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COMPARATIVE STUDY OF THE ANTIDEPRESSANT EFFECT OF ETHANOL EXTRACT OFARECA CATECHU AND IMIPRAMINE IN MICE

Pharmacology

Dr. T.janagan M.d. Pharmacology, Associate Professor, Srimuthukumaran Medical College And Hospital.

Dr.s.a.sridevi M.d. Pharmacology, Professor, Acs Medical College And Hospital.

ABSTRACT

INTRODUCTION:
Depression is a chronic illness that affects people of all ages[1]. It is one of the most prevalent forms of psychiatric disorders. Major depressive disorder is characterized by depressed mood most of the time for atleast two weeks and or loss of interest or pleasure in most activities.[2] Certain measurable behaviour can be assayed in animals which might be relevant in human depression[3]. Hence animals like mice are used as screening model to study the extract.
Aim : To compare the antidepressant effect of the ethanol extract of Areca Catechu with Imipramine in mice
Materials & Methods : It is an animal study started after the approval of animal ethical committee clearance, with the ethanol extract of areca catechu.
Results: In this study the ethanol extract of areca catechu is said to have potent anti depressant effect when compared to the conventional anti depressant imipramine.

KEYWORDS

Areca Catechu, Antidepressant Action

Review of Literature
Areca catechu is the areca palm or areca nut palm, a species of palm which is grown in India, Malaysia, Taiwan and many other countries for their seeds. Betel nut is humanity's fourth most widely used drug after nicotine, ethanol and caffeine, is chewed by millions of people living between the east coast of Africa and the western Pacific.[4]It belongs to the family Arecaceae and is erroneously called the betel tree because its fruit, the arecanut is always chewed along with the betel leaf, a leaf from the vine of the Piperaceae family. It is a medium sized and graceful palm tree growing straight to 20m tall with a trunk of 20-30 cm in diameter. The leaves are 1.5-2m long, pinnate with numerous crowded leaflets.

Areca catechu is grown for its commercially important seed crop, the areca nut. The seed contains alkaloids such as arecaine and arecoline. Nine alkaloids constitute the active ingredients of betel nut[5], the most abundant of which is arecoline – a potent muscuranic agonist that rapidly crosses the blood-brain barrier and includes a range of parasympathetic effects.[6] It is known as 'Akota' in Sanskrit and 'Adike' in Kannada. Ethanol extract of Areca catechu has been shown to have antidepressant properties.[7] In view of this the present study will be undertaken to compare the antidepressant effect of ethanol extract of Areca catechu with Imipramine in mice.

Imipramine is a tricyclic antidepressant. Hafliger and Schindler in the late 1940's synthesized a series of more than 40 iminodibenzyl derivatives of which one was Imipramine. Kuhn in 1958 found that Imipramine was relatively ineffective in quieting agitated psychotic patients, but it had a remarkable effect on depressed patients[8]. As it has side effects like dry mouth, epigastric distress, constipation, tachycardia, palpitations, increased risk of glaucoma, hypotension, urinary retention[8] - a newer antidepressant with lesser side effects can be looked for.

Depression can be defined as a pathological complex of psychological, neuroendocrine and somatic symptoms that cannot be exactly reproduced in animals. Patients with the major depression have symptoms that reflect changes in brain monoamine neurotransmitters, specifically noradrenaline, serotonin and dopamine[3]. As most of the available antidepressants have significant side effects, a newer antidepressant with not only greater efficacy and rapid onset of action but also with lesser side effects can be looked for[1] Areca catechu is said to be traditionally used in rural villages as a folk-lore medicine for people with mild – moderate depression. Areca catechu is used as an interior landscaping species in large indoor areas such as malls and hotels. Areca nut is also used for chewing along with betel leaf among the people of India and Taiwan.

LDH activity which is elevated in MI, liver and kidney damage, cancer was significantly reduced with the methanol extract of Areca nut because it has a inhibitory effect on most of the serum enzymes tested[9].

Ethanol extract of Areca palm will be tested for its antidepressant property in mice using forced swim test and tail suspension test which are behavioural provocative (despair) tests. The inability or reluctance to maintain the effort of escape is referred as "Behavioural Despair"[10]. In forced swim test the mice are forced to swim in restricted space from which they cannot escape and are induced a characteristic behaviour of immobility. This state reflects a state of despair which can be reduced by several agents which are therapeutically useful as antidepressants[1]. In tail suspension test the immobility displayed by the mice when subjected to an unavoidable and inescapable stress has been hypothesized to reflect behavioural despair which in turn may reflect depressive disorders in humans[1].

Clinically effective antidepressants reduce the immobility that mice display after active and unsuccessful attempt to escape when suspended by the tail. This act is a variant of the behavioural despair test in which immobility is induced by simply suspending a mouse by tail[1]. This test is reliable and rapid screening method for antidepressants including those involving serotonergic system. The results are then tabulated and statistical analysis using "One Way ANOVA" is done.

STUDY METHODOLOGY:

Type of Study :	Animal Study
Animals Used:	Albino Mice of Swiss Strain
Weight :	20 – 25 gms
Gender :	Male
Study Site :	Department of Pharmacology, Sree muthukumaran medical college and hospital.
Drugs Used: & Materials:	Ethanol Extract of Areca Catechu Imipramine Vertical Plexiglass Cylinder Plastic String Adhesive Tape Digital Stop Clock

Method of assessment: forced swim test, tail suspension test.

Preparation of Extract :
Ethanol extract of areca catechu will be prepared using Soxhlet apparatus.

Animals :
About 36 Albino male mice weighing 20-25 gms are bred and maintained under Standard conditions in the central animal house in sree muthukumaran medical college. They will be kept at the animal

house of the Pharmacology department of the college for 7 days at $21^0 + 1^0$C with light/dark cycle of 12:12 hours. Prior to the experiment all the animals will be fasted overnight with water *ad libitum*.

Procedure :

a) Forced Swim Test :

Here the mice are subjected to two trials. The first trial lasts for 15 minutes. 24 hours after the first trial, a second trial is performed for 6 minutes. The immobility time during second trial is measured. Three groups of 6 Albino male mice each weighing between 20-25 gms are selected for the experiment. Group I will be taken as control and will receive normal saline. Group II will receive Imipramine 10mg/kg orally 1 hour before the experiment and is taken as standard[1]. Group III will receive 50 mg ethanol extract of areca catechu and is taken as the test group.[9]

Naïve mice individually are forced to swim in a vertical plexiglass cylinder (capacity:5L, height :50cm , diameter :18cm, containing 15cm of water maintained at temperature:25^0C) .Mice placed in the cylinder first time are initially highly active, vigourously swimming in circles trying to climb the wall or diving to the bottom. After 2-3 minutes activity begins to subside and interspersed with phase of immobility or floating of increasing length. After 5 -6 minutes immobility reaches a plateau where the mice remains immobile for 80% of the time. A mouse is considered immobile when floating motionless or making only those movements necessary to keep its head above the water surface. Duration of immobility is recorded during the last 4 minutes in the 6minutes test[3]. Antidepressants decrease the immobility time. After 6 minutes mice are taken out, dried by a towel and warmed under a 100 W lamp. The water is changed after each test because urine and other chemicals released by the first mouse will affect the swimming pattern of the next mouse. The results are then tabulated and calculation is done

b) Tail Suspension Test :

Three groups of 6 Albino male mice each weighing between 20-25 gms are selected for the experiment. Group I will be taken as control and will receive normal saline. Group II will receive Imipramine 10mg/kg orally 1 hour before the experiment and is taken as standard[1]. Group III will receive 50mg of ethanol extract of areca catechu and is taken as the test group[7]. Mice are hung on a plastic string 38cm above the table top with an adhesive tape placed ~1cm from the tip of the tail. Immobility time is recorded for 8 minutes. Mice are considered immobile only when they hang passively and completely motionless for atleast one minute[3]. Both these tests are performed on 0, 7th, 15th, 30th day and the results are tabulated.

STATISTICAL ANALYSIS :

The analysis of the ethanol extract of areca catechu is done using "one way ANOVA" test.

The forced swim test (FST) is one of the most commonly used animal models for assessing antidepressant-like behavior. This protocol details using the FST in rats, which takes place over 48 h and is followed by the video analysis of the behavior. The swim test involves the scoring of active (swimming and climbing) or passive (immobility) behavior when rodents are forced to swim in a cylinder from which there is no escape. There are two versions that are used, namely the traditional and modified FSTs, which differ in their experimental setup. For both versions, a pretest of 15 min (although a number of laboratories have used a 10-min pretest with success) is included, as this accentuates the different behaviors in the 5-min swim test following drug treatment. Reduction in passive behavior is interpreted as an antidepressant-like effect of the manipulation, provided it does not increase general locomotor activity, which could provide a false positive result in the FST.

For Forced Swim Test
Test Drug : Ethanol Extract of Areca Catechu.
Standard : Imipramine 10 mg/kg
Control : Normal Saline

Mouse No:	Drug	Dose (in ml)	Duration of Immobility (in sec)						
			1st Min	2nd Min	3rd Min	4th Min	5th Min	6th Min	Total
1.	imipramine	0.3 ml	20sec	22sec	23sec	22sec	18sec	16sec	123sec
2	imipramine	0.3ml	18sec	20sec	22sec	18sec	17sec	19sec	114sec
3.	Arecacatech extract	0.3ml	16sec	16sec	20sec	15sec	13sec	16sec	95sec
4.	Arecacatechu extract	0.3ml	14 sec	19 sec	17 sec	18 sec	19 sec	14 sec	103sec
5.	Normalsaline	0.3ml	30 sec	34sec	36sec	38 sec	36 sec	32 sec	206sec
6.	Normalsaline	0.3ml	34 sec	33 sec	35sec	36 sec	38 sec	36 sec	212sec

For Tail Suspension Test
Test Drug : Ethanol Extract of Areca Catechu
Standard : Imipramine 10 mg/kg
Control : Normal Saline

Mouse No:	Drug	Dose (in ml)	Duration of Immobility (in sec)								
			1st Min	2nd Min	3rd Min	4th Min	5th Min	6th Min	7th Min	8th Min	Total
1.	imipramine	0.3 ml	20sec	22sec	20sec	22sec	15sec	16sec	20sec	22sec	117sec
2	imipramine	0.3ml	18sec	22sec	22sec	18sec	20sec	19sec	18sec	20sec	119sec
3.	Arecacatech extract	0.3ml	16sec	18sec	20sec	15sec	15sec	16sec	16sec	16sec	100sec
4.	Arecacatechu extract	0.3ml	14 sec	19 sec	14sec	18 sec	19 sec	12sec	14 sec	19 sec	97sec
5.	Normalsaline	0.3ml	30 sec	31sec	36sec	38 sec	33 sec	32 sec	30 sec	34sec	200sec
6.	Normalsaline	0.3ml	34 sec	36sec	35sec	36 sec	41 sec	36 sec	34 sec	33 sec	218sec

INFERENCE: In this study it shows that the ethanol extract of areca catechu is more potemt than tha antidepressant imipramine. It is said to show least time of immobility when compared to the control and the standard drug.

CONCLUSION: Thus the effect of areca catechu is found have an effective antidepressant effect on the mice. So in future these extracts can also be added as an adjuvant in the treatment of major depression.

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