

# Antidepressant Activity of the Methanol Stem-Bark Extract of *Ficus Vallis Choudae* (Moraceae) in Swiss Albino Mice

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## Abstract

Although remarkable advances have been made in the detection and management of mood disorders over the last few decades, the increasing worldwide prevalence of depression continues to challenge researchers and clinicians alike. In spite of the availability of antidepressant drugs depression continues to be a major medical problem. Although there are many effective antidepressants available today, the current therapy is often inadequate with unsatisfactory results in about one third of all subjects treated. Various plants are being used in complementary and alternative medicines for management of mood disorders. The methanol stem-bark extract of *Ficus vallis* was investigated for antidepressant activity using the Forced Swim Test and Tail Suspension Test models. The locomotor activity was also evaluated using the Open Field Test so as to rule out possible psycho-stimulant activity. It was observed from our study that *Ficus vallis* methanol extract showed significant ( $p < 0.05$ ) reduction in immobility at 200 and 400 mg/kg doses in the Tail Suspension Test. While in the Forced Swim Test there was a significant ( $p < 0.02$ ) with the 400 mg/kg dose when compared with normal saline. The methanol stem-bark extract of *Ficus vallis* possesses antidepressant properties in mice with significant decrease in duration of immobility.

**Keywords:** Antidepressant activity, *Ficus vallis*, Forced swim test, Tail suspension test.

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## INTRODUCTION

A medicinal plant is any plant which one or more of its organs contain substances that can be used for therapeutic purposes or which is a precursor for the synthesis of useful drugs [1]. Medicinal plants are sold in large quantities and varieties in local markets to people in search of cures for particular ailments or as usually claimed, all kinds of diseases [2].

The World Health Organization (WHO) has recommended, especially in developing countries, the initiation of programmes designed to use medicinal plants more effectively in traditional health care system [3].

*Ficus vallis* is widely spread in tropical Africa, ranging from damp sites, stream banks and into dry savannah; in Senegal to southern Nigeria [4]. In Nigeria, it is known as “Dullu” or “Bargomi” by Hausa people, and “Oguro” by the Yoruba people [4].

Traditionally, the leaves and young leafy stems are decocted and taken for jaundice, nausea, bronchial and gastro-intestinal problem. Such preparations are

emollient and astringent. In Ghana and Zaire, the combined part of the plant is used as an antidote for poisons.

*Ficus vallis* belongs to the Moraceae family having about 53 genera and 1400 species distributed throughout tropical and temperate regions worldwide.

Depression can be defined as a mental condition characterized by severe feelings of hopelessness and inadequacy, typically accompanied by a lack of energy and interest in life. Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration [5, 6].

## MATERIALS AND METHODS

### Plant Collection and Identification

A sample of the plant (stem-bark of *Ficus vallis*) was collected by scrapping the trunk. The plant was collected in the month of March from Samaru Sabon Gari Local Government Area of Kaduna state, Nigeria. Botanical identification was done at the

herbarium unit of the Department of Biological Sciences, Ahmadu Bello University Zaria. Mallam U. S. Gallah of the herbarium unit compared the sample with voucher specimen available.

The stem-bark was cleaned, and air dried under shade for 26 days. This was done until a constant weight was obtained for three consecutive days. It was then pulverized using a pestle and mortar and then sieved to obtain the fine powder. The powder was weighed and kept in an air tight container.

### Experimental Animals

Male and female mice weighing 16-33 grams obtained from the animal house facilities of the Department of Pharmacology and Toxicology, Usmanu Danfodiyo University, Sokoto were used. The rats were housed in polypropylene cages at room temperature and maintained on standard laboratory animal feed obtained from the Department and water *ad libitum*, throughout the study. These studies were carried out in, Usmanu Danfodiyo University, Sokoto in accordance with the rules governing the use of laboratory animals as accepted internationally.

### Preparation of Extract

#### Methanolic crude extract

To 500 g of the powder, 1L of 90% methanol was added and allowed to soak for 48 hours in a separating funnel. The filtrate was then collected in a conical flask and transferred to an evaporating dish where it was evaporated to dryness on a water bath at a temperature of 40°C. The extract was collected in an air tight container and labelled as methanol stem-bark extract of *Ficus vallis* and it was kept in a desiccator until ready for use.

### Phytochemical Screening

The screening was carried out in accordance with the standard protocol as described in Trease and Evans [7].

### Acute Toxicity Studies

The oral median lethal dose (LD<sub>50</sub>) of the extract in mice was conducted according to the method of Lorke [8] with modifications. The method was divided into two phases. In the initial phase, 3 groups of three mice each were treated with the methanol stem-bark extract of *Ficus vallis* at doses of 10, 100 and 1000 mg/kg body weight orally and the mice were observed for clinical signs and symptoms of toxicity within 24 h and death within 72 h.

In the second phase, 3 groups each containing one fresh mouse was administered with three more specific doses of the extract based on the result of the initial phase. The animals were also observed for clinical signs and symptoms of toxic effects and mortality for 14 days.

The LD<sub>50</sub> value was determined by calculating the geometric mean of the lowest dose that caused death and the highest dose for which the animal survived (0/1 and 1/1).

### Behavioural Tests

#### Tail suspension test

In this model first described by Steru, 1986 which is the commonly employed behavioural model for screening antidepressant like activity in mice [9]. The animals were grouped into five (5) groups of six (6) animals each. The animals were grouped into five (5) groups of six (6) animals each. Groups 3, 4 and 5 received 100, 200 and 400 mg/kg of the extract orally 1 h prior to test. Groups 1 and 5 were treated with distilled water (10 mL/kg) and fluoxetine (60 mg/kg), respectively.

The animals were moved from the animal house to the laboratory on the experiment day in their cages and were allowed to adapt to the laboratory condition for 2 hours.

Each mouse was individually suspended to the edge of a table 50cm above the floor, by adhesive tape placed approximately 1cm from the tip of the tail. Each animal under test was both acoustically and visually isolated from other animals during the test. The total period of immobility was recorded manually for 6 minutes.

Animal was considered to be immobile when it didn't show any body movement, hung passively and completely motionless. The test was conducted in a dim lighted room and each mouse was used only once in the test.

#### Forced swim test

Porsolt, 1977 first described this model which is the most frequently used model for screening antidepressant like activity in mice [10]. The animals were grouped into five (5) groups of six (6) animals each. Groups 3, 4 and 5 received 100, 200 and 400 mg/kg of the extract orally 1 h prior to test. Groups 1 and 5 were treated with distilled water (10 mL/kg) and imipramine (60 mg/kg), respectively.

The animals were moved from the animal house to the laboratory 2 hours prior to the experiment in their cages and were allowed to adapt to the laboratory condition for 2 hours.

Mice were individually forced to swim in open chamber (25 × 15 × 25 cm) containing water to a height of 15 cm and maintained at room temperature. At this height of water, animals were not able to support themselves by touching the bottom or the side walls of the chamber with their hind-paws or tail. Water in the chamber was changed after subjecting each animal to the test because "used water" has been shown to alter

the behaviour. Each animal showed vigorous movement during initial 2 minutes period of the test. The duration of immobility was manually recorded during the next 4 minutes of the total 6 minutes testing period.

Mice were considered to be immobile when they ceased struggling and remained floating motionless in water, making only those movements necessary to keep their head above water.

#### Open field test

The animals were subjected to further evaluation using the open field test, in order to eliminate any bias associated with hyperkinesias in FST or TST. The test apparatus was made of wood 50cm in length, 50cm in width, and 25cm in height. The plain floor of the box was divided into 8cm, with 16 squares on it. Mice were placed into the centre and allowed to explore the apparatus crossing the peripheral central squares for 5 minutes. After the 5 minute test, the ambulation time was recorded and mice were returned to their home cages and the open field was cleaned with 10 % ethanol to remove any odour of the previous animal and permitted to dry between tests.

Thirty mice divided into 5 groups of six mice each were used. Groups 1, 2 and 3 received 100, 200 and 400 mg/kg of the extract orally 1 h prior to test. Groups 4 and 5 were treated with distilled water (10 mL/kg) and imipramine (60 mg/kg), respectively [11].

#### Statistical Analysis

The results obtained were expressed as mean  $\pm$  S.E.M. Variance was analyzed using One-way Analysis of Variance (ANOVA),  $p < 0.05$  was considered to be statistically significant.

## RESULTS

#### Result of Phytochemical Screening

The extract showed a positive result for the presence of carbohydrates, glycosides, saponins, flavonoids, cardiac glycosides, tannins, alkaloids and triterpenes however; anthraquinones and steroids were absent.

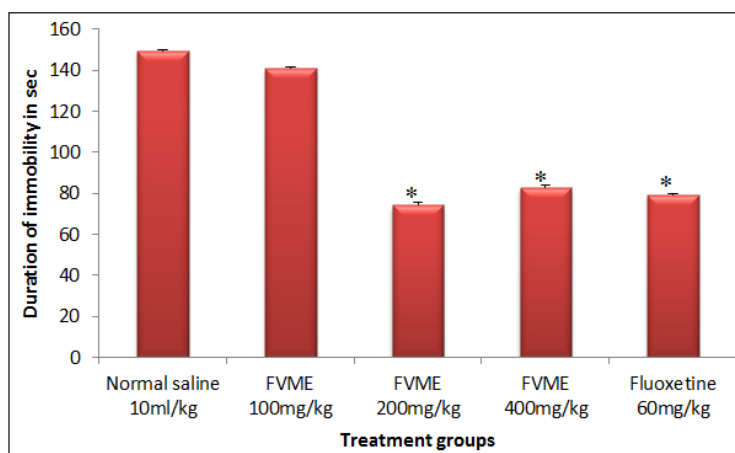
#### Acute Toxicity Study

The oral LD<sub>50</sub> in mice for the methanol stem-bark extract of *Ficus vallis* was found to be 3,800 mg/kg using the Lorke's method.

#### Tail Suspension Test

In Figure-1 below animals treated with the three doses of FVME (100, 200 and 400 mg/kg, orally) and fluoxetine showed decrease in their immobility times when compared with normal saline. The extract at doses of 200 mg/kg and 400 mg/kg decreased duration of immobility which was significant ( $p < 0.05$ ) when compared with the normal saline group. The 100 mg/kg dose only showed a slight reduction in immobility time when compared with normal saline.

The group treated with the standard agent (Fluoxetine) also showed a significant ( $p < 0.05$ ) reduction in their duration of immobility when compared with the normal saline group.



**Fig-1: Effects of FVME and Fluoxetine on duration of immobility In the TST**

Results are expressed as mean  $\pm$  S.E.M (n=6). \* $p < 0.05$  as compared to normal saline.

FVME= *Ficus vallis* methanol extract

TST= Tail suspension test

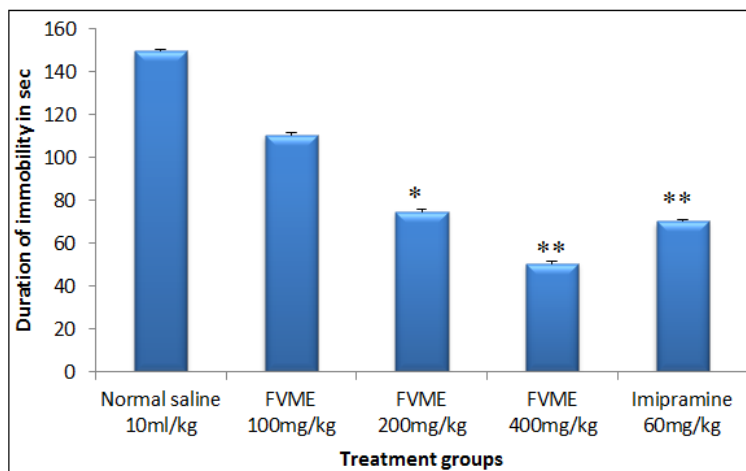
#### Forced Swim Test

In this test Figure-2 below showed animals treated with three doses of FVME (100, 200 and 400 mg/kg, orally) and imipramine showed decrease in their immobility times which was significant ( $p < 0.02$ ) when compared with normal saline.

Extract at a dose of 200 mg/kg and 400 mg/kg decreased the duration of immobility which was significant ( $p < 0.05$ ) and ( $p < 0.02$ ) respectively when compared with normal saline. Extract at the dose of

100mg/kg showed slight reduction in the duration of immobility when compared with normal saline.

The group treated with imipramine also showed a significant ( $p < 0.02$ ) reduction in their immobility time when compared with normal saline.



**Fig-2: Effects of FVME and imipramine on duration of immobility in the FST**

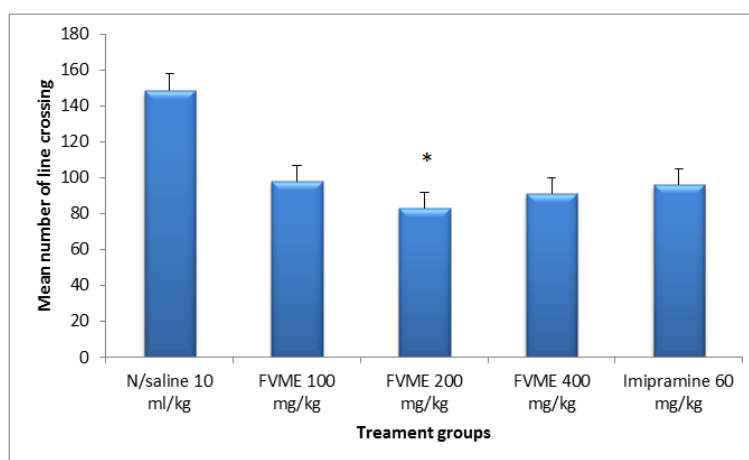
Results are expressed as mean  $\pm$  S.E.M (n=6). \*\*  $p < 0.02$  and \*  $p < 0.05$  as compared to normal saline.

FVME= *Ficus vallis* methanol extract  
FST= Forced swim test

### Open Field Test

The three doses of the extract used were able to show antidepressant-like response, but did not

exhibit significant change in locomotion except for the 200 mg/kg dose (Figure-3).



**Fig-3: Effects of FVME and imipramine on mean number of line crossing OFT**

Results are expressed as mean  $\pm$  S.E.M (n=6). \*  $p < 0.05$  as compared to normal saline.

FVME= *Ficus vallis* methanol extract  
OFT= Open field test

## DISCUSSION

The incidence of anxiety and depression in the community is very high and is associated with lots of mortality. Though several drugs are available, all are associated with some limitations and there is an urgent need for alternative medications for these disorders [12].

The immobility behaviour displayed in mice when subjected to an unavoidable and inescapable stress has been hypothesized to reflect behavioral

despair which in turn may reflect depressive disorders in humans [13]. These tests are quite sensitive and relatively specific to all major classes of antidepressant drugs [14].

In this experiment, the immobility displayed by mice when subjected to unavoidable stress such as FST and TST are thought to reflect a state of despair or lowered mood, which is thought to reflect depressive disorders in humans [15].

A study by Sharma *et al.*, 2009 showed that immobility time is reduced by treatment with antidepressant drugs [16]. In our study reduction of immobility was comparable to that observed after oral administration of fluoxetine (60 mg/kg) and imipramine (60mg/kg) in TST and FST respectively, the reference antidepressant drugs. There is, indeed, a significant correlation between clinical potency and effectiveness of antidepressants in both models [10, 17, 18].

Pre-treatment with FVME exhibited significant decrease in immobility time in TST and FST. So, the decrease in duration of immobility by FVME treated mice may be due to its attenuating effect in endogenous depression. The underlying principle of both the TST and FST is identical, but their variability in response to certain antidepressants indicates potentially different substrates and neurochemical pathways mediating performance in these tests. These issues may underlie the observed behavioral differences [19].

Furthermore, one of the most important differences between these two models is the response to drugs in both tests and the apparent increased sensitivity of the FST. The FST has not traditionally been viewed as a consistently sensitive model for detecting selective serotonin reuptake inhibitor activity, whereas these antidepressants are generally reported as active in the TST [20].

Moreover, the result obtained from the experiment is contrary to the research done by Thierry *et al.*, 1986 that proposed TST to have a greater pharmacological sensitivity as compared with the FST [21].

Cryan *et al.*, 2005 also proposed that TST detects the anti-immobility effects of a wide array of antidepressants, including tricyclic antidepressants (TCA), selective serotonin reuptake inhibitors (SSRI), monoamine oxidase inhibitors (MAOI), electroconvulsive shock (ECS), and even atypical antidepressants [20]. Thus, the activity of FVME could involve one of the mechanisms of the established agents as described above.

The results showed that the duration of immobility of extract-treated group was significantly shorter ( $p < 0.05$ ) and ( $p < 0.02$  and  $p < 0.05$ ) for TST and FST respectively than that recorded for the normal saline group. The decrease in duration of immobility indicates the degree of antidepressant activity [22].

In TST, animals treated with the three doses of FVME (100, 200 and 400 mg/kg) orally, showed decreases in their immobility times which was significant when compared with normal saline. Similarly, animals treated with fluoxetine (60 mg/kg),

as expected, showed a significant decrease in the immobility time ( $p < 0.05$ ).

Whereas, in FST animals treated with three doses of FVME (100, 200 and 400mg/kg) orally, showed decreases in their immobility times which was significant when compared with normal saline. Similarly, animals treated with imipramine (60 mg/kg), as expected, showed a significant decrease in the immobility time ( $p < 0.02$ ).

The results therefore indicated that FVME decreased duration of immobility in mice in both TST and FST models. Similar results have been obtained by other workers who tested the antidepressant potential of various plant extract [23, 24].

A model designed by Hall in 1934; the open field test was used to rule out any possible non-specific motor stimulation, because it is known that antidepressants do not increase activity that is observed in psychostimulant drugs like amphetamine. Antidepressants are known to cause slight decrease in motor activity and can cause loss of muscle tone [10].

FVME did not increase the number line crossing in Open Field Test; this shows there is no psycho-stimulant like action and also confirms the result seen in FST and TST. OFT serves as a paradigm to eliminate any bias that anti-immobility effect could be linked with hyperkinesias [25]. The Open Field Test can also be used to assess locomotor activity based on total number of square crossings [26]. Therefore, the outcome of this test is important to rule out any nonspecific activity of FVME. It is not clear how FVME was able to decrease locomotion in OFT; this decrease in locomotor activity suggests a possible sedation effect [27].

According to results of phytochemical screening and the literature, the antidepressants like potential might be due to the presence of phenols, glycosides and flavonoids. Flavonoids and glycosides are mostly hydrolysed into their aglycons by mucosal and bacterial enzymes in the intestines, and then converted to conjugated metabolites during the absorption process [28, 29].

It has been reported that some flavonoids bind with high affinity to the benzodiazepine site of the GABA receptor [30]. Their general bioavailability and particularly their presence in the brain *in vivo* appear to play an important role in the expression of their effects on the CNS [15].

Therefore, one of the antidepressant mechanisms of FVME is thought to involve flavonoids and glycosides which reach the brain tissues through the metabolizing process, protecting brain function from CNS disturbance and consequently, exerting an



antidepressant effect. Thus, FVME may have potential therapeutic value for the management of depressive disorders due to presence of flavonoids and glycosides.

## CONCLUSION

The antidepressant like activity of the methanol stem-bark extract of *Ficus vallis* was tested. The results obtained provide evidence that the methanol stem-bark extract of *Ficus vallis* possesses antidepressant properties in mice with significant decrease in duration of immobility.

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