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## Evaluation of anti depressant activity of *Calotropis gigantea* by using experimental rats

**K Naga Rani, D Kalpana, N Syamala, T Divya, G Vasu and P Venkateswara RAO**

### Abstract

Anti-Depressant activity of *Calotropis gigantea* was evaluated in Experimental rats. The present study aqueous extract of *Calotropis gigantea* leaves has shown promising results in experimental depression. These studies are valuable for identifying lead compounds for anti-depressant drugs, keeping in mind the side effects of presently used antidepressants. The standardization of the extracts, identification and isolation of active principles along with pharmacological studies of these principles may be considered for further detail studies. Still further human studies are needed to prove the safety and efficacy of long term administration of aqueous extract of *Calotropis gigantea* leaves. In the light of observations made it may be envisaged that *Calotropis gigantea* (CG) leaves extract can be used as a potential adjuvant in the treatment of depressive disorders. The extract of *Calotropis gigantea* leaves of showed the results were increased that the standard imipramine it indicates the test extract poses antidepressant activity. The investigations of aqueous extract of *Calotropis gigantea* leaves (100mg/kg and 200mg/kg) in both Forced Swim Test (FST) & Tail Suspension Test (TST) models in rats were showed invivo antidepressant activity. In this study the results were obtained increased such as imipramine. So it is concluded that the aqueous extract of *Calotropis gigantea* leaves should possessed the antidepressant activity.

**Keywords:** Anti-depressant activity, *Calotropis gigantea* (CG), forced swim test (FST) & tail suspension test (TST)

### Introduction

Depression is a chronic mental disorder that causes changes in mood, thoughts, behavior and physical health. It's a common but serious disease that can take away a person's ability to enjoy life and cause decline in capacity to undertake even the simplest daily tasks. Other than its chronic nature, symptoms associated with this mental disorder are often recurring and life threatening<sup>[1]</sup>. According to the World Health Organization (WHO) unipolar depression is one of the leading causes of disability- adjusted life year (DALY) and approximately 350 people worldwide are said to suffer from this mental disorder. As described in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM- V, 2013), the hallmark of major depressive disorder (MDD) is the occurrence of depressed mood (dysphoria) and loss of interest in activities that were rather pleasurable in the past (anhedonia) for a duration of at least two weeks. These symptoms must also be accompanied by at least four of the following manifestations such as changes in appetite or weight, sleep patterns, altered psychomotor activity, feelings of worthlessness or guilt, difficulty concentrating or making decisions and recurrent thoughts of death or suicidal ideation. Even though there are plenty of drugs developed for the management of depression, one of the challenges in dealing with this disease is that a significant portion of the patients taking antidepressants fail to attain full remission. Some patients also develop treatment resistant depression in which the patients fail to respond to the available drugs or other therapeutic approaches<sup>[2-4]</sup>.

### Medicinal plants used to treat depression<sup>[5-8]</sup>

Medicinal plants around the world have been used to treat disorders of the body and the mind since antiquity. Herbal medicine has been a reasonable alternative for the management of mental disorders such as anxiety, depression and dementia among plenty others (Klemens, 2006). Developing antidepressants from herbal sources seems to be reasonable approach due to their therapeutic efficacy and lower incidence of side effects (Rajput *et al.*, 2011). *Hypericum perforatum* commonly known as St. John's wort is the only herbal antidepressant that has been approved for the clinical management of mild to moderate cases of depression.

Hypericin and hyperforin are flavonoids present in hypericum that are claimed to be responsible for the antidepressant activity of the plant. Medicinal plants most widely used to treatment depression around the world are *Hypericum perforatum*, *Centella asiatica*, *Rhodiola rosea*, *Pfaffia paniculata*, *Rauwolfia, serpentina*, *Rhododendron molle*, *Schizandra chin*, *Thea sinensis*, *Uncaria tome*, *Valeriana officinalis* and *Withania somnifera*. There is a long history of using plants for treating many diseases in Ethiopia. This herbal based therapy is most valued and has been passed from generation to generation by word of mouth. Herbal therapy still remains to be the first line treatment option for nearly 80% of the population. Plants such as *Justicia odora*, *Whitiana somnifera*, *Calpurnia aurea* and *Asparagus leptocladodius* have traditionally been used for the treatment of depression.

## Methodology

### Plant extract

About 150 g of powdered material have to be soaked in 1000 mL distilled water at  $25 \pm 2$  °C for 48 h in a beaker and mixture needs to be stirred every 10 h using a sterile glass rod. Filtrate was obtained 3 times with the help of Whatman No. 1 filter paper and sterilized cotton filter. The solvent was obtained. This crude extract was used for the investigations of antidepressant-like effect of the aqueous extract of *Calotropis gigantea* in rats [9, 10]

### Procedure

The procedure was divided into 2 phases, phase I (observation made on day 1), and phase II (observed the animals since next 14 days). Two sets of healthy female rats (each set of 3 rats) were used for the experiment. First set animals were divided and fasted for 18 h deprived from food, water withdrawn before 4 h of the dosing, body weights were noted before and after dosing with *Calotropis gigantea* dose 20ml per body weight.

### Determining anti depression activity

#### Tail Suspension Test (TST)

Rats were weighing 160-200g are used preferentially. They are housed in plastic cages for at least 10 days prior to testing in a 12 h light cycle with food and water freely available. Animals are transported from the housing room to the testing area in their own cages and allowed to adapt to the new environment for 1 h before testing. Groups of 10 animals are treated with the test compounds or the vehicle by intra peritoneal injection 30min prior to testing. For the test the



mice are suspended on the edge of a shelf 58 cm above a table top by adhesive tape placed approximately 1 cm from the tip of the tail. The duration of immobility is recorded for a period of 5min. Mice is considered immobile when they hang passively and completely motionless for at least one min [11].

### Groups

Group I – Control (Normal saline 1 ml/kg),  
Group II – Standard (Imipramine 15 mg/kg),  
Group III – *Calotropis gigantea* 30mg/kg, Group IV – *Calotropis gigantea* 40 mg/kg, Group V – *Calotropis gigantea* 50 mg/kg.

### Forced Swim Test (FST)

Rats weighing 160–180 g are used. They are brought to the laboratory at least one day before the experiment and are housed separately in Makrolon cages with free access to food and water. Naive rats are individually forced to swim inside a vertical Plexiglas cylinder (height: 40 cm; diameter: 18 cm, containing 15 cm of water maintained at 25 °C). Rats placed in the cylinders for the first time are initially highly active, vigorously swimming in circles, trying to climb the wall or diving to the bottom. After 2–3 min activity begins to subside and to be interspersed with phases of immobility or floating of increasing length. After 5–6 min immobility reaches a plateau where the rats remain immobile for approximately 80% of the time. After 15min in the water the rats are removed and allowed to dry in a heated enclosure (32 °C) before being returned to their home cages. They were again placed in the cylinder 24 h later and the total duration of immobility is measured during a 5min test. Floating behavior during this 5min period has been found to be reproducible in different groups of rats. An animal is judged to be immobile when ever it remains floating passively in the water in a slightly hunched but upright position, its nose just above the surface. Test drugs or standard are administered one hour prior to testing. Since experiments with the standard drug (imipramine) showed that injections 1, 5 and 24 h prior the test gave the most stable results in reducing floating these times are chosen for the experiment [12]

### Groups

Group I – Control (Normal saline 1 ml/kg),  
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Group V – *Calotropis gigantea* 50 mg/kg.



**Fig 1:** Tail Suspension Test (TST) **Figure-2-** Forced Swim Test (FST)

### Plant Profile

*Calotropis* species is a shrub with thick twisted branches, the young ones bluntly quadrangular, bark ash colored, covered with a minute white woolly down (Ahirwar *et al.*, 2007) . The

species can be differentiated by the floral characteristics. *Calotropis gigantea* bears corolla lobes which are spreading, uniformly coloured, pure lavender to white, coronal scales narrow truncate shorter than the staminal column with

pubescent back, apex entire. Whereas the corolla lobes of *Calotropis procera* are erect while pink or purple spotted on the corolla lobes, corona scales equal or longer than the staminal column, glabrous on back apex bifid, auricles wanting.

**Table 1:** Taxonomical Classification

<b>Kingdom :</b>	<b>Plantae</b>
Clade:	Trachephytes
Clade:	Angiosperms
Clade:	Eudicots
Clade:	Asterids
Order:	Gentianales
Family:	Apocynaceae
Genus:	<i>Calotropis</i>
Species:	<i>C. gigantea</i>

**Medicinal Uses of Plant**

The potent bioactivity of calotropin, *Calotropis gigantea* has been used as a folk medicine in India for many years, and has been reported to have a variety of uses. In Ayurveda, Indian practitioners have used the root and leaf of *C. gigantea* in asthma and shortness of breath and the bark in liver and spleen diseases. The plant is reported as effective in treating skin,

digestive, respiratory, circulatory and neurological disorders and was used to treat fevers, elephantiasis, nausea, vomiting, and diarrhea. The milky juice of *Calotropis gigantea* was used against arthritis, cancer, and as an antidote for snake

bite. However, these reports are of folk uses and more research is needed to confirm the clinical usefulness of the leaves, latex, and bark. Recent studies have displayed use of calotropin as a contraceptive and as a promising cancer medication. In one study of the cancer-fighting properties of *Calotropis gigantea*, DCM extracts were demonstrated to be strongly cytotoxic against non-small cell lung carcinoma (A549), colon carcinoma (HCT 116), and hepatocellular carcinoma (Hep G2). These extracts show promise as cancer medications and warrant further clinical research. The plant extract also shows anti depressant activity, anti microbial activity, anti diuretic activity, anti oxidant activity etc.

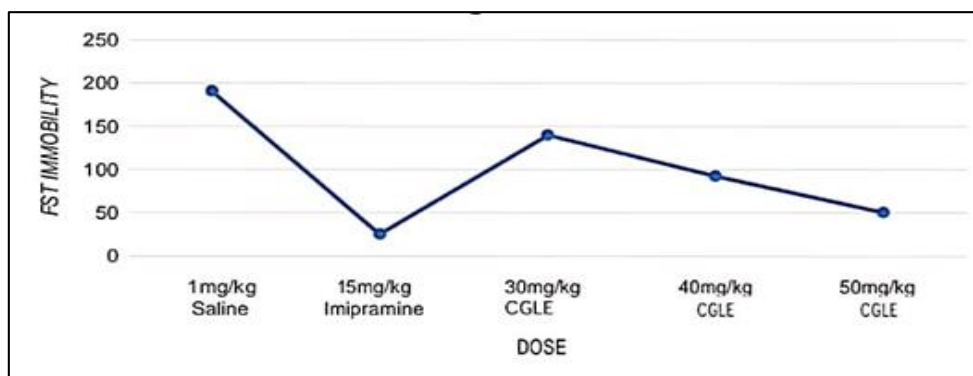


**Fig 3:** *Calotropis gigantea* Plant

**Results**

**Table 2:** Results of Anti-Depressant Activity

S.NO	GROUPS	DOSE	FST(immobility)	TST(immobility)
1	<b>Group I – Control (Normal saline)</b>	1mg/kg	199.0 ± 3.21	157.12 ± 05.24
2	<b>Group II – Standard (Imipramine)</b>	15mg/kg	30.02 ± 2.09	161.25 ± 02.75
3	<b>Group III –CGLE</b>	30mg/kg	147.08 ± 3.67	135.16 ± 2.88
4	<b>Group IV –CGLE</b>	40mg/kg	99.05 ± 2.75	157.15 ± 02.33
5	<b>Group V –CGLE</b>	50mg/kg	48.13 ± 3.27	175.33± 09.56



**Fig 4:** Results graph of Forced Swim Test (FST)

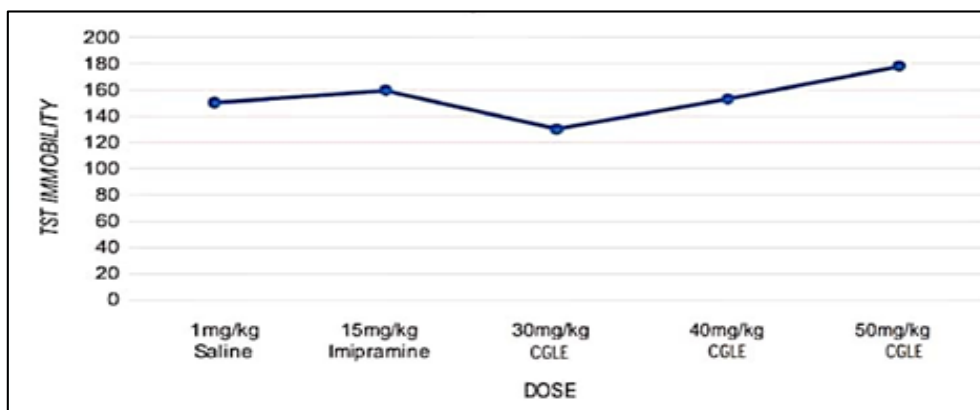


Fig 5: Results graph of Tail Suspension Test (TST)

### Conclusion

The present study aqueous extract of *Calotropis gigantea* leaves has shown promising results in experimental depression. These studies are valuable for identifying lead compounds for anti-depressant drugs, keeping in mind the side effects of presently used antidepressants. The standardization of the extracts, identification and isolation of active principles along with pharmacological studies of these principles may be considered for further detail studies. Still further human studies are needed to prove the safety and efficacy of long term administration of aqueous extract of *Calotropis gigantea* leaves. In the light of observations made it may be envisaged that *Calotropis gigantea* leaves extract can be used as a potential adjuvant in the treatment of depressive disorders. The qualitative analysis of aqueous extract of *Calotropis gigantea* leaves revealed the presence of alkaloids, flavonoids, Saponins, Phenolic compounds & triterpenoids etc. The extract of *Calotropis gigantea* leaves showed the results were increased that the standard imipramine it indicates the test extract poses antidepressant activity. The investigations of aqueous extract of *Calotropis gigantea* leaves (100mg/kg and 200mg/kg) in both Forced Swim Test (FST) & Tail Suspension Test (TST) models in rats were showed *in vivo* antidepressant activity. In this study the results were obtained increased such as imipramine. So it is concluded that the aqueous extract of *Calotropis gigantea* leaves should possess the antidepressant activity.

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