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Research Article

**EVALUATION OF ANTIDEPRESSANT ACTIVITY OF TOTAL  
EXTRACTS FROM PLANT ARECA CATECHU IN ANIMAL  
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Rampally, Kesara, Rangareddy, Telangana, India.<sup>2,3</sup>KGR Institute of Technology and Management, Rampally, Kesara, Rangareddy, Telangana,  
India.**Abstract:**

*In the present study, Areca Catechu significantly increased the frequency of 5-HTP induced head twitches, Clonidine induced aggression and L-DOPA induced hyperactivity and aggressive behavior indicating its enhanced activity on serotonergic, noradrenergic and dopaminergic pathways respectively. Our results also confirm the involvement of serotonergic, noradrenergic and dopaminergic pathways in depression. Pretreatment with Areca Catechu, also significantly increased the levels of SOD and Catalase with simultaneous decrease in LPO levels in rat brain, suggesting its strong antioxidant activity. Since oxidative stress is reported to play an important role in depression, the antioxidant activity of Areca Catechu might be a part of the mechanism for its antidepressant activity. Results from behavioral experiments indicate that the antidepressant activity of Areca Catechu, might be due to the facilitatory effect on serotonergic, noradrenergic and dopaminergic systems apart from the antioxidant activity. The results from the present study confirm the antidepressant activity of Areca Catechu, since it reduced the immobility in both FST and TST.*

**Key Words:** *Areca Catechu, antidepressant activity.***Corresponding author:****Dr.Gampa Vijaya Kumar,**

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**INTRODUCTION:**

Depression is the most common of the affective disorders (disorders of mood rather than disturbances of thought or cognition); it may range from a very mild condition, bordering on normality, to severe (psychotic) depression accompanied by hallucinations and delusions. There are two types and they are Unipolar and Bipolar

Unipolar depression is commonly (about 75% of cases) non-familial, clearly associated with stressful life-events and accompanied by symptoms of anxiety and agitation; this type is sometimes termed reactive depression. Other patients (about 25%, sometimes termed endogenous depression) show a familial pattern, unrelated to external stresses, and with a somewhat different symptomatology<sup>2</sup>. This distinction is made clinically, but there is little evidence that antidepressant drugs show significant selectivity between these conditions.

Bipolar depression, which usually appears in early adult life, is less common and results in oscillating depression and mania over a period of a few weeks. There is a strong hereditary tendency, but no specific gene or genes have been identified either by genetic linkage studies of affected families, or by comparison of affected and non-affected individuals.

Theories of Depression

*The Monoamine Theory*

The monoamine biochemical theory of depression is the monoamine hypothesis, proposed by, which states that depression caused by a functional deficit of monoamine transmitters at certain sites in the brain, while mania results from functional excess.<sup>3</sup>

The monoamine hypothesis grew originally out of associations between the clinical effects of various drugs that cause or alleviate symptoms of depression and their neurochemical effects on monoaminergic transmission in the brain.

*Pharmacological Evidence*

The pharmacological evidence does not enable a clear distinction to be drawn between the noradrenaline and 5-HT theories of depression. Clinically, it seems that inhibitors of noradrenaline reuptake and of 5-HT reuptake are equally effective as antidepressants though individual patients may respond better to one or the other.

**AIM OF THE STUDY**

Aim of the present study was to evaluate the antidepressant activity of *Areca Catechu*(AC) in experimental models of depression using rats.

- To study the effect of AC on behavior models of depression like forced swim test, tail suspension test.
- To study the effect of AC on mechanism based models of depression like 5-HTP induced head twitches, clonidine induced aggression and

L-Dopa induced hyperactivity and aggressive behavior.

To study the effect of AC on anti-oxidant levels of brain.

**Materials**

Drugs and Chemicals

Thiobarbituric acid and DTNB reagent (HiMedia Laboratories Ltd., Mumbai)

Trichloroacetic acid (Qualigens Fine Chemicals, Mumbai)

Riboflavin (Astra IDL, Bangalore)

Sodium dihydrogen phosphate and Disodium hydrogen phosphate (S.D. Fine Chemicals, Mumbai)

Lorazepam (Ranbaxy, India)

1,1,3,3,-Tetraethoxy propane, O-Dianisidine, Imipramine hydrochloride, 5-Hydroxy Tryptophan (5-HTP), Clonidine and L-DOPA (Sigma, St. Louis, USA) were used in the study.

The other chemicals and solvents used were of analytical grade and purchased from commercial suppliers. Imipramine (IMP), 5-HTP, clonidine, L-DOPA, Lorazepam was administered intraperitoneally by dissolving in normal saline.

**METHODOLOGY**

Collection and Authentication of Plant Material

Extraction of Plant Material

- ✓ Cold Extraction (Methanol Extraction)
- ✓ Evaporation of Solvent
- ✓ % Yield value of Methanol Extract from Aerial Parts of *Areca Catechu* Plant.

Preliminary Phytochemical Screening

- ✓ Detection of Alkaloids:
- ✓ Detection of Carbohydrates:
- ✓ Detection of saponins
- ✓ Detection of steroids.
- ✓ Detection of Phenols
- ✓ Detection of Tannins
- ✓ Detection of Tannins

**Animals**

- ✓ Healthy adult male mice of 5 weeks old with average weight in the range of 40-60gms were selected.
- ✓ Acute toxicity studies
- ✓ *In vivo* models of depression employed in the study
- ✓ Forced swimming test (FST)
- ✓ Tail suspension test (TST)
- ✓ 5-HTP induced head twitches in mice
- ✓ Clonidine-induced aggression in mice
- ✓ L-dopa-induced hyper activity and aggressive behavior in mice (LHA)
- ✓ Statistical analysis

**RESULTS AND DISCUSSION:**

%Yield value of Ethanolic Extract from Aerial Parts of *Areca Catechu* was found to be **26.1%**

**Preliminary Phytochemical Screening**

Investigation revealed the presence of steroid, Alkaloid, saponins, Tannins, phenols & Flavonoid in Ethanolic Extract of *Areca Catechu*(AC)

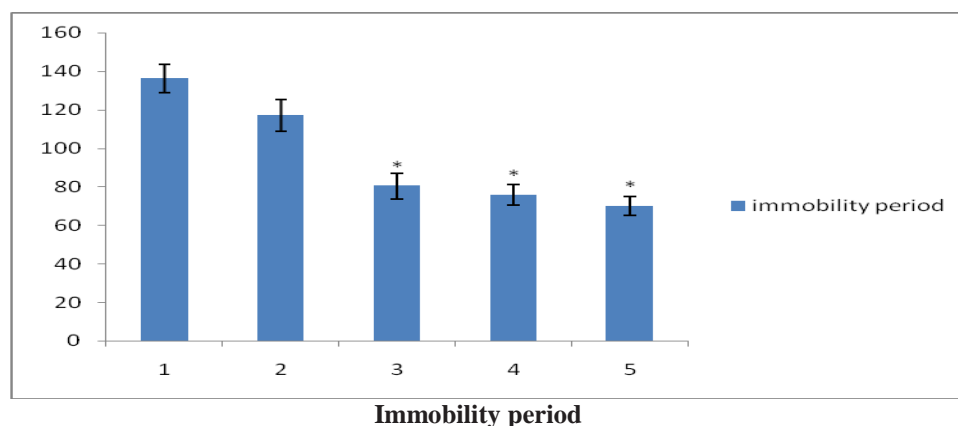
**Acute toxicity studies**

As per (OECD) draft guidelines 423 Female albino mice were administered *Areca Catechu* and doses was be selected in the sequence (1.75- 5000) using the default dose progression factor, for the purpose of

toxicity study. Animals are observed individually at least once during the first 30 minutes after dosing, periodically during the first 24 hours and daily thereafter, for a total of 14 days,. In all the cases, no death was observed within 14 days. Attention was also given to observation of tremors and convulsions, salivation, diarrhoea, lethargy, sleep and coma. Overall results suggested the LD<sub>50</sub> value as 2000 mg/kg. Hence therapeutic dose was calculated as 1/10<sup>th</sup> and 1/20<sup>th</sup> i.e. 100mg/kg and 200 mg/kg of the lethal dose for the purpose of antidiabetic investigations.

**Table 1: Forced Swim Test (FST)**

Group no.	Treatment (dose in mg/kg)	Immobility period (sec) Mean $\pm$ SEM
I	Control (0.3% CMC) + FST	136.3 $\pm$ 7.3
II	<i>Areca Catechu</i> (100 mg/kg, p.o.) + FST	125.2 $\pm$ 10.3
III	<i>Areca Catechu</i> (200 mg/kg, p.o.) + FST	98.5 $\pm$ 8.6*
IV	<i>Areca Catechu</i> (400 mg/kg, p.o.) + FST	82.0 $\pm$ 7.4*
V	Imipramine (15 mg/kg, i.p.) + FST	70.1 $\pm$ 5.0*



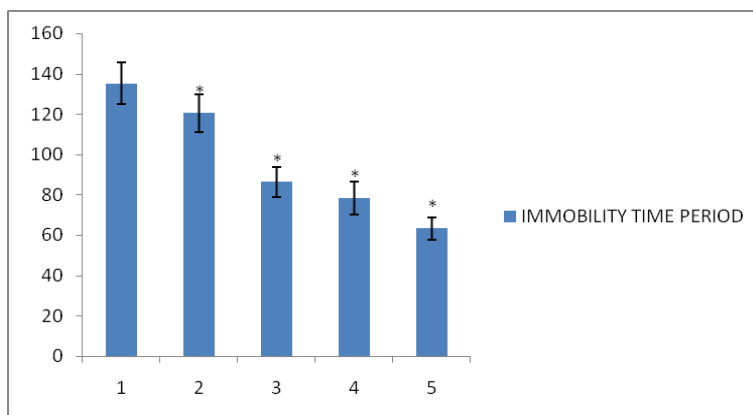
Effect of AC (100, 200 and 400 mg/kg, p.o.) and Imipramine (IMP; 15 mg/kg) on forced swim test (FST) in rats. Each column represents mean  $\pm$  S.E.M. of immobility period (sec), n = 6. \* = p < 0.001 compared to control

**Tail Suspension Test (TST)****Effect of AC and Imipramine (IMP) on tail suspension test (TST) in mice**

Each column represents mean  $\pm$  S.E.M. of immobility period (sec), n = 6. a = p < 0.001 compared to control

**Table 2: Effect of AC and Imipramine (IMP) on tail suspension test (TST) in mice**

Group no.	Treatment (dose in mg/kg)	Immobility period (sec)
I	Control (0.3% CMC) + TST	135.2 $\pm$ 10.3
II	<i>Areca Catechu</i> (100 mg/kg, p.o.) + TST	110.6 $\pm$ 10.2 <sup>a</sup>
III	<i>Areca Catechu</i> (200 mg/kg, p.o.) + TST	98.4 $\pm$ 9.3 <sup>a</sup>
IV	<i>Areca Catechu</i> (400 mg/kg, p.o.) + TST	80.3 $\pm$ 7.1 <sup>a</sup>
V	Imipramine (15 mg/kg, i.p.) + TST	63.4 $\pm$ 5.5 <sup>a</sup>



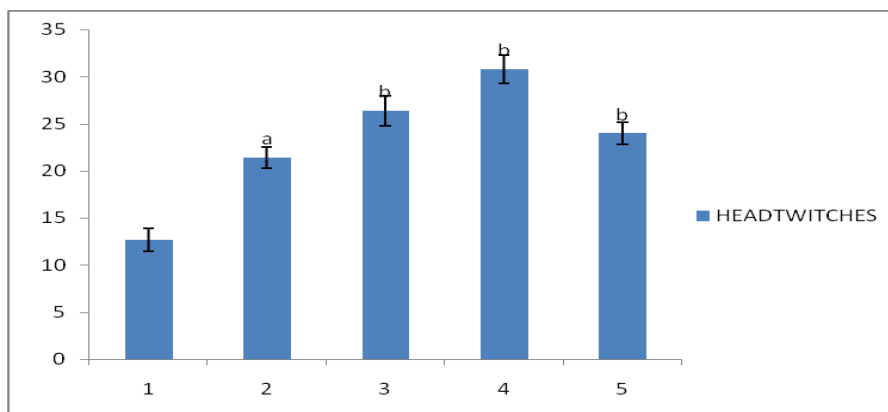
5-HTP induced head twitches in mice

**Effect of AC on 5-HTP-induced head twitches in mice.**

Each column represents mean  $\pm$  S.E.M. of number of head twitches, n = 6. a = p<0.01, b = p<0.001 compared to control

**Table 3: Effect of AC and Imipramine (IMP) on tail suspension test (TST) in mice**

Group no.	Treatment (dose in mg/kg)	Head twitches Mean $\pm$ SEM
I	Control (0.3% CMC)	12.7 $\pm$ 1.2
II	<i>Areca Catechu</i> (100 mg/kg, p.o.)	20.8 $\pm$ 2.1 <sup>a</sup>
III	<i>Areca Catechu</i> (200 mg/kg, p.o.)	29.0 $\pm$ 2.6 <sup>b</sup>
IV	<i>Areca Catechu</i> (400 mg/kg, p.o.)	37.8 $\pm$ 3.5 <sup>b</sup>
V	Imipramine (15 mg/kg, i.p.)	24.0 $\pm$ 2.2 <sup>b</sup>



L-DOPA induced hyperactivity and aggressive behavior in mice

**Effect of AC and Lorazepam on L-DOPA-induced hyperactivity and aggressive behavior in mice.**

Each column represents mean  $\pm$  S.E.M. of number of head twitches, n = 6. a = p<0.001, compared to control

**Table 4: Effect of AC and Lorazepam on L-DOPA-induced hyperactivity and aggressive behavior in mice**

Group o.	Treatment (dose in mg/kg)	Behavioral score
I	Control (0.3% CMC)	1
II	<i>Areca Catechu</i> (100 mg/kg, p.o.)	2.0 $\pm$ 0.2 <sup>a</sup>
III	<i>Areca Catechu</i> (200 mg/kg, p.o.)	2.0 $\pm$ 0.2 <sup>a</sup>
IV	<i>Areca Catechu</i> (400 mg/kg, p.o.)	2.6 $\pm$ 0.2 <sup>a</sup>
V	Lorazepam (2.5 mg/kg, i.p.)	2.1 $\pm$ 0.2 <sup>a</sup>

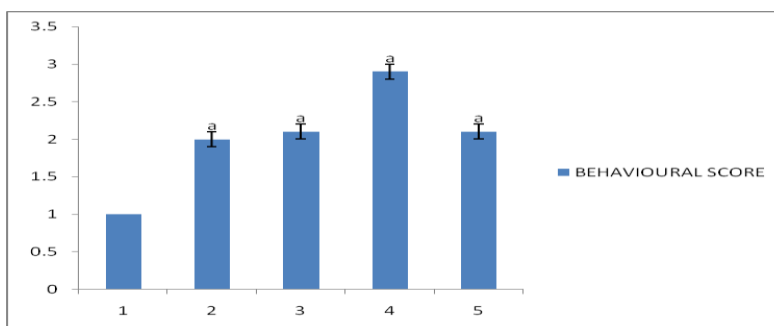
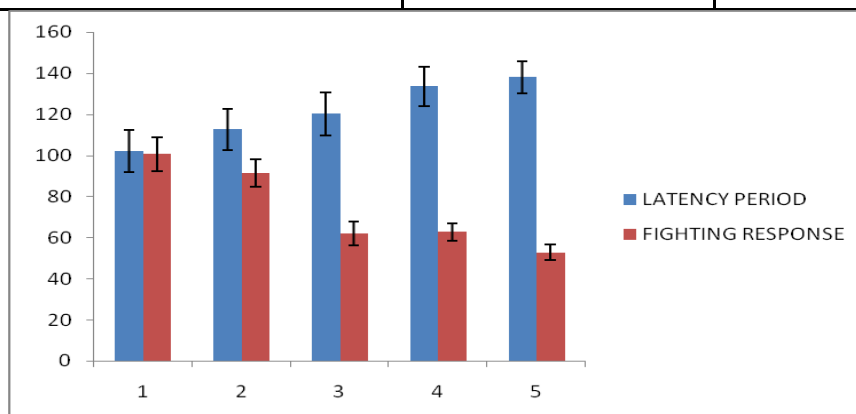


Table 5: Clonidine induced aggression in mice

Group no.	Treatment (dose in mg/kg)	% Response( MEAN ± SEM)	
		Latency to 1 <sup>st</sup> attack	Fighting response
I	Control (0.3% CMC)	102.1 ± 10.1	100.6 ± 8.3
II	<i>Areca Catechu</i> (100 mg/kg, p.o.)	122.6 ± 12.1 <sup>a</sup>	89.5 ± 8.6 <sup>a</sup>
III	<i>Areca Catechu</i> (200 mg/kg, p.o.)	130.5 ± 12.5 <sup>b</sup>	67.9 ± 6.6 <sup>b</sup>
IV	<i>Areca Catechu</i> (400 mg/kg, p.o.)	133.7 ± 9.6 <sup>b</sup>	64.5 ± 6.2 <sup>b</sup>
V	Lorazepam (2.5 mg/kg, i.p.)	140.0 ± 8.0 <sup>b</sup>	42.6 ± 4.8 <sup>b</sup>



#### Effect of AC (100, 200 and 400 mg/kg, p.o.) and Lorazepam (2.5 mg/kg) on clonidine induced aggression in mice

#### CONCLUSION:

The results from the present study confirm the antidepressant activity of *Areca Catechu*, since it reduced the immobility in both FST and TST.

In the present study, *Areca Catechu* significantly increased the frequency of 5-HTP induced head twitches, Clonidine induced aggression and L-DOPA induced hyperactivity and aggressive behavior indicating its enhanced activity on serotonergic, noradrenergic and dopaminergic pathways respectively. Our results also confirm the involvement of serotonergic, noradrenergic and dopaminergic pathways in depression.

Pretreatment with *Areca Catechu*, also significantly increased the levels of SOD and Catalase with simultaneous decrease in LPO levels in rat brain,

suggesting its strong antioxidant activity. Since oxidative stress is reported to play an important role in depression, the antioxidant activity of *Areca Catechu* might be a part of the mechanism for its antidepressant activity.

Results from behavioral experiments indicate that the antidepressant activity of *Areca Catechu*, might be due to the facilitatory effect on serotonergic, noradrenergic and dopaminergic systems apart from the antioxidant activity.

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