

Evaluation of antidepressant like activity in *Amaranthus caudatus*

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Abstract

Depression is a chronic illness that affects mental stability, personal and social relations. Herbal drugs possess least side effects compared to synthetic medicines. *Amaranthus caudatus* belongs to family Amaranthaceae. Antidepressant activity of methanolic extract of whole plant of *Amaranthus caudatus* (MEAC) was investigated by using forced swimming test (FST) and tail suspension test (TST) models. Animals are divided into five groups, group 1 receives normal saline, group 2 and 3 receives escitalopram (4 mg/kg) and imipramine (4 mg/kg) and group 4 and 5 receives MEAC (100 and 200 mg/kg) dose respectively. Preliminary phytochemical analysis showed the presence of phenolic compounds, steroids, alkaloids, flavonoids, saponins and amino acids in methanol extract of *A. caudatus*. It has been observed from our study that both the *Amaranthus caudatus* extract at higher concentration showed significant ($p < 0.01$) reduction in immobility in tail suspension and forced swim model which comparable to escitalopram and imipramine. It is concluded that *A. caudatus* possess antidepressant activity may be due to the presence of polyphenolic compounds and flavonoids. However further study is needed to understand mechanism of action and to identify active component responsible for antidepressant like activity.

Keyword: *Amaranthus caudatus*, Antidepressant activity, Tail suspension test, Forced swimming test.

1. INTRODUCTION

Depression is one the most prevalent forms of psychiatric disorders and is a leading cause for mortality.¹ Lifetime prevalence of depression in the general population is 4.4-20%² and suicides occur is up to 15% of individuals with severe major depression.³ Therefore, major depression is a serious public health problem and causes a considerable heavy psychological and economic burden for families.⁴ The presently using drugs can impose a variety of side-effects including

cardiac toxicity, hypopiesia, sexual dysfunction, body weight gain, and sleep disorder. During the last decade, there is a growing interest in the therapeutic effects of natural products on mental disorders. *Amaranthus caudatus* was investigation for antidepressant activity.

Amaranthus caudatus Linn, (Amaranthaceae), are spread throughout the world, growing under a wide range of climatic conditions and they are able to produce grains and leafy edible vegetables.⁵ *A. caudatus* traditionally used in jaundice, amoebiasis, kidney diseases,^{6,7} as blood purifier, diuretic,

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abortifacient, vermifuge and astringent.⁸ *A. caudatus* is reported for its antiatherosclerotic,⁹ hepatoprotective,¹⁰ antihelmintic,¹¹ antinociceptive and antipyretic activities.¹² *A. caudatus* seeds showed cholesterol lowering, *in vitro* antioxidant and alpha amylase inhibition activities.¹³⁻¹⁵ The Amaranth seed oil is used as nutraceutical resource from Ecuadorian flora.¹⁶ *A. caudatus* contains antimicrobial peptides,¹⁷ agglutinin,¹⁸ triterpenoid saponins and ionol derived glycoside,¹⁹ vitamin E isomers,²⁰ and amaranthin.²¹ The main aim of the study is to investigate antidepressant activity in whole plant extract of *A. caudatus*.

2. MATERIALS AND METHODS

2.1. Collection of plant material and extraction

The fresh plant of *A. caudatus* was collected from Chickballapur (Karnataka, India), and was authenticated by Prof. Venkatesh, B.K., Department of Botany, Government First Grade College, Chickballapur, Karnataka (India). A voucher specimen (SKVCP 12) was deposited in college herbarium. The whole plant was shaded dried and coarsely powdered. The coarse powder was exhaustively extracted with methanol by soxhlet apparatus and extract was concentrated to dryness in vacuum.

2.2. Preliminary phytochemical screening

The methanol extract of *A. caudatus* was screened for the presence of various phytoconstituents like flavonoids, saponins, glycosides, terpenoids aminoacids, alkaloids, carbohydrates, phenolic compounds and proteins as described by Kokate.²²

2.3. Animals

Albino Wistar rats (150–250 g) of either sex were acclimatized to the experimental room at a temperature of $23 \pm 2^\circ\text{C}$, controlled humidity conditions (50–55%) and 12 h light and 12 h dark cycles. They were caged with a maximum of two animals in a polypropylene cage and were fed with

standard food pellets (Kamadenu Enterprises, Bangalore) and water *ad libitum*. The protocol was approved by the Institutional Animal Ethical Committee (IAEC) (Ref. No. IAEC/SKVCP/PGCOL/11-12/04) of Sri K.V College of Pharmacy, Karnataka (117/1999/CPCSEA).

2.4. Acute toxicity studies

Methanol extract of *A. caudatus* was studied for acute oral toxicity as per revised OECD (Organization for Economical Co-operation and Development) guidelines No. 423.²³ In acute oral toxicity study single dose of *A. caudatus* extract (2,000 mg/kg) was administered test group and control group received normal saline alone. After administration of extract, animals were observed for four hours with an interval of one hour for behavioral changes and for 14 days for any mortality.

The extract was devoid of any toxicity in rats when given in doses up to 2000 mg/kg by an oral route. Hence, for further studies 200–400 mg/kg doses of the extract were used.

2.5. Antidepressant activity

2.5.1. Forced swimming test.

For the forced swim test (FST), rats of either sex were individually forced to swim in an open cylindrical container (diameter 10 cm, height 25 cm) containing 19 cm of water at $25 \pm 1^\circ\text{C}$. Rats were divided into five groups ($n=6$): control (normal saline), 4 mg/kg escitalopram (ESC), 4 mg/kg imipramine, 100 and 200 mg/kg MEAC. The total duration of immobility was recorded during the last 6 min of the 10 min period. Each mouse was judged to be immobile when it ceased struggling and remained floating motionless in the water, making only those movements to keep its head above water. A decrease in the duration of immobility is indicative of an antidepressant like effect.²⁴

2.5.2. Tail suspension test

The tail suspension method used in this study was similar to those described

by Steru et al.²⁵ The rats were suspended upside down on a metal rod at a height of 50 cm from the ground with the help of an adhesive tape placed approximately 1 cm from the tip of the tail. Rats were divided into five groups (n=6): control (normal saline), 4 mg/kg ESC, 4 mg/kg imipramine, 100 and 200 mg/kg MEAC. Rats were suspended on the edge of a table 50 cm above the floor by the adhesive tape placed approximately 1 cm from tip of the tail. Immobility time was recorded during a 6 minute period. Animal was considered to be immobile when it did not show any movement of the body, hanged passively and completely motionless.

2.6. Statistical analysis

All the values were expressed as Mean±S.E.M. The results were analyzed statistically by one-way ANOVA followed by Dunett Multiple comparison test, $p < 0.05$ were considered significant.

3. RESULTS AND DISCUSSION

Depressive disorder is a prevalent psychiatric disorder, which affects 21% of the world population.²⁶ Medications such as selective reversible inhibitors of monoamine oxidase A, tricyclic antidepressants, serotonin–noradrenaline reuptake inhibitors and selective serotonin reuptake inhibitors are clinically employed for drug therapy.²⁷ However, these drugs can impose a variety of side-effects including cardiac toxicity, hypoplasia, sexual dysfunction, body weight gain, and sleep disorder.²⁸⁻³¹ During the last decade, there is a growing interest in the therapeutic effects of natural products on mental disorders.

Escitalopram is classical selective serotonin reuptake inhibitors SSRIs, it is bound at the primary site of pre-synaptic serotonin transporter (SERT) with a very high affinity, and it has higher serotonergic activity than the classical SSRIs.³² Imipramine prevents reuptake of noradrenaline and serotonin resulting in their increased availability in the synapse and therefore an increase

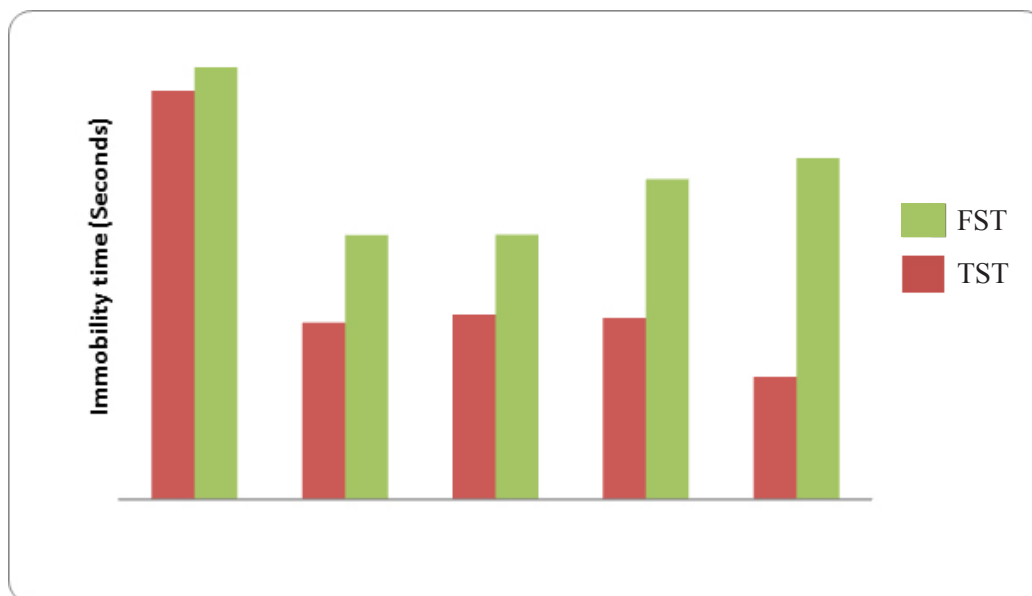
in adrenergic and serotonergic neurotransmission.³³

Preliminary phytochemical analysis showed the presence of carbohydrates, steroids, alkaloids, phenolic compounds, flavonoids, saponins and amino acids in methanol extract of *A. caudatus*.

Acute toxicity studies methanolic extract of *Amaranthus caudatus* showed neither behavioural changes nor mortality at dose 2,000 mg/kg.

In this study, we used two animal models, FST and TST. Both the paradigms are widely accepted behavioral models for assessing pharmacological antidepressant activity.^{34,35} Characteristic behavior scored in these tests is termed immobility, reflecting behavioral despair as seen in human depression.^{36,37} In addition, it is well known that many antidepressant drugs are able to reduce the immobility time in rodents.³⁵ The antidepressant effects of methanolic extract of *Amaranthus caudatus* (100 and 200 mg/kg) and escitalopram and imipramine were studied by observing the changes in the duration of immobility in the two models: Forced swim test (FST) and tail suspension test (TST). MEAC produced a marked reduction in immobility time at doses of 100 and 200 mg/kg in the rat FST and TST ($p < 0.01$), with a profile comparable to that observed for the classical antidepressant drug ESC and imipramine (Figure 1). 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.³⁸ Moreover, TST is proposed to have a greater pharmacological sensitivity as compared with FST.^{38,39}

The presence of Flavonoids and phenolic compounds have been reported to have multiple biological effects such as central nervous system disorders,⁴⁰ antioxidant activity,⁴¹ analgesic,⁴² inhibition of mast cell histamine release antiulcerogenic,⁴³ cytotoxic, antihypertensive, hypolipidemic, antiplatelet and neurodegenerative diseases.⁴⁴



Date represents Mean \pm S.E.M. n=6 ** p<0.01 when compared with control

Figure 1. Effect of methonolic extract of *Amaranthus caudatus* on immobility time in FST and TST

4. CONCLUSION

Our study indicates that the whole plant of *Amaranthus caudatus* showed antidepressant activity. Further studies are required to know the phytochemical responsible for antidepressant activity.

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