

Acanthus ilicifolius, A saline plant of southeast coast as CNS depressant

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Abstract

The marine world offers an extremely rich resource for important compounds of structurally novel and biologically active metabolites. Traditionally, mangrove plants are used in folklore medicine for the treatment of several ailments throughout worldwide. Though numerous mangroves and mangal associates are recommended in traditional medicine as active against various diseases, very little attempts have been made to investigate the veracity of these assertions in controlled experiments. *Acanthus ilicifolius* Linn, (sea holly) (acanthaceae) is popularly recognized for its full scope of secondary metabolites and its traditional usage and this saline plant found along with mangroves in the coastal regions of India commonly in the southeast coasts. The leaves of *Acanthus ilicifolius* were collected, shade dried, pulverized into the coarse powder and subjected to defatting with petroleum ether and then extracted with ethanol using Soxhlet apparatus. Evaluation of ethanolic extract of leaves of *Acanthus ilicifolius* on CNS depressant. Various tests namely Forced Swimming Test (FST), Tail Suspension Test (TST) behavioural study were performed in mice. In FST extract at the doses of 100, 250, and 500mg/kg significantly $P < 0.0001$ increased the immobility times when compared with the control group. In case of TST significantly increase the immobility time with increase in dose when compared to standard drug. These depressive pattern may be due to the drug interact with GABA ergic system.

Keywords: marine plants, *acanthus ilicifolius*, CNS depressant, forced swimming test (FST), tail suspension test (TST), GABA

Introduction

Every parts of plants has medicinal properties include flower, root, stem, leafs, fruits, seed barks and whole plants. However, it has been observed that some plants are not safe because they contain toxic compounds which exhibits adverse effects in the body. Herbal medicine is widely practiced worldwide. The World Health Organisation (WHO) reported that 4 Billion people (80% of the world's population) use herbal medicine for some aspect of primary healthcare. Herbal medicine has been recognized by WHO as essential components for primary health care and about 11% of the 252 drugs are derived from plants [1]. Mangrove form the interface ecosystem that occur at the confluence of river and sea in tropical and subtropical areas. The term 'mangrove' describes both the ecosystem and the plant families that are adopted to live in the tidal saline environment [2]. Mangrove plant extracts have been used for centuries to treat health disorders. Plant – derived substances have recently become great interest owing to their versatile application [3]. Different classes of CNS depressants work in different ways, but all have the ability to reduce activity of the Central Nervous System and lowers the awareness in the brain. Indications of CNS depressant are Insomnia, Anxiety, Epilepsy, tension before surgery, Panic attacks.

Insomnia

Insomnia is the term applied collectively to complaints involving the chronic inability to obtain adequate sleep. Insomnia affects upto 40% of the general population yearly and is a significant cause of morbidity and mortality [4]. Insomnia results due to an imbalance between sleep inducing neurotransmitters Gamma – Amino Butyric Acid (GABA).

Anxiety

Individuals who suffer from anxiety disorders may also suffer from other co-morbidities such as mental health disorders, sleep disorders, irritable bowel syndrome, and other physical conditions [29]. Neurochemicals such as Serotonin, GABA, Dopamine, Norepinephrin, and many others have also recently been linked to anxiety disorders. Each chemical plays a very different, but equally important, role in anxiety regulation. Dysregulations in the noradrenergic systems are hypothesized to occur in anxiety disorders. Noradrenaline modulates autonomic arousal mechanisms, including increased heart rate and respiration. This leads to a physiological cascade resulting in panic symptoms such as paraesthesia, Numbness and tightness in the chest. Generalised Anxiety Disorder (GAD) is associated with noradrenergic overactivity, serotonin receptor (5-HT1A, 5-HT2C) dysregulation and a decrease in the number of benzodiazepine sites on the GABA - benzodiazepine receptor complex [5].

Epilepsy

“Epilepsy” is the condition of recurrent, unprovoked seizures. Epilepsy has numerous causes, each reflecting underlying brain dysfunction. Epilepsy is one of the most common neurologic conditions, with an incidence of approximately 50 new cases per year per 100,000 population. About 1% of the population suffers from epilepsy, and about one-third of patients have refractory epilepsy [6].

A seizure can be conceptualized as occurring when there is a distortion of the normal balance between excitation (E) and inhibition (I) in the brain. This E/I imbalance can result from an alteration at many levels of brain function. The factors that alter E/I balance can be genetic or acquired. Genetic pathologies leading to epilepsy can occur anywhere from the circuit level (e.g., abnormal synaptic connectivity in cortical dysplasia) to the receptor level (e.g., abnormal γ -aminobutyric acid [GABA] receptor subunits in Angel man syndrome) to abnormal ionic channel function (e.g., potassium channel mutations in benign familial neonatal epilepsy [BFNE]) [6].

Materials and Methods

Animals

Male Swiss albino mice weighing between 20 – 25g were used for the present study. The animals were maintained under standard environmental conditions ($25 \pm 2^\circ\text{C}$) and relative humidity (45 to 55%) and were fed with standard pellet diet and water *ad libitum* and also were exposed to 12-h light and 12-h dark cycle [7].

Plant Material

Acanthus ilicifolius Linn. (Acanthaceae) found with mangroves along the coastal regions of India commonly in the southeast coasts namely Thiruvallur, Chennai, Chengalpattu, Pichavaram, Thiruvarur, Nagapattinam.

The leaves of *Acanthus ilicifolius* were collected, shade dried, pulverized into the coarse powder and subjected to defatting with petroleum ether and then extracted with ethanol using Soxhlet apparatus.

Methods

Screening of CNS Depressant

1. Forced Swimming Test (FST)
2. Tail Suspension Test (TST)

Animals: Albino Mice

The animals were divided into five groups of six mice each.

Group I - Control group (2% DMSO in distilled water)

Group II - Standard group (Diazepam at the dose of 5mg/kg)

Group III - Test (Ethanol extract in 2% DMSO at the dose of 100mg/kg)

Group IV - Test (Ethanol extract in 2% DMSO at the dose of 250mg/kg)

Group V - Test (Ethanol extract in 2% DMSO at the dose of

500mg/kg)

Forced Swimming Test

Procedure

Forced Swim Test (FST) is the most frequently used behavioral model for screening CNS depressant activity in rodents. Mice were individually forced to swim in open glass chamber (25×15×25cm) containing fresh water to a height of 15cm and maintained at $26 \pm 1^\circ\text{C}$. 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 in the chamber was changed after subjecting each animal. Each animal showed vigorous movement during initial 2mins period of the test. The duration of immobility was manually recorded during the next 4mins of the total 6mins 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. Following swimming session, mice were towel dried and returned to their housing conditions.

Tail Suspension Test [8]

Procedure

Mice were suspended on the edge of the table, 50cm above the floor, with the help of adhesive tape placed approximately 1cm from the tip of the tail. The duration of immobility was observed for a period of 6mins. The duration of immobility was recorded during the last 4mins of the observation period. Mice were considered to be immobile only when they hung passively and were completely motionless. The animal was considered immobile when it did not show any movement of the body except for those required for respiration and hung passively. Before treatment animals were individually trained in 15mins sessions and for 30mins. Each animal was placed on Tail Suspension Test in similar environment for a period of 6min and duration of immobility time for each animal were recorded.

Statistical Analysis

All the data of CNS depressant activity was expressed as mean \pm S.E.M of animals in each group. The statistical analysis was carried out using one way ANOVA followed by Turkey's t-test. All analyses were performed using the ANOVA statistical software (Graph pad and PRISM software version 9.0.1 (151)).

Results and Discussion

Results

Forced Swimming Test

The extract at the doses of 100, 250, and 500mg/kg significantly increased the time of immobility when compared with the control group (Fig. No. 1). Similarly, the standard drug diazepam (5mg/kg, *i.p.*), showed a significant increase in the duration of immobility.

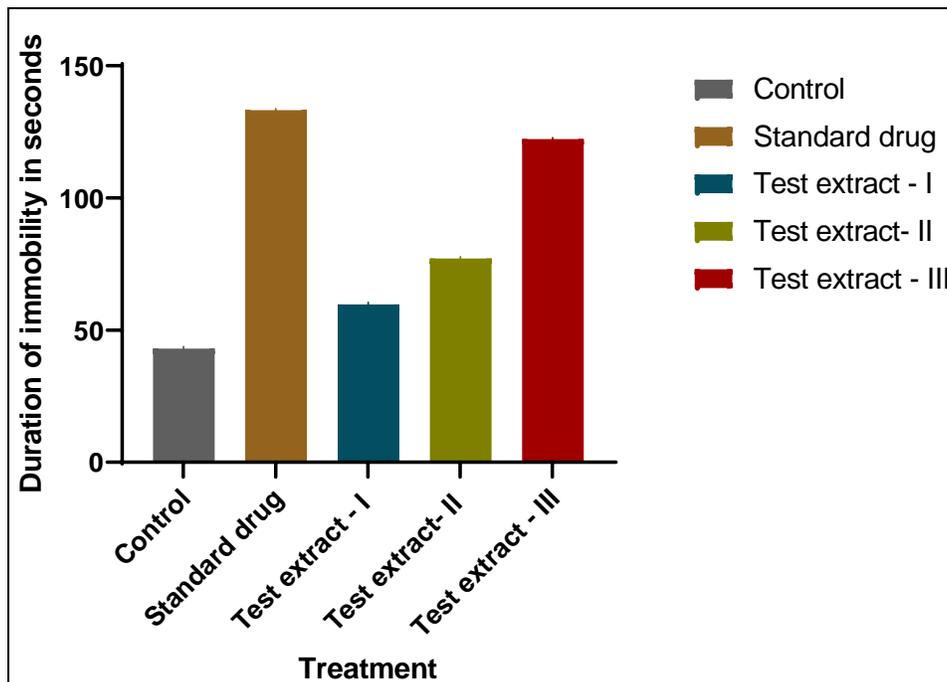


Fig 1: Effect of *Acanthus ilicifolius* extracts at different doses in Forced swimming test

Test extract I- 100mg/kg
 Test extract II- 250mg/kg
 Test extract III- 500mg/kg
 Standard drug (diazepam) - 5mg/kg

Tail Suspension Test

The results for CNS depressant activity of test extracts in Tail suspension test are given in Fig. No. 2.

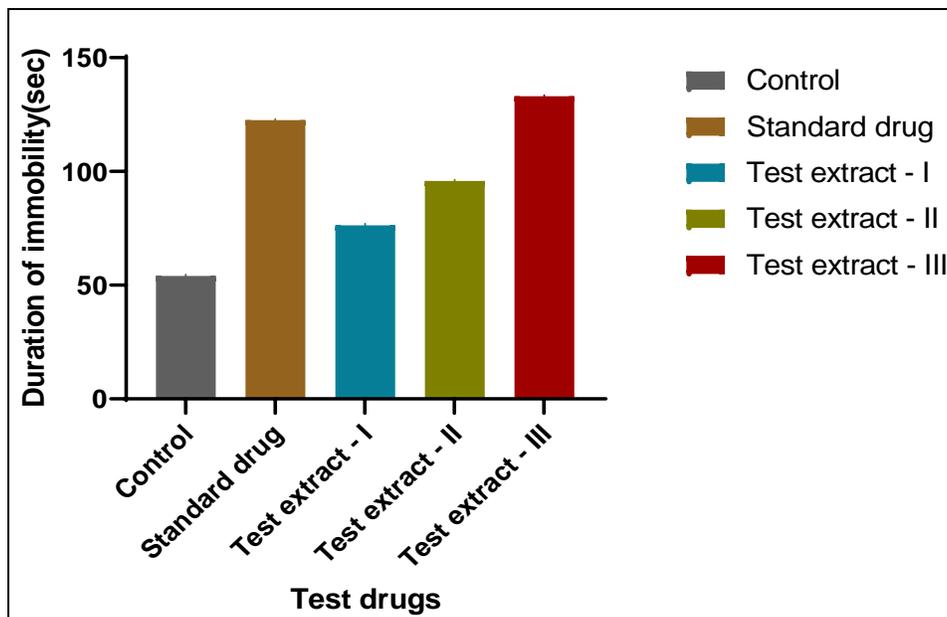


Fig 2: Effect of *Acanthus ilicifolius* extracts at different doses in Tail suspension test

Test extract I- 100mg/kg
 Test extract II - 250mg/kg
 Test extract III- 500mg/kg
 Standard drug (diazepam) - 5mg/kg

Discussion

In FST, Treatment with Ethanolic Extract of Leaves of

Acanthus ilicifolius at different doses (100mg/kg, 250mg/kg, 500mg/kg *p.o*) showed significant CNS depressant effect compared with the standard drug diazepam (5mg/kg, *i.p.*) treated group. These significant depressive pattern caused in forced swimming test may be due to the effect of test drug on inhibitory receptors present in the Central Nervous System.^[9] The modulatory receptors increases the frequency of cl-

channel opening induced by submaximal concentration of GABA. Inducing hyperpolarization due to influx of Cl^- ions and decrease the firing rate of neurons^[88]. In tail suspension test, Evaluation of EELAI using tail suspension test in mice showed increase in the immobility time. The results confirmed its dose dependent CNS depressive effect and it is summarised in Fig. No.2 the result may be due to the binding of test drug with the inhibitory receptor namely GABA^[9].

Conclusion

The present study has duly supported the traditional use of a mangrove plant known as *Acanthus ilicifolius* as CNS depressant. In forced swimming test, test compound showed increase in immobility time equal to that of standard drug. These significant depressive pattern caused in forced swimming test may be due to the inhibitory effect of test drug on inhibitory receptors present in the Central Nervous System and in tail suspension test also produced dose dependent depressive effect by interacting with GABAergic system.

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