Research Article

A STUDY ON ANTI-DEPRESSANT ACTIVITY OF FRESH FRUIT JUICE OF *ACTINIDIA DELICIOSA* IN EXPERIMENTAL MICE

Muhammed muzammil*, Satish S, Praveenkumar C , Tripthi Salyan and AR Shabaraya

Department of Pharmacology, Srinivas College of Pharmacy, Valachil, Post Farangipete, Mangalore - 574143, Karnataka, India.

ABSTRACT

The present study involves evaluation of anti-depressant activity of fresh fruit juice of *Actinidia deliciosa* in experimental mice. The acute toxicity studies conducted on fresh fruit juice of *Actinidia deliciosa* was found to be non-toxic at a dose of 10ml/kg. Two doses of *Actinidia deliciosa* 1 ml/kg and 2 ml/kg of the extract and standard group of animals shows beneficial effect against depression in Tail Suspension Test, Learned Helplessness Test. Estimation of brain dopamine was carried out, both the lower (1ml/kg) and higher dose (2ml/kg) of *Actinidia deliciosa* fruit juice showed dose dependent significant decrease in depression and increase in dopamine when compared with depressive control. The result obtained was comparable with that of the standard drug Imipramine. The finding of the present study provides the evidence that the fresh fruit juice of *Actinidia deliciosa* may be beneficial against depression.

Key Words: Anti-depressant activity, *Actinidia deliciosa*, Imipramine.

INTRODUCTION

Depression is a common mental disorder characterized by sadness, loss of interest or pleasure, feelings of low self-worth, disturbed sleep and poor concentration and is considered as an affective disorder characterized by change in mood, lack of interest in the surroundings, psychomotor retardation and melancholia. Even though there are plenty of drugs developed for the management of depression, one of the challenges in dealing with this disease is that a significant portion of the patients taking antidepressants fail to attain full remission. [1]

The drawbacks of using medications such as Serotonin- Noradrenaline Reuptake Inhibitors can cause side effects. The drugs of plant origin are gaining increasing popularity due to the side effects caused by the synthetic medications and are being investigated for remedies of a number of disorders including antidepressant activity.

Number of plants being used for the treatment of depression. "*Actinidia deliciosa*" is one among them and also literature review revealed that fruits of *Actinidia deliciosa* possess antidepressant activity[2], though there is paucity of scientific data for its antidepressant activity, hence the present study was selected to investigate antidepressant activity of *Actinidia deliciosa* in mice.

PLANT PROFILE[3]

Family: Actinidiaceae
Genus : Actinidia
Species: *Actinidia deliciosa*
Botanical name: *Actinidia deliciosa*
Synonym: kiwi phal (Sanskrit), Kiwi fruit or Chinese gooseberry (English), kiwi phal (Hindi), kiwi hannu (Kannada), kedu (Marathi).

MATERIALS AND METHODS

Experimental animals

Swiss albino mice (22-25g) of either sex were procured from animal house of Srinivas college of Pharmacy Mangalore, Karnataka. They will be maintained under standard conditions (temperature 22 ± 2oC, relative humidity 50±5% and 12 h light/dark cycle).The animals were housed in sanitized polypropylene cages containing sterile paddy husk as bedding, they had free access to standard pellet diet and water.

PREPARATION OF THE FRUIT JUICE

The method of juicing includes, weighing the fresh flesh of the fruit, cut into appropriate sizes and mixed using a mixer for two minutes. Then obtained juice is refrigerated and used for the anti-depressant studies.

DETERMINATION OF ACUTE TOXICITY (LD50)[4]

The acute toxic study was carried out to determine a safe dose for fresh juice of *Actinidia delicosa*. Experimental animals were administered orally with a single dose of fresh juice of *Actinidia delicosa* at different dose levels and observed for mortality, body weight effects, and the clinical signs after the administration. For the study two dose were selected i.e, 1ml/kg as low dose and 2ml/kg as high dose.

PHARMACOLOGICAL SCREENING OF ANTI DEPRESSION

Tail suspension test (TST)[5]

The total duration of immobility induced by tail suspension was measured, as a means of evaluating potential antidepressants. Mice were suspended on the edge of a table 50 cm above the floor by the adhesive tape placed approximately 1 cm from the tip of the tail. Immobility was recorded during a 6 min period to be immobile when it did not show any movement of body and hanged passively.

Learned helplessness test[6]

Mice of either sex were placed in a compartment with steel mesh grid floor. Repeated shocks (15 sec duration, 0.8mA every min) are applied and this serves as stress to the animals. Mice are exposed for 1 hour without any escape route. Control animals are place in the chamber for 1 hour without shock. This forms the first phase of the model where animal is exposed to inescapable shock treatment. In the second phase there is conditioned avoidance training where after chronic exposure, the animal is trained. A cue (buzzer or light signal) precedes the shock and simultaneously a door opened for safe chamber, which is unelectrified, and the animal is allowed to escape towards it and avoid the noxious stimulus (electric shock). This is termed as the escape response. Failure to exhibit response by an animal is said to be an indicative of its depressive state. Antidepressants reduce escape failure.

BIOCHEMICAL PARAMETERS

Dopamine assay[7]

- To 0.02ml of the Hcl phase, 0.005 ml 0.4 ml Hcl and 0.01ml Sodium Acetate buffer (pH 6.9) was added, followed by 0.01 ml iodine solution for oxidation.
- The reaction was stopped after 2 min by the addition of 0.1ml sodium thiosulphate in 5 M Sodium hydroxide.
- 10 M Acetic acid was added 1.5 minute later. The solution was then heated to 100oC for 6 min.
- When the samples again reach room temperature, excitation and emission spectra were read (330 to 375 nm) in a spectrofluorometer.
- Compare the tissue values (fluorescence of tissue extracts minus fluorescence of tissue blank) with an internal reagent standard (fluorescence of internal reagent standard minus fluorescence of internal reagent blank).
- Tissue blanks for the assay were prepared by adding the reagents of the oxidation step in reversed order (sodium thiosulphate before iodine).
- Internal reagent standards were obtained by adding 0.005 ml bi – distilled water and 0.1 ml HclButanol to 20 ng of dopamine standard.

EVALUATION

The mice of despair swim test were sacrificed on 21st of the experiment day and estimated the dopamine level in brain.

STATISTICAL ANALYSIS

All data were expressed as Mean±SEM. The statistical significance between groups were compared using one way ANOVA, followed by Turkey (multiple comparison test).

RESULT AND DISCUSSION

Determination of acute toxicity (LD50) of *Actinidia deliciosa* fruit juice

Actinidia deliciosa was studied for acute toxicity at dose 10ml/kg by p.o. route according to OECD guideline no.425. Animals were administered with single dose of 10ml/kg and observed for its behavioural, neurological and mortality profile during two days and 14 days study period. There was no mortality amongst the dosed groups of animals and did not show

any toxicity or behavioural changes and the extract found to be safe or non-toxic in mice.

TAIL SUSPENSION TEST

In TST, on day one, mean immobility period was reduced in animals treated with imipramine 10 ml/kg as standard, fresh fruit juice of *actinidia deliciosa* at two doses 1 ml/kg and 2 ml/kg as test group also reduced compared to control group, after 21 days of administration, decrease in mean duration of immobility in all groups of animals treated with test drug was found to be statistically significant comparable to that of control group

Table 1: Effect of *Actinidia deliciosa* fruit juice in tail suspension test on mice

Dose	Duration of immobility			
	Day 1	Day 7	Day 14	Day 21
Control	211.3±0.7350	218.4±0.855	209.9±0.4900	204.8±1.370
Imipramine (10mg/kg)	123±1.555***	129.8±0.2200***	140.3±0.8500***	125.4±1.060***
Actinidia deliciosa (1ml/kg)	141.1±1.055***	128.3±0.8200***	136.8±0.2050***	136.5±0.700***
Actinidia deliciosa (2ml/kg)	130.4±0.9250***	132.3±1.145***	128.5±1.080***	136.5±0.9700***

Values are expressed as the mean ± SEM. n=6. Data were analyzed by one-way ANOVA followed by Tukey's comparision test. *p<0.05, **p<0.01, ***p<0.001, as compared to depressive control mice.

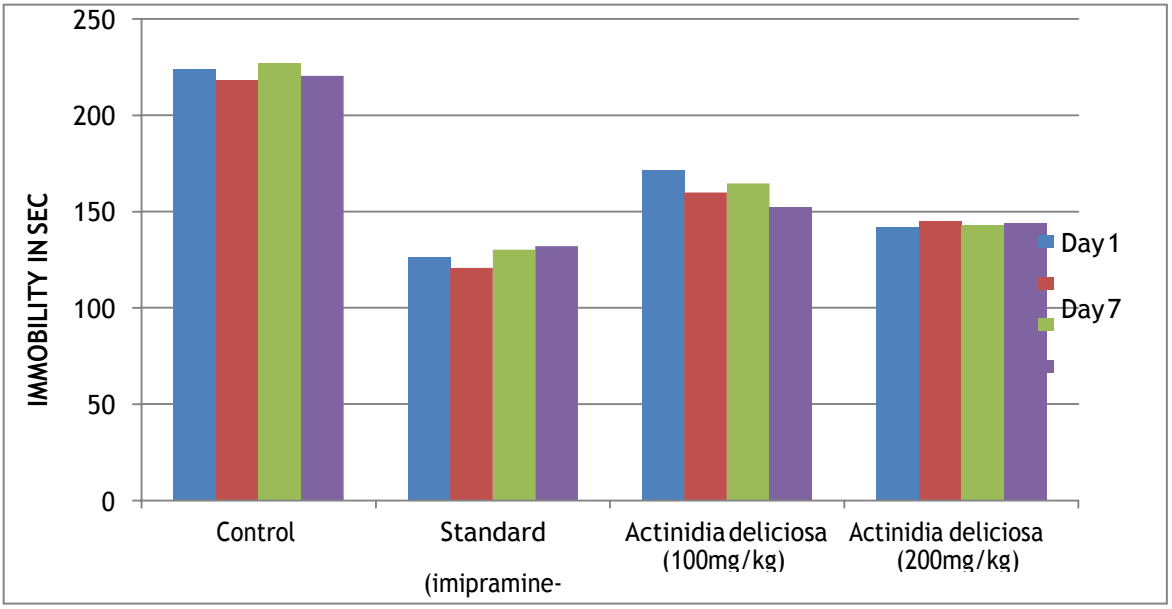

Fig. 1: Effect of *Actinidia deliciosa* fruit juice in tail suspension test on mice

LEARNED HELPLESSNESS TEST

In learned helplessness test, on day one, escape failure period was reduced in animals treated with imipramine 10 mg/kg as standard, fresh fruit juice of *actinidia deliciosa* at two doses 1 ml/kg and 2 ml/kg as test group also reduced compared to control group, after 21 days of administration, decrease in mean duration of escape failure in all groups of animals treated with test drug was found to be statistically significant comparable to that of control group. In this study, all the drug preparations were done in distilled water and administered orally once daily for 21 days. The animals were tested on 1st, 7th, 14th, and 21st day for the escape failure and escape response.

Table 2: Effect of *Actinidia deliciosa* fruit juice in learned helplessness test on mice: escape failure

Escape failure				
Dose	**Day 1**	**Day 7**	**Day 14**	**Day 21**
Control	28.85±0.3250	25.70±0.6850	25.14±0.8200	25.46±0.8950
Imipramine (10ml/kg)	21.40±0.1650***	20.78±1.115***	21.57±1.415***	21.66±0.0950***
Actinidia deliciosa (1ml/kg)	15.56±1.330***	14.22±0.6350***	18.36±0.8750***	16.14±0.1800***
Actinidia deliciosa (2ml/kg)	13.54±0.6900***	16.12±0.6650***	18.45±1.115***	18.92±0.4000***

Values are expressed as the mean ± SEM. n=6. Data were analyzed by one-way ANOVA followed by Tukey's comparision test. *p<0.05, **p<0.01, ***p<0.001, as compared to depressive control mice.

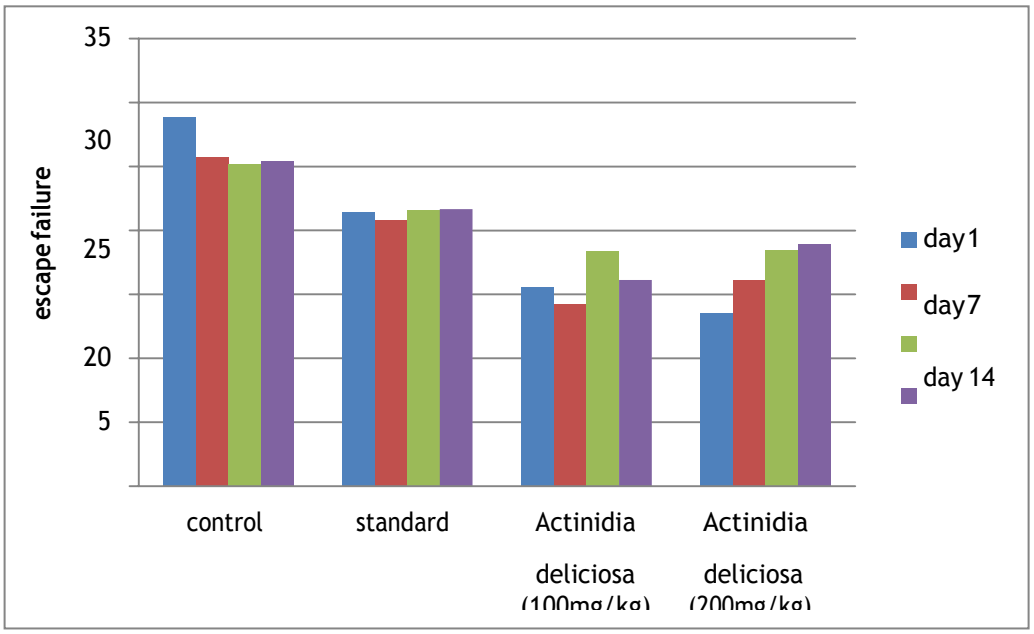

Fig. 2: Effect of *Actinidia deliciosa* fruit juice in learned helplessness test on mice: escape failure

BIOCHEMICAL PARAMETER

DOPAMINE

Dopamine assay is assessed by fluorimeter, read at 330nm-375nm. In standard treated animal dopamine level was significally increased as compared to control group, but in test treated animal lower doses does not show any significant increase but high doses increases the dopamine level significally.

Table 3: Effect of *Actinidia deliciosa* fruit juice in estimation of dopamine level in the brain of mice

Group	Dopamine concentration(µg/ml)
Control	160.9±0.075
Standard	205.4±1.820***
Low dose(1ml/kg)	149.9±2.090**
High dose(2ml/kg)	176.7±0.3240*

Values are expressed as the mean ± SEM. n=6. Data were analyzed by one-way ANOVA followed by Tukey's comparision test.
*p<0.05, **p<0.01, ***p<0.001,as compared to depressive control mice

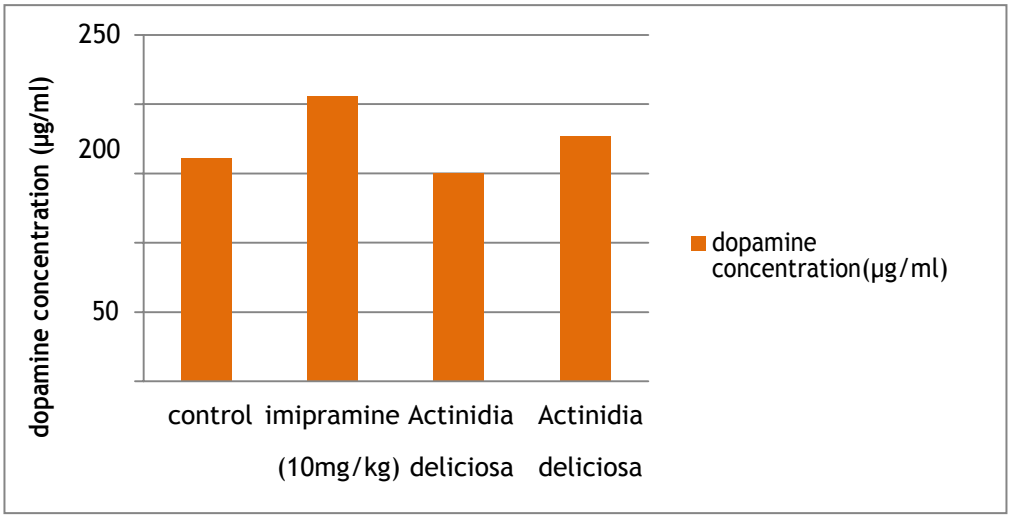

Fig. 3: Effect of *Actinidia deliciosa* fruit juice in estimation of dopamine level in the brain of mice

CONCLUSION

In the present study after analysing the data obtained from the result we conclude that the fruit juice found to have significant antidepressant activity in Tail suspension Test, Learned Helplessness test models. Biochemical tests have also supported that this fruit juice have comparable antidepressant activity without showing side effects. Thus the present study showed that fruit of *Actinidia deliciosa* possesses antidepressant activity.

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REFERENCES

1. Al- Harbi K. Treatment resistant depression therapeutic trends, challenges and future directions. Patient preference and adherence 2012; 6: 369-388.
2. Lal S, Ahmed N, Singh SR, Singh SR. Kiwi fruit: Miracle berry;Feature article science report July 2010: 52-54.
3. Rehecho S, Hidalgo O, Garcia-Iniguez de Cirano M, Navarro I,Astiasaran I, Ansorena D, et al. Chemical composition, mineral content and antioxidant activity of *Verbena officinalis* L. LWT Food Sci Tech 2011;44:875-82.
4. Cheng A.L, Hsu C.H, Lin J.K, Hsu M.M, Ho Y.F, Shen T.S, Ko J.Y. et al. Anticancer Res 2011; 21: 2895.
5. Calvo MI. Anti-inflammatory and analgesic activity of the topical preparation of *Verbena officinalis* L. J Ethnopharmacol 2006;107(3):380-2.
6. Casanova E, García-Mina JM, Calvo MI. Antioxidant and antifungal activity of *Verbena officinalis* L. leaves. Plant Foods Hum Nutr 2008;63(3):93-7.
7. Mamedov N. Adaptogenic, geriatric, stimulant and antidepressant plants of RussianFar East. J Cell Mol Bio, 2005, 4:71-75