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Original Research Article

Screening of Antidepressant Effect of Hydro Ethanolic Extract of *Caryoyta urens* on Wistar Rats

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Abstract: A person's thoughts, behavior, feelings and sense of wellbeing are important acts for the good sustainable life in the society and also for the personal life. Low mood, exercise rumination of negative thoughts, misery, apathy and pessimism, low self-esteem, feeling of guilty adequacy and ugliness ,indecisiveness ,loss of motivation, anhedonia, loss of reward, these are the symptoms of depression, which is a leading disorder making the human life uncomfortable.
Biologically depression is an extremely common psychiatric condition, about which a variety of neurochemical theories exist and for which a corresponding variety of different types of drugs are used for treatment. Imbalanced state of neurotransmitters serotonin, dopamine, and norepihephrine will lead to the depression and anxiety. By evaluation of traditional claim using modern scientific experimental methods, Aiming to develop a drug obtained from plant origin to treat depression using various experimental animal models. On the observation, exploratory behaviors of the animals towards the plant extract with the help of various models involving in the methodology, the antidepressant activity of chemical constituents present in the plant extract, and on admission of the drug to the experiment animals, conducting the exploratory methods, found the antidepressant activity in the extract.
Keywords: Neurotransmitters, Psychiatric condition, Antidepressants, Anhedonia, Anxiety.

INTRODUCTION

Major depressive disorder (MDD), often simply called as depression, is a mental disorder characterized by a pervasive and persistent low mood that is accompanied by low self-esteem and by a loss of interest or pleasure in normally enjoyable activities. The term "depression" is used in a number of different ways. Major depressive disorder is a disabling condition that adversely affects a person's family, work or school life, sleeping and eating habits, and general health [1].

The diagnosis of major depressive disorder is based on the patient's self-reported experiences, behaviour reported by relatives or friends, and a mental status examination. There is no laboratory test for major depression, although physicians generally request tests for physical conditions that may cause similar symptoms. The most common time of onset is between the ages of 20 and 30 years, with a later peak between 30 and 40 years [2]. The bio psychosocial model proposes that biological, psychological, and social factors all play a role in causing depression [3]. Depression may be directly caused by damage to the cerebellum as is seen in cerebellar cognitive affective syndrome [4-6]. It is said that variation among the serotonin transporter (5-HTT) gene affects the chances that people who have dealt with very stressful life events will go on to experience depression. To be specific, depression may follow such events, but seems more likely to appear in people with one or two short alleles of the 5-HTT gene [7].

Most biological theories focus on: The monoamine chemicals serotonin, norepinephrine and dopamine, which are naturally present in the brain and assist communication between nerve cells. This cluster of symptoms (syndrome) was named, described and classified as one of the mood disorders in the 1980 edition of the American Psychiatric Association's diagnostic manual [8]. Antidepressants influence the overall balance of three neurotransmitters: serotonin, norepinephrine, and dopamine. Some antidepressants act on neurotransmitter receptors.

Antidepressant medications increase the levels of one or more of the monoamines the neurotransmitters serotonin, norepinephrine and dopamine in the synaptic cleft between neurons in the brain. Some medications affect the monoamine receptors directly. Serotonin is hypothesized to regulate other neurotransmitter

systems; decreased serotonin activity may allow these systems to act in unusual and erratic ways [9]. According to this "permissive hypothesis", depression arises when low serotonin levels promote low levels of norepinephrine, another monoamine neurotransmitter [10]. Antidepressants enhance the levels of norepinephrine directly, whereas others raise the levels of dopamine, a third monoamine neurotransmitter. These observations gave rise to the monoamine hypothesis of depression. In its contemporary formulation, the monoamine hypothesis postulates that a deficiency of certain neurotransmitters is responsible for the corresponding features of depression: "Norepinephrine may be related to alertness and energy as well as anxiety, attention, and interest in life; lack of serotonin to anxiety, obsessions, and compulsions; and dopamine to attention, motivation, pleasure, and reward, as well as interest in life" [11].

Typically, people are treated with antidepressant medication and, in many cases, also receive counseling, particularly cognitive behavioural therapy (CBT) [12]. Synthetic drugs available for treatment of depression have various adverse effects including drowsiness, ataxia with benzodiazepines and insomnia, libido with selective serotonin reuptake inhibitors. Drugs obtained from natural sources are perceived to have fewer side effects while having same ability to cure disorders in much the same way as their synthetic counterparts. Therefore, present study was undertaken to evaluate anti-depressant effect of hydro ethanolic extract of *caryota urens Fruit.*

MATERIALS AND METHODS

Description of the plant drug

A genus of palms, distributed in the tropical parts of indo- Malaysia, Sri Lanka, the Solomon Island and north-eastern Australia. Seven species, two of which have been introduced, are found to occur in India [13]. *Caryota urens* is a species of flowering plant in the palm family from the Indian Subcontinent and Southeast Asia where they grow in fields and rainforest clearings. The epithet *urens* is Latin for "stinging" alluding to the chemicals in the fruit. They are commonly called solitary fishtail palm, toddy palm, wine palm, jaggery palm; its leaf is used as fishing rod after trimming the branches of the leaf and drying. *Caryota urens* species is a solitary-trunked tree that measure up to 12 m (39 ft.) in height and up to 30 cm (12 in) wide. Widely-spaced leaf-scar rings cover its gray trunk which culminate in a 6 m (20 ft.) wide, 6 m tall leaf crown. The bipinnate leaves are triangular in shape, bright to deep green, 3.5 m (11 ft.) long, and held on 60 cm (24 in) long petioles. The obdeltoid pinnae are 30 cm long with a pointed edge and a jagged edge. The 3m (9.8ft) long inflorescences emerge at each leaf node, from top to bottom, producing pendent clusters of white, unisexual flowers. The fruit matures to a round, 1 cm (0.39 in) drupe, red in color with one seed. Like all *Caryotas*, the fruit contains oxalic acid, a skin and membrane irritant. As these plants are monocarpic, the completion of the flower and fruiting process results in the death of the tree. Elephants love this plant - both leaf & the pulp. Pulp of the fully grown up plant is cut, sun dried, powdered and is edible. This powder is considered cool and nutritious in Coastal districts of Karnataka [14].

Collection and authentication of plant material

The fruit of *Caryota urens* was collected from Chennai at the month of February 2016; the specimen was identified and authenticated by Dr. D. Aravind, M.D. (S), M.Sc. Consultant (Pharmacognosy), National institute of siddha, Chennai and a voucher specimen was deposited at C. L. Baid Metha College of Pharmacy for future reference. All procedures described were reviewed and approved by the Institutional Animals Ethical Committee.

Preparation Of Plant Extract:

The fruits were shade dried at room temperature. The dried parts were subjected to size reduction to a coarse powder by using dry grinder and passed through sieve No.30. This powder was packed into soxhlet apparatus and extracted with Hydro ethanol at a temperature range of 55˚C. The extracts was dried at 45˚C in hot air oven till semisolid to solid mass was obtained and was stored in airtight containers in refrigerator below 8˚C. These extracts was suspended in CMC Sodium and used for further studies.

Percentage Yield:

The percentage yield of the Hydro ethanolic extract of *Caryota urens* fruits was found to be 83.57% .

Experimental Animals

The adult Rats (200-400g) of either sex were obtained from the animal house in C. L. Baid Metha College of Pharmacy, Chennai. The animals were maintained in a well-ventilated room with 12:12 hour light/dark cycle in polypropylene cages.

Standard pellet feed (Hindustan Lever Limited., Bangalore) and safe drinking water was provided throughout experimentation period. Animals were acclimatized to laboratory conditions one week prior to initiation of experiments. Animal Ethical committee clearance was obtained from IAEC (Institutional Animal Ethics Committee) of CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals) of C. L. Baid Metha college of Pharmacy.

Acute Oral Toxicity Studies [15]

Healthy adult Rats weighing 200-400gm were used for the study, since the herbal extracts are relatively nontoxic, the starting dose level of hydro ethanolic extract of Caryota urens fruits was selected as 2000mg/kg p.o. and the extract was administered orally to rats which were fasted over night with water *ad libitum*. Body weights of the rats before and after treatment were noted. Any changes in skin and eyes and mucous membrane and also respiratory, circulatory, autonomic, CNS, motor activity, behavior pattern were observed and also signs of tremors, convulsion, salivation, diarrhea, lethargy, sleep and coma were noted. The onset of toxicity and signs of toxicity also noted.

Oral Acute Toxicity Testing by OECD guidelines 423 [16]

The Acute Oral Toxicity Study was done according to OECD guidelines 423 (Acute Toxic Class Method). A single dose of 2000 mg/kg body weight of the HEECU was administered through p.o to 3 animals each and observed for 3 days. Animals were observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours and daily thereafter for a period of 1 day for all toxicity signs. There was no considerable change in body weight in before and after treatment and no sign of toxicity were observed. LD50 cut off dose per kg body weight was categorized as x (unclassified) and a Globally Harmonized System (GHS) class also comes under x (unclassified). The results are shown in Table-1.

Table-1: Result of oral Acute Toxicity Testing

Sl. No	Extract	Dose/kg Body weight	Weight of animals		Signs of toxicity	Onset of toxicity	Duration of study
			Before	After			
1.	HEEFCU	2000 mg	280gm	282gm	No signs of Toxicity	Nil	7 days
2.	HEEFCU	2000mg	350gm	354 gm		Nil	7 days
3	HEEFCU	2000 mg	220gm	222 gm		Nil	7 days

***Invivo* Pharmacological Studies**

Grouping of Animals:

Rats of either sex weighing 200-400gms are used for the study. They were divided into 3 groups of 6 animals each and maintained at an ambient temperature relative humidity with 12 hrs light/ dark cycle.

GROUP 1--- control.

GROUP 2--- Treated with low dose of CU Hydro ethanolic extract (200mg/kg/oral)

GROUP 3---Treated with high dose of CU Hydro ethanolic extract (400mg/kg/oral)

GROUP 4---Treated with standard drug.

Forced swimming test [17]

The Rat from each group II, III, IV will be placed in the cylinder 24 h later after doses of HEECU (200 and 400mg/kg) respectively and their activity will be recorded. The recordings will be analyzed to find the duration of immobility, swimming behavior and climbing behavior in the 5 min test period using stopwatch. An animal will be judged to be immobile whenever it remains floating passively in the water in a slightly hunched but upright position, its nose just above the surface, with no additional activity other than that necessary to keep its head above water. Swimming is defined as active movement throughout the swim chamber, which includes crossing into another quadrant. Climbing activity (also termed thrashing) consist of upward directed movements of the forepaws along the side of the swim chamber. The data obtained will be recorded and compared.

Actophotometer [18]

The locomotor activity (horizontal activity) can be easily measured using an actophotometer which operates on photoelectric cells which are connected in circuit with a counter. When the beam of light falling on the photo cell is cut off by the animal, a count is recorded. An actophotometer could have either circular or square arena in which the animal moves. After 30min of drug administration, the animals were subjected to the actophotometer and checked for their locomotor activity for a period of 5 min. The basal activity score of all the animals was calculated.

Elevated Plus Maze [19]

HEECU (200and 400 mg/kg) were uniformly suspended in 1% CMC SODIUM was administered to the animals (of Group – III, IV respectively). Then after 3HRS, the parameters were observed by placing the animal in the elevated plus maze. The plus-maze apparatus consisting of two open arms (30cm×5 cm) and two enclosed arms (30cm×5cm×5cm), extending from a central platform (5cm×5 cm) and raised 50cm above floor level. Each mouse was placed at the center of the maze with its head facing the open arm. During the 5 min experiment, the behavior of the mouse was recorded as the number of entries into the open or closed arms and time spent by the RAT in each of the arms. An arm entry was defined as the entry of all four paws into the arm.

RESULTS AND DISCUSSION

Preliminary phytochemical investigation for ethanolic extract of *Caryota urens*

The results that the preliminary phytochemical screening of the hydroethanolic extracts of fruits of *CARYOTA URENS* were shown below in table**.** The alcoholic extract gave positive result of Alkaloids, tannins, flavonoids, phenol, Quinones, and sugar.

Table-2: Preliminary phytochemical screening of the hydroethanolic extracts of fruits

Sl no.	Category	Result
1	Alkaloids	+ve
2	Sugar	+ve
3	Steroids	-ve
4	Proteins	-ve
5	Tannins	+ve
6	Flavonoids	+ve
7	Saponins test	-ve
8	Phenols test	+ve
9	Glycosides	-ve
10	Anthraquinones	-ve
11	Quinones	+ve
12	Terpenoids	-ve

Table-3: Effect of HEECU on forced swimming test

Animal groups	Swimming	Climbing	Immobility
Control	21.83±1.447	74.00±1.633	100.5±1.565
HEECU 200 mg/kg	39.83±1.352	117.3±0.7601	75.33±1.333
HEECU 400 mg/kg	48.17±1.014	138.0±1.291	67.83±0.8724
Fluoxetine	166.3±2.362	167.2±1.515	39.83±3.156

Table-4: Effect of HEECU on Actophotometer

Animal groups	Locomotor score (seconds)
Control	126.3±1.585
HEECU 200 mg/kg	217.5±0.8851
HEECU 400 mg/kg	271.7±3.051
Fluoxetine	308.66±8.22

Table-5: Effect of HEECU on Elevated plus Maze

Animal groups	Total time travelled	No. of entries in open arm	No. of entries in closed arm
Control	5 minutes	3.000±0.3651	4.167±0.4014
HEECU 200 mg/kg	5 minutes	5.000±0.3651	8.000±0.5164
HEECU 400 mg/kg	5 minutes	7.500±0.5627	9.167±0.4773
Fluoxetine	5 minutes	4.800±0.47	10.66±0.42

DISSCUSION

Effect of heecu on FST

The duration of the swimming and climbing was significantly increased in animals treated with high dose of HEECU 400mg/kg and low dose of HEECU 200mg/kg when compared to control, but lesser than the standard drug durations. The duration of the immobility was significantly decreased in animals treated with high dose of HEECU 400mg/kg and low dose of HEECU 200mg/kg when compared to control, but higher than the standard drug duration.

Effect of heecu on elevated plus maze

The number of entries in open arm was significantly increased in animals treated with HEECU 400 mg/kg. The standard drug treated animals exhibit same effect as of low dose 200 mg/kg. The number of entries in closed arm was significantly decreased in animals treated with 400 mg/kg when compared to control. The low dose treated animals shows same number of entries as that of the standard.

Effect of heeuv on actophotometer

The locomotor activity was significantly

decreased in animals treated with HEECU 200 mg/kg when compared to control. The locomotor activity was significantly decreased in animals treated with HEECU 400 mg/kg when compared to control. A significant increase in locomotor activity was observed in animals treated with HEECU 400 mg/kg when compared with the standard drug.

CONCLUSION

The assessment of depression related behavior in animal models is based on the assumption that depression in animal is comparable to depression in humans. Depressive reaction is an adaptive reaction of an individual when confronted with danger and threat. Behavioral and psychological responses accompanying depression prepare and individual to react appropriately to such situations. The Forced swim test method measures the response of an animal to unfamiliar environment. The parameters swimming, climbing and immobility are sensitive to depressive state of the animal. In present study, a significant increase is showed in swimming, climbing and immobility

The elevated plus maze is a screening test for depression properties of a compound. The fear of balancing on relatively narrow raised platform increases time spent in close arm thus proving the Antidepressant activity. The actophotometer test measures the depressive response of an animal. The locomotor score is increased in the present study, indicating the decrease in the depression of that animal. In summary, the Hydro Ethanolic Extract of *Caryota urens* produces a significant antidepressant effect as observed in many animal models like FST method, actophotometer and elevated plus maze methods. By this study, exploratory behaviors of the animals were studied by various models as described above

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