]. This consideration implies that there is a need for new antidepressant agents with lesser side effects and quick on the set of action [10]. Owing to the belief that most preparations from medicinal plants have lesser side and adverse effects, researchers interests were shifted to investigating specific novel pharmacotherapies from medicinal plants against psychopharmacological disorders.

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*Calliandra* is a genus of flowering plants in the pea family, *Fabaceae*, in the mimosoid clade of the subfamily *Caesalpinioideae* with about 140 species that are native to tropical and subtropical regions of the Americas [11].

Despite the widely popular use of *C.portoricensis* for treating various disorders, there is an absence of scientific reports about the evaluation of its antidepressant effects, hence was the need toevaluate the antidepressant effect of the extract from *C. portoricensis*in the models predictive of antidepressant action.

## MATERIALS AND METHOD

**Collection of Plant:** Fresh leaves of *C. Portoricensis* were collected in large quantitative from Ikwo Local Government Area of Ebonyi State and was authenticated by Mr. LateefAkeemAdeyanju in herbarium of National Institute for Pharmaceutical Research and Development Idu, Industrial Area, Abuja.

**Animals:** Albino mice (20- 30g) of both sexes were obtained from the animal house of National Institute of Pharmaceutical Research and Development (NIPRD) Industrial area. They were housed at a controlled temperature of 24± 2°C with free access to food and water and constant 12 h light/dark cycle. The animals were placed in the experimental room 48 h before the test for acclimatization.They were divided into seven groups of five (5) miceeach and coded using picric acid.

**Preparation of Plant Sample:** *C. portoricensis* leaves were thoroughly washed and spread on clean benches and allowed to air dry at room temperature. When the leaves were dried, they were gathered and pulverized into powder using a mortar and pestle. The fine powder was sieved with fine mesh and the chaff was discarded. 50 gram of the sieved powder was macerated in 200ml 70 % of ethanol at room temperature for 48h. The extraction mixture was sieved with a white sieve cloth and filtrate allowed to evaporate to dryness.

**Experimental Groups:** In this experiment seven groups of five mice each were used:Normal saline as the negative control, Fluoxetine (10 mg/kg) as positive control**,** extract groups - 1000,500**,** 250, 125 and 62.5 mg/kg respectively.

**Acute Toxicity Study:** Both feed and water were withdrawn from the mice overnight (Fasting) before administration of the test compounds. In the first phase of the study ethanolic extract of *C. portoricensis*was administered orally in increasing doses of 10, 100 and 1000 $mgkg^{-1}$ body weight. Immediately after dosing, the mice were observed continuously for 4 hours for any symptoms of toxicity like motor activity, tremors, convulsions, tonic extension, musclespasm, loss of frightening reflex, ataxia, sedation, hypnosis, diarrhea, salivation and writhing. The mice were checked after 24 hours for any mortality.

The second phase of the study consisted of three fresh mice, one per group, with each receiving oral doses of 1600, 2900 and 5000 mg/kgbody weight of *C. portoricensis*, respectively based on the result of the first phase. They were also observed critically for signs of toxicity and mortality for the first 4 hours and subsequently for 24 hours. Observations at both phases continued for a further 14 days. The $LD_{50}$ was calculated as the square root of the product of the lowest lethal dose and highest non-lethal dose of the extract, i.e. the geometric mean of the successive dose that produced 0 and 100 % survival rates.

$$LD_{50} = \text{vmaximum non-lethal dose} \times \text{minimum lethal dose}$$

**The Forced Swimming Test:** This model was used to evaluate the antidepressant effect of *C. portoricensis* in mice. Animals were placed in pyrex cylinders (20 × 40 cm) which were filled with water at 24-25 °C with a 30 cm depth and behaviors were monitored. Normal saline (Negative control), fluoxetine 10 mg/kg (Positive control) and five doses of ethanolic extract were administered orally an hour prior to the test session. The duration of test was 5 minutes and immobility time was measured over the 5 minutes period Immobility was assigned to period when no additional activity was observed [12].

**Tail Suspension Test (TST):** Mice were suspended 50cm above the floor by adhesive tape in the tail suspension apparatus. They were placed at the hook in such a way that they hanged approximately 2 cm from the base of the tail. Immobility time was recorded during a 5 minutes window period. Animal was considered to be immobile when it did not show any movement of the body, hanged passively and completely motionless.

**Phytochemical Studies:** The extract of *C. portoricensis*was screened for the presence of various phytoconstituents like steroids, alkaloids, glycosides, flavonoids, carbohydrates, proteins and phenolic compounds.

## RESULTS

**Phytochemical Screening:** Qualitative phytochemical analysis of plant extract *C.portoricensis* showed the positive chemical reaction for alkaloid, flavonoid, saponin, phenol, glycosides, tannins, phlobatannins, anthraquines and carbohydrate were found present in the samples.On quantitative analysis of alkaloid, Flavonoid, Saponin, Tannin, Phenol andGlycosides they were found to be present0.40, 5.80, 4.30, 21.68, 37.27and 0.13 % respectively as shown in the Fig. (1).

**Effect of Ethanolic Extract of *C. Portoricensis* on Open Field:** In the acute toxicity study ethanolic extract of *C. portoricensis* did not show any mortality in the mice. Even at this higher dose of 1600 mg $kg^{-1}$, no gross behavioral changes were observed therefore the doses 62.5, 125, 250, 500, 1000 mg $kg^{-1}$ of *C. portoricensis* were used for evaluation of locomotor activity. The result obtained showed a locomotor effect on increasing the dose, a significant difference ($p<0.05$) was observed when compared against control.The plant was found to have a locomotory effect more at 250 mg/kg as mean values in bars with asterisks (*) shows a significant difference at $p<0.05$ at increasing doses as shown in the Fig. 2

**Effect of Ethanolic Extract of *C. portoricensis* on Forced Swim:** Results from this study showed that the administration of the ethanolic extract of *C.portoricensis*(62.5, 125, 250, 500and 1000 mg/kg doses) when compared to the control group produced a significant ($p<0.05$) decrease in immobility time 191.20±18.79, 186.60±13.72, 192.60±10.53, 183.60±5.49 and176.80±8.34 respectively. Fluoxetine showed a

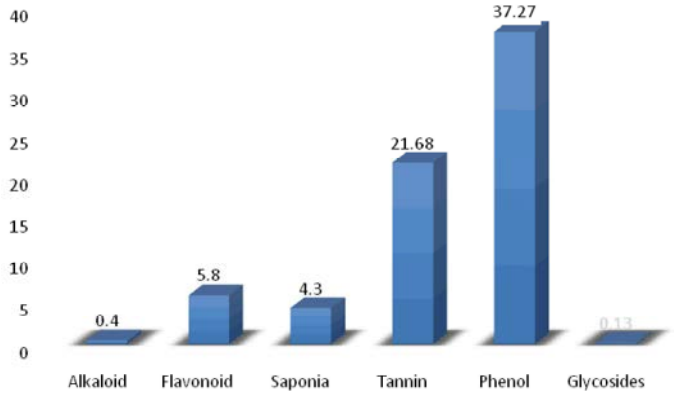


Fig. 1: Phytochemical Constituents of plant extract *C.portoricensis*.

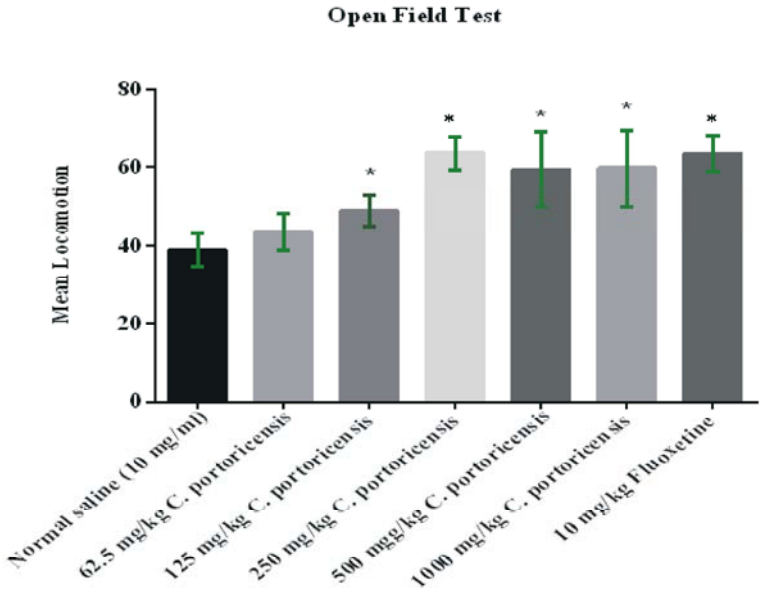


Fig. 2: Effect of ethanolic extract of *C portoricensis*on open field test

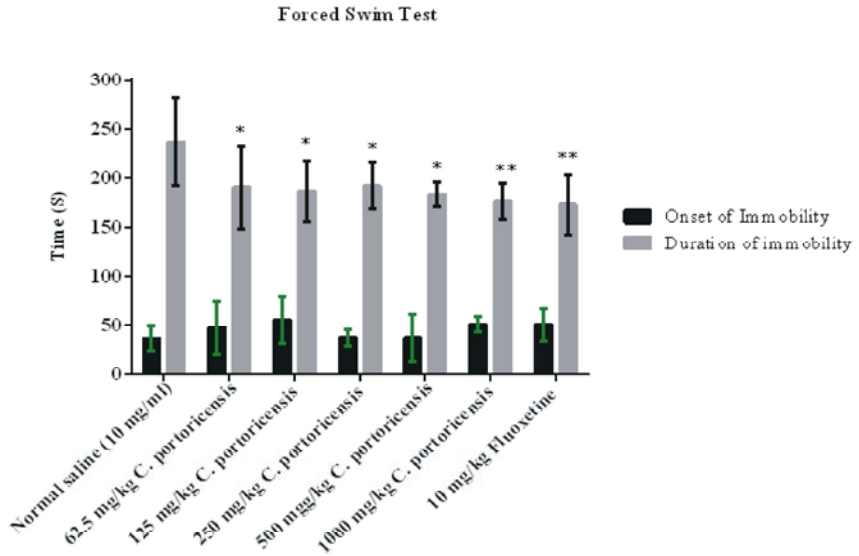


Fig. 3: Effect of ethanolic extract of *C.portoricense* on forced swim test

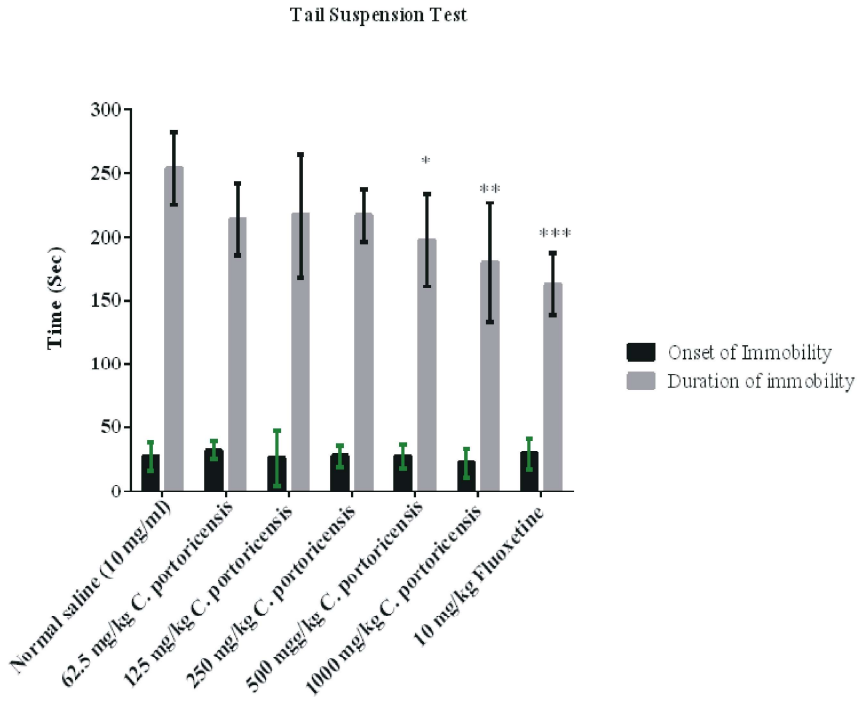


Fig. 4: Effect of ethanolic extract of *C portoricensis* on tail suspension test

significant ($p<0.05$) decrease in immobility period 173.40±13.70, as compared to normal control in forced swim test. There was however no differences in the onset of immobility for the forced swim, indicating that the extract did not have any effect in the speed at which it brings the mice out of a depressed state, mean values in bars with asterisks showed significant difference at $p<0.05$ at increasing dose as shown in the Fig. 3.

**Effect of Ethanolic Extract of *C. portoricensis*on Tail Suspension Test:** Results showed that doses 62.5, 125, 250, 500 and 1000 mg/kg showed a significant ($p<0.05$) decrease in immobility time of213.80±12.82, 217.20±21.74, 216.67±9.20, 197.60±16.35 and 180.20±20.80 seconds respectively when compared to the control which had 163.20±10.82 seconds. Also, there was increased swimming time in the mice when compared with the

control group. However,flouxetine at the dose of 10 mg showed a significant decrease ($p<0.05$) in immobility period when compared with normal saline control. Mean values in bars with asterisks (*) showed significant differences at $p<0.05$ at increasing doses as shown in the Fig. 4.

## DISCUSSION

Depression is one of the most prevalent and disabling neuropsychiatric diseases. The available antidepressant drugs though safe and effective half of the patientsexhibits new partial, refractory or intolerant responses to treatment, thus emphasizing the need to discover antidepressants. A growing number of herbal medicines are being introduced into psychiatric practice, many of which have comparable efficacies to prescription medications with lower side effects. This makes herbal therapies a desirable alternative treatment for severe depression [13].

The present study was carried out to evaluate the antidepressant effect of the extract of *C. portoricensis*in the models predictive of antidepressant action.

The result of phytochemical screening as shown in fig 1 revealed that *Calliandraportoricensis* contained alkaloid, flavonoid, saponin, phenol, glycosides, tannins, phlobatannins and anthraquines in variable quantities with phenol (37.27 %) and tannin (21.68 %) being the dominant compounds. Similar phytochemical screenings reportedthat the fresh root and leaf extracts of *C. portoricensis* revealed the presence of alkaloids, glycosides, saponins, tannins, flavonoids, reducing compounds, polyphenols, anthraquines, hydroxymethyl and anthraquines[14, 15]. The high content of phenol in the plant extract is an indication that the plant leaves could have ameliorative reactions in tissues and organs. It is also suggested that this high content of phenols in *C. portoricensis*brings about the neutralization effect on vipera venom which may be due to the complexation between the polyphenols and venom peptides [16].

The oral acute toxicity study as presented in fig 2 showed that the $LD_{50}$ of the ethanolic extract of *C.portoricensis* was above 2000 mg/kg. This shows that the extract is safe at the dose tested. This inference was also reported in the toxicity studies of *C. portoricensis* by [17]. This is contrary to the work carried out byOnyeama *et al.* [14] whoreported that the $LD_{50}$ value of their ethanolic extract of *C. portoricensis* in mice was 150mg/kg, implying the extract was relatively toxic in mice.

In acute study, ethanolic extracts were administered 60 min prior to the test and it was observed from the result that (EECP) showed significant ($p<0.05$) decrease in immobility in tail suspension and forced swim model of depression at increasing dose (125, 250, 500 and 1000 mg/kg) of ethanolic extract of *C. portoricensis* suggesting of plant extract *C.portoricensis* that the administration of the extract at any dose can drastically reduce immobility time in mice.

Doses significantly ($p<0.05$) increased the number of line crossing in open field, suggesting that the extract increased the locomotor activity of the mice, 250 mg/kg showed a higher locomotive effect. In a similar study, Peter and John [18] reported that the aqueous extracts of both root and stem of *C. portoricensis* possess anticonvulsant and antidepressant activity when given intraperitoneally.

The antidepressant effect demonstrated by this study could have been due to the phytochemical constituent present in the extract. They might be acting either singular or in synergy to exert their effects. In this study, the lower dose of extract of *C. portoricensis* caused a significant reduction in immobility time and increased swimming time. Therefore the results suggest that antidepressant-like effect of ethanolic extract of *C. portoricensis* might be mediated by reuptake inhibition of CNS neurotransmitters.

## CONCLUSIONS

The present study revealed that theethanolic extract of *C. portoricensis*is rich in important phytochemicals with phenol being predominant. The research showed antidepressant activities with seemingly no negative effects. Hence, ethanolic extract of *C. portoricensis* may have potential therapeutic value for the management of depressive disorders.

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