

ANTIDEPRESSANT ACTIVITY OF *PHYLLANTHUS AMARUS* ETHANOLIC EXTRACT IN  
EXPERIMENTAL ANIMAL MODEL.Sheeba Damodar KP<sup>1</sup>, Shyamjith Manikkoth<sup>2\*</sup> and Deepa B<sup>3</sup><sup>1</sup> Department of Pharmacology, Academy of Medical Sciences, Pariyaram, Kannur<sup>2</sup>Department of Pharmacology, Yenepoya Medical College, Yenepoya University, Mangalore<sup>3</sup>Department of Pharmacology, K.S.Hegde Medical Academy, Nitte University, MangaloreCorresponding Author\*: Email: [shyamjithpubs@gmail.com](mailto:shyamjithpubs@gmail.com) Mobile: +919480361961**ABSTRACT**

**Objectives:** The aim of the study was to investigate the antidepressant effect of *Phyllanthus amarus* ethanolic extract in Wistar albino rats.

**Methods:** The ethanolic extract of leaves of *Phyllanthus amarus* [PAEE] at a dose of 100mg/kg/body weight was administered orally for ten days. On tenth day, after one hour, the animals were taken for forced swimming test, to assess the level of depression.

**Results:** The results indicate PAEE has significant antidepressant activity

**Conclusions:** The antidepressant activity of *Phyllanthus amarus* can be due to its effect on brain neurotransmitters or due to antioxidant property.

**Key Words:** *Phyllanthus amarus*, ethanolic extract, antidepressant

**INTRODUCTION**

Depression is a most prevalent diverse mood disorder. It's a chronic disorder which upsets a person's mood, thoughts, physical health and performance. Symptoms of this mind disorder are biological elements like impedance of thought, sleep disorder, loss of appetite and libido. The symptoms of emotional factors are sadness, apathy, pessimism, low self-respect, feeling of guilt, loss of enthusiasm and indecisiveness. The main two types of depression are unipolar depression and bipolar depression. Depression is one of the five leading causes of disability and disease burden worldwide. Prevalence rate of this disorder is more in woman, school dropouts and in geriatric persons (Dingra et al, 2006; Mangala et al, 2011; Suttajit, 2009). The most successful groups of antidepressants are tricyclic antidepressants [TCAs], selective reversible inhibitors of monoamine oxidase-A [MAO-A], selective serotonin reuptake inhibitors [SSRIs] and selective noradrenaline reuptake inhibitors [SNRIs]. Even though they are highly effective in alleviating the symptoms of depression, these drugs do not give complete cure. Moreover, these drugs are often associated with frequent side effects (Suttajit, 2009; Landén et al, 2006; David J Nutt, 2006). The significance of many indigenous medicinal plants and their phytoconstituents in the management of depression with minimal side effect profile arise in this context. *Phyllanthus amarus* (Syn. *Phyllanthus niruri*) is a perennial herb generally seen in the tropical and subtropical regions of both hemispheres. It belongs to Euphorbiaceae family. *Phyllanthus amarus* is widely used all over the world for treating ailments like jaundice, asthma, hepatitis, urogenital problems, dysentery, dyspepsia, arthritis, malaria, etc. Numerous pre-clinical studies proved that this plant possess antiviral, analgesic, anticonvulsant, antioxidant, antimicrobial, antiemetic, anticataleptic, antitumour, hepatoprotective, hypoglycaemic and hypolipidemic activities (Aruna Kumar R et al, 2010; Bhat SS et al, 2015; Bhattacharyya, 2003; Bhattacharjee R, 2007; Deepa et al, 2015; Hanumanthachar Joshi et al 2007; Priyanka Sharma, 2009; Shetti AA et al, 2012; Rashmi Mathur et al, 2011; Rajeshwar Y et al, 2008; Shyamjith M et al, 2011; Sundeep Hegde et al, 2014).

This research work was conducted to evaluate the effect of ethanolic extract of *Phyllanthus amarus* leaves on depression induced by forced swimming, which is an established model for screening antidepressant drugs.

## MATERIALS AND METHODS

### Drugs and Chemicals

Imipramine (Intas Laboratories Pvt Ltd) was obtained from a pharmacy in Mangalore. It was administered at a dose of 15 mg/kg orally.

### Plant materials

*Phyllanthus amarus* were cultivated during the month of June. The fresh leaves were collected in the month of September. They were authenticated by Dr.Noeline J.Pinto, Head of Botany department, St.Agnes College, Mangalore, Karnataka, India. They were shade dried, and then powdered.

### Sample Preparation and Extraction

*Phyllanthus amarus* ethanolic extract (PAEE): A weighed quantity (500 g) of the coarse powder was taken and extracted with ethanol (90 %) in a Soxhlet apparatus. The extract was concentrated on a water bath at a temperature not exceeding 60°C. The percentage yield of the extract was 20%. The ethanolic extract was dissolved in distilled water. It was administered at a dose of 100mg/kg body weight orally for 10 days.

### Animals

Adult Wistar albino rats of either sex weighing 175-200 g were used in this study after obtaining Institutional Animal Ethical Committee Clearance (IAEC), Yenepoya University. The rats were maintained under standard conditions in the Animal House (CPCSEA approved, Reg No: 347) under Department of Pharmacology, Yenepoya University, Mangalore. They were kept in polypropylene cages (U.N.Shah manufacturers, Mumbai) under standard housing conditions and maintained on standard pellet diet (Amrut Lab Animal Feed, Pranav Agro Industries Ltd, Sangli, Maharashtra), and water ad libitum. The animals were maintained on a 12:12 hour light-dark cycle.

### Experimental design

#### Effect of PAEE on Depression in Forced Swimming Test

Eighteen animals were used in this study. The animals were divided into three groups. Each group consisted of 3 males and 3 females (n=12).

Group I            Distilled Water [DW] orally for 10 days

Group II           Imipramine orally for 10 days

Group III          PAEE orally for 10 days

The standard and test drugs were administered orally for ten days. On tenth day, after one hour, the animals were taken for forced swimming test, to assess the level of depression. Once the experiments were over, the animals were rehabilitated.

### Forced Swimming Test

One of the most widely used animal models for antidepressant screening is the forced swimming test [FST]. This test is the most widely used in vivo model for assessing antidepressant activity and is relatively sensitive and specific to all major classes of antidepressants. The development of immobility when the rats are placed in an inescapable cylinder filled with water replicates the termination of persistent escape-directed behaviour. The apparatus consisted of a clear plexiglass cylinder (50 cm high×21 cm diameter) filled to a 30 cm depth with water (25±1 °C). 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 was changed between each swimming session. During the test session, the immobility time was recorded for 5 minutes, when the rats make no further attempts to escape, and makes only movements to keep its head above the water. Immobility depicts a state of lowered mood in which the animals had given up hope of finding an exit. This state is claimed to produce a condition similar to human depression (Dingra et al, 2006; Mangala et al, 2011; Suttajit, 2009).

### Statistical analysis

Results were expressed as mean ± S.D. One-way analysis of variance (ANOVA) was carried out and the statistical comparisons among the groups were performed with Tukey Kramer multiple comparison test using Prism statistical package program. P<0.05 was considered significant.

## RESULTS

### Effect of PAEE on Depression

The data revealed that [table1], there was a considerable decrease ( $p < 0.001$ ) in immobility time in PAEE and Imipramine treated groups. It is also noteworthy that reduction in catalepsy state in plant extract treated group was highly significant ( $p < 0.001$ ) on comparing with the scopolamine treated group.

**Table 1: Effect of PAEE on Haloperidol induced catalepsy**

Group	Immobility time in seconds
I (Control)	137.166±18.736
II (Imipramine)	86.5 ± 3.425 <sup>a</sup>
III (PAEE)	93.0±3.69 <sup>a</sup>

The observations were analysed by One Way ANOVA, followed by Tukey Kramer multiple comparison test, n = 06.  
a:  $p < 0.001$  considered extremely significant on comparing group II, III with group I

## DISCUSSION

In this study, ethanolic extract of *Phyllanthus amarus* showed significant antidepressant activity in the animal model of depression as evidenced by decrease in immobility time in FST. Relatively little information exists on the antidepressant activity of *Phyllanthus amarus*.

The antidepressant activity of this plant can be credited to the various phytochemicals present in its ethanolic extract. There are ample studies showing that phytochemicals like alkaloids, phytosterols, saponins, triterpenoids, carbohydrates, flavonoids, tannins, phenolic compounds shows antidepressant activity (Evans WC, 2002).

In a previous HPLC-LCMS analysis carried out on the ethanolic extract of *P. amarus* by Bhat SS et al, 2015, it was postulated that the active components of PAEE are Phyllanthine and Nirphyllin.

Phyllanthine, is a derivative of securinine. Securinine compound is found to possess GABA-A antagonistic property. This agent might have shown antidepressant activity by the blockade of GABA-A receptors and thereby increasing the levels of serotonin, like Bicuculline, another GABA-A antagonist. Its role in alleviating depression by altering the levels of dopamine cannot be ruled out. Like Picrotoxin, a GABA-A antagonist, it might have increased the level of dopamine, there by showing an antidepressant property (Wierońska et al, 2012; Schlicker E et al, 1984; Rick Shin et al, 2010).

Nirphyllin the second active component as seen by the HPLC-LCMS analysis belongs to the group of Lignans. Lignans are known to have antioxidant property. Nirphyllin being a lignan, might have shown antidepressant property by virtue of its free radical scavenging activity, since reactive oxygen species have a role in the etiology of major depression (Bhat SS et al, 2015; Wilson R Cunha, 2012).

## CONCLUSION

This preclinical study has proved that, *Phyllanthus amarus* has got a therapeutic role in depression. The active constituent responsible for this action has to be identified. This will help in explaining the exact mechanism of its antidepressant property.

**Conflict of Interest:** Nil

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