Evaluation of anti-depressant activity of *Garcinia cambogia* on experimentally induced depression in mice

Abdula Hashif[1], Prasanna Shama Khandige[1]*, Prashant Nayak[2]

[1]Department of Pharmacology, NITTE (Deemed to be university) N. G. S. M. Institute of Pharmaceutical Sciences, Paneer Campus, Deralakatte, Mangalore- 575018, India.
[2]Department of Pharmaceutics, NITTE (Deemed to be university) N. G. S. M. Institute of Pharmaceutical Sciences, Paneer Campus, Deralakatte, Mangalore- 575018, India.

ABSTRACT

Context: Depressive is a prevalent psychiatric disorder. The currently using drugs can impose a variety adverse effects including, hyperpiesia, sexual dysfunction cardiac toxicity, body weight gain, and sleep disorder.

Aim: The present study was aimed to assess the antidepressant activity of *Garcinia cambogia* plant in experimental animal mouse.

Materials and Methods: Antidepressant activity was investigated in Albino mice by using Forced swimming test (FST) and Tail suspension test (TST) models. Imipramine(10mg/kg) was used as standard drug and *Garcinia cambogia*(100, 400mg/kg) was used as test drug.

Results: *Garcinia cambogia* showed significant decrease in duration of immobility in both TST and FST models.

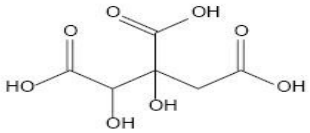
Conclusion: *Garcinia cambogia* has shown anti-depressant activity in both TST and FST models.

KEYWORDS: *Garcinia cambogia*, tail suspension test, forced swim test.

INTRODUCTION:

Depression is one of the fast growing diseases in the world. It affects all age group but more common in women. Major depression is also caused genetically. Other reasons for an individual to develop depression are combination of biological, environmental imbalance in brain chemical and psychological parameters. There are two major forms of depression they are unipolar depression in which mood swing in one direction only. The other one is bipolar depression categorized by cyclic manifestation of depression followed by mania. About 60% of the unipolar depressed cases shows symptomatology of reactive depression categorized by inconsistent feeling of unhappiness, anguish and fretfulness as a repercussion of sorrow of loved one, joblessness corporeal illness and social problems[1]. TCA where the first generation drugs for depression, which block the neuronal reuptake of norepinephrine and serotonin. The blockade occurs as soon as administering the drug there is an immediate increase in the synaptic concentration of serotonin and norepinephrine. Now- a – days SSRIs is more commonly use which block the neuronal reuptake of noradrenaline. Their efficiency in the treatment of depression supports the hypothesis that serotonin dysfunction plays important role in pathophysiology of depression [2].

The present study is an effort to evaluate the anti-depressant potential of *Garcinia cambogia* preparation. Many drugs are available for the treatment of depression. However these drugs possess severe side effects, drug interactions and show the incidences of relapses. The commonly observed major side effects of antidepressants are sedation, muscle relaxation, memory disturbance and dependency. This enhances the need to explore new drugs with less side effects and more efficacy[3]. Thus the present investigation is intended in scientifically validating the anti-depressant potential of *Garcinia cambogia*. Hydroxycitric acid (HCA) is the main constituent of *Garcinia cambogia* . A review on earlier studies conducted, revealed that HCA has been shown to increase the levels of serotonin, a neurotransmitter that influences mood, sexual desire, social behavior and appetite. Low serotonin levels are connected to depression and anxiety. As the serotonin level, mood improves. Studies on lab animals show that HCA helps to increase serotonin levels[4].



(-)-Hydroxycitric acid

Figure 1: Structure of 9(-)- hydroxycitric acid

MATERIAL AND METHODS:

Plant material and preparations:

The fruits of *Garcinia cambogia* were collected from the native place at Kerala, India during the month of August. These fruits are then shade dried and coarse powdered for extraction. This extraction is further dried and then stored in a desiccator for future use.

Experimental animals:

Mice of either sex, 4-6 weeks, weighing (20-30g) was obtained from central animal house, N-CARE, Paneer, Mangalore. The rats were appropriately grouped and then sheltered in distinct cages. The cages were kept under standard lab conditions of temperature 25 ± 2° with appropriate dark and light cycle of 12 hours. Standard food and water was freely accessed to the animals. The investigation was done in accordance to the guidelines of the CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals), New Delhi, India. And the research work was permitted and approved by the Institutional Animal Ethics Committee (**NGSMIPS/IAEC/MAY-2018/68**).

Drug treatment and acute toxicity:

Acute oral toxicity study was carried out to determine the lethal dose, i.e LD50, of the fruit extract suspension of *Garcinia cambogia*. These studies were conducted on female mice of 20 to 30g body weight by using "Up and Down Method" as per OECD 425 guidelines. The suspension of fruit extract (2000 mg/kg) was administered orally to the rats which were fasted overnight. These animals are watched once in 30 minutes interval for about 4 hours inorder to check any behavioural and neurological changes and finally till the death after 24 hours of administration[5].

Experimental design:

Albino mice of either sex weighing between 20-30g were randomly allocated into four groups.

Each group having six animals (i.e. n=6) were utilized to evaluate the anti-depressant activity. The groups of animals are summarized below:

Group I (normal control): The animals were administered with single oral dose of the vehicle on 14th day

Group ll (standard group): The animals were administered with single dose of Imipramine (10mg/kg p.o) on 14th day.

Group lll: The animals were daily administered with single oral dose of the *Garcinia cambogia* 100 mg/kg, p.o once a day for 14 days.

Group IV: The animals were administered with single oral dose of the *Garcinia cambogia* 400 mg/kg, p.o once a day for 14 days.

About 1 hour after administration of drugs, trials were carried out and antidepressant activity was assessed by using 2 models: forced swim test(FST) and tail suspension test(TST).

Tail Suspension Test (TST)

Tail suspension test is an invitro behavioral model for the immobility time. The animals were passively suspended 50cm above the floor. Tail was sticked by using adhesive tape and it is placed 1cm from tip of the tail. Immobility time (animals didn't show any movement expect lungs) was recorded during the 6 minute tail suspension test. From the total minute, the duration of immobility will be recorded for a period of 4 minutes. Immobility time of the test was compared with the standard drug [6].

Forced swim test (FST)

In both tail suspension and forced swim test not inducing depression in mice. In both experiments animals were placed in inescapable situations. The main aim of these experiments are to find out the learned helplessness by measuring out the immobility time. These experiments will help to study both acute and chronic effect of antidepressant drug. Before doing the experiment animals were trained for 24hrs in the same conditions. Swimming apparatus (height 25 cm and diameter 12 cm) filled water up to 15cm height. Mice were individually placed in the apparatus. Immobility time will be recorded for 6min in which 4 min duration will be taken [7].

Statistical analysis:

All the values are expressed as Mean ± SEM. Statistical analysis will be carried out by using ANOVA test followed by post hoc multiple comparison test using SPSS software. A P value less than 0.05 will be considered as statistically significant.

RESULTS AND DISCUSSION:

The *Garcinia cambogia* extract was subjected for toxicity studies. The extract was found to be nontoxic up to 2000mg/kg body weight given orally. The animals are found to be stable after 24 hours of drug administration. There was no mortality or any signs of toxicity. Hence, the fruit extract is found to be safe. So, for the present study, the two dose levels i.e, 100mg/kg and 400mg/kg body weight were selected.

Depression is a serious disorder which is increasing day by day. It is a neuronal disorder which is mainly affected by variations in the neurotransmitters like serotonin, dopamine, noradrenaline and 5-hydroxy tryptamine. Depression occurs irrespective of age, mainly seen in women. Suicidal tendency in depressed patients are common. Stress is one of the main reason for an individual to develop depression[8]. Several drugs are available in market today;all of these drugs have one or another side effects so it is essential to find out an alternative drug which effectively reduces depression in patients without any serious side effect[9] [10].

Imipramine is most commonly used as a standard drug which mainly act by blocking NE reuptake. In forced swim test and tail suspension test total immobility time was increased when animal was administered with imipramine. The concentration of biogenic amine in brain drastically increased due to the blocked biogenic amine reuptake. Second choice of drug which can be used as a standard drug is Fluoxetine, which act by inhibiting reuptake of 5-HT[11].
In the present study *Garcinia cambogia* was used to evaluate antidepressant activity on mice, showed significant results when compared with control group and non-significant when compared with standard group. *Garcinia cambogia* showed significant results by decreasing total immobility time. The mice were said to be immobile when it ceased all its body movement expect necessary movement. Initially mice showed vigorous movement which is reduced after 1-2 min, when the mice stay immobile from then the immobility is noted for each min for 6min. Average of each min is calculated in seconds. *Garcinia cambogia* was proved to be as capable as the standard drug Imipramine in treating depression.

Table 1: Effect of *Garcinia cambogia* on time of immobility in tail suspension test (TST) and forced swim test (FST) in mice model

Groups	Treatment	Time of immobility(s)	
		TST	FST
Group1	Control (10mg/kg)	73.33±4.68	72.83±8.09
Group II	Standard(10mg/kg)	48.16±4.97	47.33±2.70
Group III	*Garcinia cambogia*(100mg/kg)	56.66±6.68	59.5±3.76
GroupIV	*Garcinia cambogia*(400mg/kg)	50.66±5.6	49.83±3.58

The values are expressed as Mean± SEM, n=6 mice in each group. Significance $P<0.05$ compared to control

CONCLUSION:

The present study showed the anti-depressant activity of aqueous extract of *Garcinia cambogia.* In TST and FST high dose (400mg/kg) of *Garcinia cambogia* revealed as significance when it was analysed using ANOVA. From the results it was concluded that the treatment with *Garcinia cambogia* can help in reducing the duration of immobility time in rodents exposed to TST and FST. Evaluvation of *Garcinia cambogia* for CNS related activities using few more models may further justify the therapeutic benefits in the treatment of depression.

ACKNOWLEDGEMENT:

The authors are grateful to the authorities of N.G.S.M. Institute of Pharmaceutical Sciences, Mangalore for the facilities.

CONFLICT OF INTEREST:

The authors declare no conflict of interest.

REFERENCES:

[1] Jithesh M. Panchagavya Ghrita A Promising Drug in Ayurvedic Psychiatry. Asian Journal of Pharmaceutical Research and Development. 2013; 1(3):7-15.
[2] Sharma RK, Bhagwan D. Apasmara Chikitsa. In: Charaka Samhitha with Ayurveda Deepika commentary of Chakrapanidatta. Reprint ed 3. Varanasi: Chowkamba Sanskrit series. 2003. p. 453.
[3] Semwal R, Semwal D, Vermaak I, Viljoen A. A comprehensive scientific overview of Garciniacambogia. Fitoterapia. 2015;102:134-148.
[4] Heymsfield S, Allison D, Vasselli J, Pietrobelli A, Greenfield D, Nunez C. Garciniacambogia (Hydroxycitric Acid) as a Potential Antiobesity Agent. *JAMA*. 1998;280(18):1596-1598.
[5] New OECD 425 guidelines. OECD Guidelines for testing animals. 2011; 26(3):1-26.
[6] Steru L, Chermat R, Thierry B, Simon P. The tail suspension test: a new method for screening antidepressants in mice. Psychopharmacology (Berl). 1985; 85(3):367-370.
[7] Porsolt RD, Bertin A, Jalfre M. Behavioral despair in mice: A primary screening test for antidepressants. Archives Internationales de Pharmacodynamie et de Therapy 1977; 229(2):327-336.
[8] Ahemad AAE, Rashed NM, Rasheed NM. Antidepressant like activity of rosiglitazone in the rat forced swim and mice tail suspension test. Sudi pharmaceutical J 2009; 1(17):51-61.
[9] Harsat JA, Bruyene TD, Bracker JP, Vauquellin G.isoquinoline derivatives isolated from the fruit of Annona muricata as 5-HT ergic 5-HT 1A receptor agonist in rats. J pharm Pharmacol. 1997;49(11):1145-9.
[10] Hararat JA, Pieters l, Backer JPD, Vlietinck AJ. Screening of plant from suriname for 5-HT (1a) liugands: Bioactive isoquinoline alkaloid from the fruit of Annona Muricata. Phytomedicine 1997; 4(2):133-40.
[11] Manavi C, Pinki V, Gautam P. comparative evaluvation of Bacopa monniera and Panax quniquefolium in experimental and depressive models in mice. Indian J Exp Biol.2010; 48(4):306-31.

Authors:
First Author- Abdula Hashif, Department of Pharmacology, NITTE (Deemed to be university) N.G.S.M. Institute of Pharmaceutical Sciences, Paneer Campus, Deralakatte, Mangalore- 575018, India.

Second Author- Prasanna Shama Khandige, Department of Pharmacology, NITTE (Deemed to be university) N.G.S.M. Institute of Pharmaceutical Sciences, Paneer Campus, Deralakatte, Mangalore- 575018, India.

Third Author- Prashant Nayak, Department of Pharmaceutics, NITTE (Deemed to be university) N.G.S.M. Institute of Pharmaceutical Sciences, Paneer Campus, Deralakatte, Mangalore- 575018, India

Corresponding author-
Prasanna Shama Khandige

Department of Pharmacology, NITTE (Deemed to be university) N. G. S. M. Institute of Pharmaceutical Sciences, Paneer Campus, Deralakatte, Mangalore- 575018, India.