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PHARMACOLOGICAL INVESTIGATION OF *PIPER LONGUM* FOR ANTIDEPRESSANT ACTIVITY

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ABSTRACT

The present study is undertaken with a view to investigating the probable antidepressant activity of *Piper longum* Fruits although the exact cause of depression is not known biological, genetic and environmental factors are thought to play a key role. Depression is often associated with various conditions including emotional upset (e.g., divorce, death in the family, major financial problems), co-existing medical conditions (e.g., stroke, heart attack, cancer), hormonal disorders (e.g., underactive thyroid, menopause) and problem substance use (i.e., alcohol and other drugs). Depression also often co-occurs with other mental illnesses, including bipolar disorder, schizophrenia and anxiety disorders. Whatever the trigger, it is believed that the underlying biological basis of depression is a depletion in the levels of neurotransmitters such as serotonin, norepinephrine, and/or dopamine in the central nervous system.

KEYWORDS: Antidepressant, Actophotometer test, Tail suspension Test, hydroalcoholic extract (HAE), locomotor activity, *Piper longum* Fruits.

INTRODUCTION

Although the exact cause of depression is not known, biological, genetic and environmental factors are thought to play a role. Depression is often associated with various conditions including emotional upset (e.g., divorce, death in the family, major financial problems), co-existing medical conditions (e.g., stroke, heart attack, cancer), hormonal disorders (e.g., underactive thyroid, menopause) and problem substance use (i.e., alcohol and other drugs). Depression also often co-occurs with other mental illnesses, including bipolar disorder, schizophrenia and anxiety disorders. Whatever the trigger, it is believed that the underlying

biological basis of depression is a depletion in the levels of neurotransmitters such as serotonin, norepinephrine, and/or dopamine in the central nervous system (Shalam, *et, al*.231–234).

Type of Depression

- Dysthymic disorder
- *Psychotic depression*
- *Postpartum depression*
- *Seasonal affective disorder.*

Depressions Symptoms

A person may be depressed if, for more than two weeks, he or she has felt sad, down or miserable most of the time or has lost interest or pleasure in usual activities, and has also experienced several of the signs and symptoms across at least three of the categories below.

It's important to note that everyone experiences some of these symptoms from time to time and it may not necessarily mean a person is depressed. Equally, not every person who is experiencing depression will have all of these symptoms.

Behavior

- not going out anymore
- not getting things done at work/school
- withdrawing from close family and friends
- relying on alcohol and sedatives
- not doing usually enjoyable activities
- unable to concentrate.

Feelings

- Overwhelmed
- Guilty
- Irritable
- Frustrated
- Lacking in confidence
- Unhappy
- Indecisive

- Disappointed
- Miserable
- Sad.

Thoughts

- 'I’m a failure.'
- 'It’s my fault.'
- 'Nothing good ever happens to me.'
- 'I’m worthless.'
- 'Life’s not worth living.'
- 'People would be better off without me.'

METHODS

Suspended mice by the tail with tape from the strain gauge (strain gauge is the hook connected to the vertical bar). Mice should be positioned such that the base of their tail is aligned with the bottom of the bar. Each mouse is given 1 trial that lasts 6 minutes. The total duration of immobility is calculated as the time the force of the mouse's movements is below a preset threshold.

- If a mouse climbs its tail gently pull it back down and continue the trial
- Mice that climb their tails for more than 20% of the trial (i.e. 72 seconds) will be eliminated from the final analysis.

Actophotometer Test (**Rotarod Test)**: The locomotor activity can be easily studied with the help of actophotometer, the rats were grouped and treated with drugs. Each animal was placed individually in actophotometer and the basal activity score of all the animals was recorded(. Bisht BS, *et, al*. 414-416)

- ❖ Assessment of pharmacological activity.
  - Actophotometer Test.
  - Tail suspension Test.

RESULT

Phytochemical Screening of the extract of *Piper longum fruits*

S. No.	Chemical Constituent	Test	Result
1.	Alkaloid	Mayers test	+ve
		Dragendroff test	+ve
		Wagers test	+ve
		Mayers test	+ve
2.	Carbohydrate	Mollisch's test	+ve
		Fehling test	+ve
3.	Glycoside	Modified Borntragers	+ve
		Legal test	+ve
		Baljet test	+ve
4.	Saponin	Froth test	-ve
5.	Phytosterols	Salkowaski test	+ve
6.	Tannins	Gelatin test	+ve
7.	Flavonoid	Alkaline reagent	-ve
		Lead acetate test	-ve
		Shinoda test	-ve
8.	Protein	Ninhydrin test	-ve

Antidepressant activity

Effect of on locomotor activity

It is evident from Table No.1.1, 1.2, 1.3 and Fig no.1, of locomotor activity, that the conditional avoidance response in the Control was 138.3±11.6 fluoxetine 25mg/kg, were (170.2±6.1, 180.2±5.7) and hydroalcoholic extract (HAE) of *Piper longum* fruits at 25 mg/kg, were 169.2±4.5, 176.3±4.9, respectively.

Table: 1.1 Effect of control (without administration) on locomotor activity in depressed rats using actophotometer test.

S. No.	Body weight (gms)	Activity score(sec.)
1.	168	**160**
2.	157	**128**
3.	165	**89**
4.	170	**132**
5.	180	**156**
6.	192	**165**
(Mean ± SEM)		**138.3±11.6**

Table: 1.2. Effect of fluoxetine (25 mg/kg) on locomotor activity (in sec.) in depressed rats using actophotometer test.

S. No.	Body weight	Activity score before (sec.)	Activity score After (sec.)
1.	123	163	**172**
2.	146	162	**170**
3.	160	150	**166**
4.	165	173	**178**
5.	170	181	**199**
6.	192	192	**196**
(Mean ± SEM)		170.2±6.1	**180.2±5.7**

Table: 1.3 Effect of Piperine (25 mg/kg) on locomotor activity in depressed rats using actophotometer test.

S. No.	Body weight	Activity score before(sec.)	Activity score after (sec.)
1.	139	160	**170**
2.	156	165	**172**
3.	146	156	**160**
4.	175	170	**175**
5.	181	179	**189**
6.	190	185	**192**
(Mean ± SEM)		169.2±4.5	**176.3±4.9**

Mean value of Control, Test, and Standard

S. No.	Treatment	Mean value	
		Before	After
1.	Control	138.3±11.65	
2.	Fluoxetine	170.2±6.1	180.2±5.7**
3.	Piperine	169.2±4.5	176.3±4.9*

Value are mean ± SEM (n=6) one-way anova followed by the Tukey's multiple comparison method tests where * represented significant at $p<0.05$, ** represented highly significant at $p<0.01$, *** represent very high significant at $p<0.001$ and ns represent no significant, compared to control.

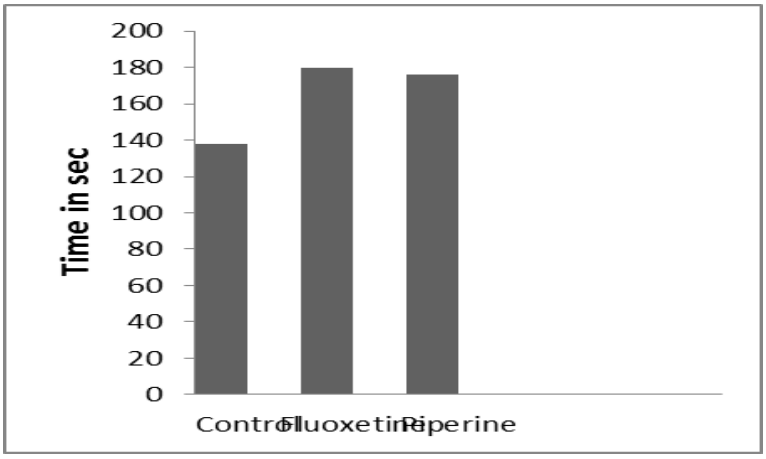

Figure. 1. X-axis Actophotometer Test comparing control, Piperine, and Fluoxetine as standard.

Effect of on Tail suspension test

It is evident from Table No.2.1, 2.2, 2.3, and Fig no.2, of, Tail suspension test, that the conditional avoidance response in the Control was 3.71±0.6, fluoxetine 25mg/kg, were (11.04±0.39, 7.3±0.74) and hydroalcoholic extract (HAE) of *Piper longum* fruits at 25 mg/kg, were 11.9±0.42, 8.5±0.72, respectively.

Table: 2.1. Effect of control (without administration) in depressed rats using Tail suspension test.

S. No.	Body weight	Activity score (sec.)
1.	130	4.34
2.	152	5.14
3.	135	2.23
4.	160	4.83
5.	192	3.66
6.	179	3.11
(Mean ± SEM)		**3.71±0.6**

Table: 2.2 Effect of fluoxetine (25 mg/kg) in depressed rats using Tail suspension test.

S. No.	Body weight	Activity score before(sec.)	Activity score after (sec.)
1.	140	10.20	5.40
2.	161	11.12	8.59
3.	139	11.23	7.51
4.	162	12.80	10.19
5.	185	10.68	5.59
6.	170	10.19	6.98
(Mean ± SEM)		**11.04±0.39**	**7.3±0.74**

Table: 2.3 Effect of piperine (25 mg/kg) in depressed rats using Tail suspension test.

S. No.	Body weight	Activity score before(sec.)	Activity score After(sec.)
1.	153	9.90	6.98
2.	146	11.23	8.03
3.	140	10.20	6.86
4.	178	11.90	10.67
5.	181	12.28	10.85
6.	182	9.98	7.89
(Mean ±SEM)		**11.9±0.42**	**8.5±0.72**

Mean value of Control, Test, and Standard

S. No.	Treatment	Mean value	
		Before	After
1	Control	3.71±0.63	
2	Fluoxitene	11.04±0.39	7.3±0.74**
3	Piperine	11.9±0.42	8.5±0.72*

Value are mean ± SEM (n=6) one-way anova followed by the Tukey's multiple comparison method tests where * represented significant at p<0.05, ** represented highly significant at p<0.01, *** represent very high significant at p<0.001 and ns represent no significant, compared to control.

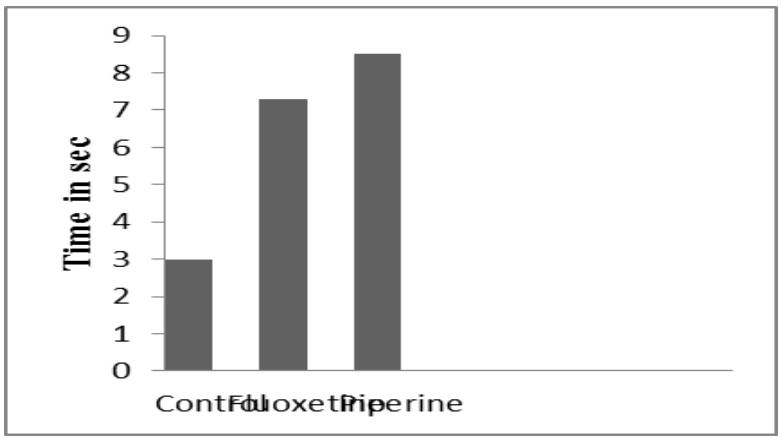

Figure 2: X-axis Tail Suspension test comparing control, Piperine and Fluoxetine with standard.

DISCUSSIONS

The natural source has a significant contribution in the modern system of medicine and herbs work synergistically with the body and without disturbing the balance. The plant Piper longum was selected for the study based on the literature survey. The fruits of the plant were extracted by Soxhlet method using ethanol.

In the present study (25 mg/kg) produced a significant antidepressant effect in (TST) Tail Suspension test and Actophotometer test. These models of depression are widely used to screen new antidepressant drugs. The tests are quite sensitive and relatively specific to all major classes of antidepressant drugs including TCAs, SSRIs, MAOI, Atypical antidepressants. TST (Tail Suspension Test) is less stressful than FST (Forced swim test) and has greater pharmacological sensitivity. In antidepressant test conditioned avoidance response was evaluated using (TST) Tail Suspension test and Actophotometer test. Latency period to be 169.2±4.5, 176.3±4, 11.9±0.42, 8.5±0.72, 16.8±0.94, 19.0±0.89 for Piper longum (25mg/kg), Fluoxetine and control groups respectively.

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