

A descriptive review on the pharmacological screening methods on antidepressant activity of different plants extracts and comparison with tea extracts (*Camellia sinensis*)

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ABSTRACT

Depression is the most common mental disorder occurring due to neurotransmitter imbalance. Antidepressants are the drugs which are used to treat neurotransmitter imbalance in depression. Antidepressants work by altering the bioamines level like norepinephrine, serotonin and dopamine neurotransmitters, which are directly related with general well being and cognitive function of brain. Various herbal remedies and dietary supplements are used to cure depression due to their CNS stimulating property. They may modulate neurotransmission through direct impact on receptors and they may also influence neurotransmitter synthesis or distribution such as GABA modulation, dopaminergic modulation. Tea (*Camellia sinensis*) contains many CNS active chemical constituents such as polyphenols, caffeine, theanine etc. among them the unique amino acids such as L-theanine, which having significant antidepressant activity in associated with very little side effect in comparison with conventional formulations. In this review work, focus was given to find the reported antidepressant activity of Tea. Then a comparison was established to find the antidepressant activity among tea and other plant on the basis of reported data. Experimental findings of common pharmacological screening methods for antidepressant activity in animal such as forced swimming test, tail suspension test and open field test etc. with its immobility and locomotion data were considered as the basis to compare the antidepressant activity. In these review it was found that Tea having a bit of better antidepressant which can be explored to substitute the known antidepressant in future.

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1. Introduction

Depression is the most common affective mental disorder, defined as disorder of mood rather than disturbances of thought or cognition. It is psychobiologic phenomena resulting from abnormal brain mechanism sign and symptoms of depression are feelings of helplessness and hopelessness, Loss of interest in daily activities, significant weight loss or weight gain, a change of more than 5% of body weight in a month.

About 5 in 100 adults have depression every year. Sometimes it is mild or lasts just a few weeks. However, an episode of depression serious enough to require treatment occurs in about 1 in 4 women and 1 in 10 men at some point in their lives. Some people have two or more episodes of depression at various times in their lives (Reynolds, 2003).

There are some conventional antidepressant drugs which are used to treat depression classified on the basis of their mechanism of action, predominantly help to fix neurotransmitter imbalance, thus reduce depressive symptoms. These are the drugs which can elevate our mood in depressive illness. Antidepressants are drugs used for the treatment of depression and other conditions including anxiety disorders, obsessive compulsive disorder, eating disorders, chronic pain, neuropathic pain and, in some cases, dysmenorrhea, snoring, migraines, attention-deficit hyperactivity disorder (ADHD), substance abuse and sleep disorders. They can be used alone or in combination with other medications. All these drugs affect monoaminergic transmissions in the brain and have other associated properties. Some herbal and natural remedies are also used to

treat depression (Richard, 2018).

To measure antidepressant action of drugs and remedies there are some pharmacological screening techniques in animal. These of pharmacological screening techniques are using full tools to compare and measure antidepressant activity with the existing drugs those having significant side effects. Hence, the need of introduction of more safe new drugs to treat depression is a challenge of today (Cryan & Mombereauet, 2004).

2. Chemical components and effects on health of tea leaves

Tea leaves contain catechins, a type of antioxidant. In a freshly picked tea leaf, catechins can give up to 30 % of the dry weight. Catechins are in the highest concentration found in white and green teas. The amounts of carbohydrates, fat, and protein found in tea are negligible. In tea plants there are various types of phenolics and tannin, but it contains no tannic acid. The tea leaves contain L-theanine, a stimulant like caffeine at about 2-4 % of its dry weight (30-90 mg per 250 g). Tea also contains small amounts of theobromine and theophylline, flavinoids, amino acids, vitamins and several polysaccharides (Juneja et al., 1999). Physiological activity of the tea components on different system are given in the table 1.

3. Tea as antidepressant

Tea have many chemical constituents but main constituents which increases the antidepressant activity are caffeine and L-theanine (Sirshendu et al., 2014; Juneja et al., 1999). The Caffeine helps to increase artificially like gamma aminobutyric acid and serotonin level to improve mental alertness, concentration, physical and cognitive ability found within 30-120 minutes after ingestion L-theanine, is another T tea constituent having stimulatory effects. It is proposed to induce tranquillity and psychological well while maintaining high levels of alertness counteract caffeine's arousing effects by lowering the body's central nervous system response. Gamma aminobutyric acid levels, which is significantly high in the mechanism of L-theanine action is suggested the key to modulate anxious consequences of cognitive overstimulation where increase an individual's speed of information processing and improving complex activities (Juneja et al., 1999).

The effects of calming in green tea may seem contradictory to the stimulatory property of tea's caffeine, but it can be explained by the action of L-theanine. This amino acid actually acts antagonistically against the stimulatory effects of caffeine on the nervous system. Research on human volunteers has demonstrated that L-theanine creates a sense of relaxation in approximately within 3040 minutes after ingestion via at least two different mechanisms. First, this amino acid directly stimulates the production of alpha brain waves, creating a state of deep relaxation and mental alertness similar to what is achieved through meditation. Second, L-theanine is involved in the formation of the inhibitory neurotransmitter, gamma amino butyric acid (GABA). GABA influences the levels of two neurotransmitters, dopamine and serotonin, producing the key factor for relaxation effect (Sadakata & Kobayishi., 1992).

4. Toxicology of L- theanine

There were no reported side effects in studies investigating L-theanine within animals. L-theanine has also shown to produce no drowsiness in humans showed studies. In some cases of cancer chemotherapy demonstrating that L-theanine enhanced the therapeutic efficacy of doxorubicin without inducing side effects (Ruxton., 2008). No consistent, statistically significant treatment-related adverse effects on the behaviour, morbidity, mortality, body weight, food consumption and efficiency, clinical chemistry, haematology, urinalysis, or gross pathology, organ weights or in histopathology were found out till date (Imrana et al., 2010).

Major advantages of antidepressant Herbal derived drug, remedies over the conventional drugs. There are a number advantages associated with using herbal medicines as opposed to pharmaceutical products. Examples include the following:

- **Reduced risk of side effects:** Most herbal medicines are well tolerated by the patient, with fewer unintended consequences than pharmaceutical drugs. Herbs typically have fewer side effects than traditional medicine, and may be safer to use over time.
- **Effectives with chronic conditions:** Herbal medicines tend to be more effective for long-standing health complaints that don't respond well to traditional medicine. One example is the herbs and alternative remedies used to treat depression. Alternative treatments for depression, on the other hand, have few side effects.
- **Lower cost:** Another advantage to herbal medicine is cost. Herbs cost much less than prescription medications. Research, testing, and marketing add considerably to the cost of prescription medicines. Herbs tend to be inexpensive compared to drugs.
- **Widespread availability:** Yet another advantage of herbal medicines is their availability. Herbs are available without a proper prescription. People can get some cultivated plants like of plant some shankhapushpi, peppermint and chamomile from nearby village at home having antidepressant action. To some remote parts of the world herbs may be the only treatment available to the majority of people in the treatment and cure of depression (Richard, 2018; Jhansi et al., 2014).

5. Pharmacological Screening Methods for Depression

The evaluation of antidepressant action of drugs, herbal components and remedies there are some pharmacological screening techniques used. These screening procedure are indexed in various types of behavioural changes observed before and after giving the drug and these also compared with the standard medicine. So need to evaluate more safe drugs and also need to find more efficacious drugs to treat depressive symptoms (Cryan & Mombereauet, 2004).

5.1. Force Swimming Test (FST)

The forced swim test is a widely used behavioral test in which the effects of antidepressant drugs and efficacy of new antidepressant compounds are tested and predicted, using rodents. An analysis of the video recording is then done for

Table 1: Activity of the components of tea on different system physiology

Components	Effect	Reference
Catechins (Astringency component)	Decreases blood cholesterol, Body fat reduction, Cancer prevention effect, Antioxidant, Tooth decay prevention, antibacterial effect, Anti-influenza effect, Inhibits high blood pressure, Anti-hyperglycemic effect, Bad breath prevention (deodorizing effect).	Sirshendu et al., 2014
Vitamins		
<i>Vitamin E</i>	Maintenance of healthy skin and mucus Membrane (collagen formation); Antioxidant	Juneja et al., 1999
<i>Vitamin B₂</i>	Maintenance of healthy skin and mucus membrane	
<i>Folic acid</i>	Prevention of fetal neural tube defects (NTD) Prevention of arterial sclerosis	
<i>β-carotene</i>	Maintenance of nighttime vision	
<i>Vitamin C</i>	Maintenance of nighttime vision	
Saponins	Lowering of blood pressure; Anti-influenza effect	Sirshendu et al., 2014
Fluorine	Prevention of tooth decay.	Harbowy, 1997
γ-aminobutyric acid (GABA)	Lowering of blood pressure.	Juneja et al; 1999)
Minerals (Potassium, calcium, phosphorus, manganese, etc.)	Biological regulators.	Harbowy, 1997
Chlorophyll	Deodorizing effect.	Sirshendu et al., 2014
Acting on CNS		
Theanine	Neuronal cell protection, Relaxation effect (promotes α wave production).	Jhansi et al., 2014
Caffeine (Bitterness component in tea)	Increases alertness, (decreases tiredness and drowsiness) Increases stamina, Hangover prevention.	Sadakata & Kobayishi, 1992

scoring the behavior, which is based on two kinds of behavior 1) active–swimming and climbing, and 2) passive–immobility.

Procedure: Animals are subjected to two trials during which they are forced to swim in an acrylic glass cylinder filled with water, and from which they cannot escape. The first trial lasts 15 minutes. Then, after 24-hours, a second trial is performed that lasts 5 minutes. The time that the test animal spends in the second trial without making any movements beyond those required to keep its head above water is measured. This immobility time is decreased by various types of antidepressants. Another common variant of this behavioural test specifically used for mice is conducted only for one trial and lasts six minutes (Petit et al., 2005).

5.2. Tail Suspension Test (TST)

The tail suspension test (TST) is an experimental method used in scientific research to measure stress in rodents. It is based on the observation that if a rat is subjected to short term inescapable stress then the rat will become immobile. It is used to measure the effectiveness of anti-depressant like agents but there is significant controversy over its interpretation and usefulness. Immobility in the TST is defined as when the animal doesn't want to put in the effort to try to escape. This represents a common symptom in depression where people who suffer from depression do not put a lot of effort into activities due to stress.

Procedure: The animal is hung from a tube by its tail for five minutes approximately 10 cm away from the ground. During this time the animal will try to escape and reach for the ground. The time it takes until it remains immobile is measured. Each animal is tested only once and out of view from the other animals. Within the study there should be two sets of rats, one group which is the control which has been injected with saline and the group being tested which has been injected with the anti-depressant like agents (Cryan & Mombereau, 2004).

5.3. Open Field Test

Open field test is developed by Calvin S. Hall, the open field test is an experimental test used to assay general locomotor activity levels, anxiety, and willingness to explore in animals (usually rodents) in scientific research.

Procedure: The open field is an arena with walls to prevent escape. Commonly, the field is marked with a grid and square crossings. The centre of the field is marked with a different color to differentiate from the other squares. In the modern open field apparatus, infrared beams or video cameras with associated software can be used to automate the assessment process.

Behavioural patterns measured in the open field test include:

- *Line crossings* – Frequency with which the rodent crosses grid lines with all four paws (a measure of locomotor activity), sometimes divided into activity near the wall and activity in the center
- *Center square entries* – Frequency with which the rodent enters the center square with all four paws
- *Center square duration* – Duration of time spent in the central square
- *Rearing* – Frequency with which the rodent stands on its hind legs in the field. Rearing-up behavior in which the forepaws of the animal are unsupported and the similar behavior in which the forepaws rest against the walls of the enclosure have different underlying genetic and neural mechanisms and unsupported rearing might be a more direct measure of anxiety.
- *Stretch attend postures* – Frequency with which rodent demonstrated forward elongation of the head and shoulders followed by retraction to the original position. High frequency indicates high levels of anxiety.
- *Defecation and urination* – The frequency of defecation and urination is controversial. Some scientists argue that

Table 2: Antidepressant activity of various plants extracts with comparison to Tea (*Camellia sinensis*) extracts using Forced Swimming Method

Test	Extracts	Treatment/Doses (mg/kg)	Data (Sec± SEM)	Animal	Reference
Forced Swimming Test	<i>Camellia sinensis</i>	400	60.00±11.5	Rat	Imrana et al., 2010.
	Imipramine	10	57.13±2.13		
	<i>Zingiber officinale</i>	400	119.10±1.11	Mice	Singh et al., 2012.
	Imipramine	10	98.00±4.5		
	<i>Baptisia tinctoria</i>	400	65.00±8.94	Rat	Richa & Kumar, 2017
	Imipramine	15	62.33±9.20		
	<i>Citrus paradisi</i>	400	114.91±3.1	Mice	Vikas et al., 2010.
	<i>Diazepam</i>	2	108.36±1.563		
	<i>Cucurbita pepo</i>	400	120.76±8.3	Rat	Umadevi et al., 2011
	Imipramine	30	110.46±2.371		
	<i>Centella asiatica</i>	400	61.34±9.4	Rat	Tomás et al., 2015
	Midazolam	1.5	49.12±1.1		
	<i>Withania Somnifera</i>	50	50.5±2.47	Mice	Bharathi et al., 2015
	Imipramine	15	27.66±2.01		
	<i>Apocynum venetum</i>	125	105.57±5.11	Mice	Veronika et al., 2001
	Imipramine	20	91.41±4.14		
	<i>Clitoria Ternatea</i>	300	58.63±10.46	Rat	Parvati et al., 2013
	Imipramine	15	65.22±8.19		
	<i>Spirulina</i>	400	71.37± 3.54	Rat	Santosh et al., 2014
	Imipramine	15	70.17±6.128		
	<i>Rosa damascena</i>	90	84.28±2.14	Mice	Hassan et al., 2017
	Imipramine	15	75.25±5.8		
	<i>Passiflora foetida</i>	300	47.67±4.58	Rat	Santosh et al., 2011
	Imipramine	15	38.5±6.27		
	<i>Moringa oleifera</i>	200	75.39± 4.23	Mice	Ginpret et al., 2015
	Fluoxetine	20	69.13±6.38		
	<i>Emblica officinalis</i>	400	67.50±5.03	Rat	Sudhakar et al., 2010
	Imipramine	10	57.33±9.81		
	<i>Holoptelea integri folia</i>	100	105.72±2.70	Mice	Ravindra et al., 2014
	Fluoxetin	10	116.13±2.05		
<i>Terminillia bellirica</i>	200	196.7±1.9	Mice	Dinesh et al., 2015	
Imipramine	15	146.6±2.2			
<i>Bauhinia variegata</i>	200	100.5±6.7	Rat	Pragati et al., 2015.	
Imipramine	15	33±2.3			
<i>Beta vulgaris</i>	400	65.34±5.4	Mice	Mihir et al., 2017.	
Fluoxethin	20	25.5±4.6			
<i>Cassia tora</i>	400	76.43±3.551	Mice	Udit et al., 2017	
Piracetam	120	45.54±2.586			
<i>Curcumin longa</i>	100	98.3 ± 16.0	Mice	Jayesh et al. 2011	
Imipramine	15	45.8 ± 9.4			
<i>Myristica fragrans</i>	500	163.0±11.7	Mice	Ghulam et al.2012	
Imipramine	15	161.6±6.1			

increase in defecation shows increased anxiety. Other scientists disagree and state that defecation and urination show signs of emotionality but cannot be assumed to be anxiety (Hall, 1932).

6. Comparative study of antidepressant activity between different plant extracts and tea (*Camellia sinensis*) extracts by using different pharmacological screening with data collection

In this study the different plant extracts and standard antidepressant drugs with different doses (mg/kg) are treated in animals such as rat /mice which give optimum and different antidepressant activities as data (sec ± SEM) indicates immobility time which are compare with data of Tea (*Camellia sinensis*) by different pharmacological screening methods such as forced swimming test, tail suspension test

and open field test. In **Table 2** shown that decrease immobility in second on different plant extracts treated mice or rat by using forced swimming test. In **Table 3** shown that decrease immobility in second on different plant extracts treated mice or rat by using tail suspension test. In **Table 4** shown that decrease in locomotor activity in second on different plant extracts treated mice or rat by using open field test which claims antidepressant activity.

Discussion

The present review study demonstrated that the tea having psychological benefits along with physiological benefits. The comparative study shows that tea extracts having significant amount of antidepressant properties in comparison with herbal plant and synthetic drug as reported in different research paper. In addition, as measured by forced

Table 3: Antidepressant activity of various plants extracts with comparison to Tea (*Camellia sinensis*) extracts using Tail Suspension Method (TST).

Test	Extracts	Treatment/ Doses (mg/kg)	Data (Sec± SEM)	Animal	Reference
Tail suspension test	<i>Camellia sinensis</i>	400	85.72 ± 4.6	Rat	Imrana et al. 2012
	Imipramine	10	78.62±2.481		
	<i>Zingiber officinale</i>	400	135.00±9.29	Mice	Singh et al.2012
	Imipramine	10	132±2.45		
	<i>Clitoria Ternatea</i>	300	79.17±8.93	Mice	Parvati et al., 2013
	Imipramine	15	76.92±6.85		
	<i>Passiflora foetida</i>	300	95.17±3.64	Mice	Santosh et al., 2011
	Fluoxetine	20	73.33±3.24		
	<i>Moringa oleifera</i>	200	187.42±6.13	Mice	Ginpret et al., 2015
	Fluoxetine	20	170±3.24		
	<i>Emblica officinalis</i>	400	161.33±03.55	Mice	Sudhakar et al., 2010.
	Imipramine	10	163.66±06.27		
	<i>Holoptelea integrifolia</i>	300	70.78±1.10	Mice	Ravindra et al., 2014
	Fluoxetine	10	71.29±1.23		
	<i>Terminillia bellirica</i>	200	221.7±5.4	Mice	Dinesh et al., 2007
	Imipramine	15	146.6±2		
	<i>Bauhinia variegata</i>	200	120.2±5.8	Rat	Pragati et al. 2015
	Imipramine	15	39.4±2.5		
	<i>Beta vulgaris</i>	400	70.54±4.7	Mice	Mihir et al., 2017
	Fluoxetine	20	48.2±3.4		
<i>Cassia tora</i>	120	89.459±12.342	Mice	Udit et al., 2017	
Piracetam	400	57.402±13.112			
<i>Curcumin longa</i>	100	69.7 ± 21.7	Mice	Jayesh et al., 2011	
Imipramine	15	64.5 ± 23.4			
<i>Myristica fragrans</i>	500	147.5±15.7	Mice	Ghulam et al., 2012	
Imipramine	15	122.1±13.1			

Table 4: Antidepressant activity of various plants extracts with comparison to Tea (*Camellia sinensis*) extracts using open Field Method.

Test	Extracts	Treatment/ Doses (mg/kg)	Data (Sec± SEM)	Animal	Reference
Open field test	<i>Camellia sinensis</i>	400	53.8 ± 3.6	Mice	Mohammad et al., 2013
	Imipramine	10	32.6 ± 4.6		
	<i>Apocynum venetum</i>	60	82±6.7	Mice	Veronika et al., 2001
	Imipramine	20	74±6.9		
	<i>Baptisia tinctoria</i>	400	58.44±7.88	Mice	Richa et al., 2017
	Imipramine	10	56.87±6.58		
	<i>Clitoria Ternatea</i>	300	234.4±25.72	Mice	Parvati et al., 2017
	diazepam	3	86.21±4.30		
	<i>Passiflora foetida</i>	300	95.17±3.64	Mice	Santosh et al., 2011
	Fluoxetine	20	73.33±3.24		
	<i>Moringa oleifera</i>	200	187.42±6.13	Mice	Ginpret et al., 2015
	Fluoxetine	20	170±3.24		
	<i>Emblica officinalis</i>	400	161.33±03.55	Mice	Sudhakar et al., 2010
	Imipramine	10	163.66±06.27		

swimming test, tail suspension test and open field tests, showed that immobility time and locomotion are diminish than comparison to other extracts of various plants, which is much higher than other antidepressant activity having plants. Tea can be considered as a moderate antidepressant herbal formulation which contains antidepressant activity having chemical constituents such as L-theanine and caffeine. As shown in the table extracts having good antidepressant activity in mice and rat than most of other antidepressant plants. Which is a good evidence for allowance of further research and modification into suitable formulation for human administration. The comparative study of anti-depres-

-sant activity between different plant extracts and tea extracts by using different pharmacological screening data shows- In table 2 in experiment of forced swimming method, the study gives that tea has lower antidepressant activity than *Withania Somnifera*, *Passiflora foetida*, *Clitoria Ternatea* but has greater activity than *Zingiber officinale*, *Baptisia tinctoria*, *Citrus paradise*, *Cucurbita pepo*, *Centella asiatica*, *Apocynum venetum*, *Spirulina*, *Rosa damascene*, *Moringa oleifera*, *Emblica officinalis*, *Holoptelea integri folia*, *Terminillia bellirica*, *Bauhinia variegata*, *Beta vulgaris*, *Cassia tora*, *Curcumin*, *Myristica fragrans*.

In **Table 3** using animal model of tail suspension method, the study gives that tea has lower antidepressant activity than *Clitoria Ternatea*, *Holoptelea integrifolia*, *Curcumin longa*, *Beta vulgaris* and has greater antidepressant activity than *Zingiber officinale*, *Passiflora foetida*, *Moringa oleifera*, *Embllica officinalis*, *Terminillia bellirica*, *Bauhinia variegata*, *Myristica fragrans*, *Cassia tora*.

In **Table 3** under open field method, the study gives that the tea has greater antidepressant activity than *Embllica officinalis*, *Moringa oleifera*, *Passiflora foetida*, *Clitoria Ternatea*, *Apocynum venetum*, *Baptisia tinctoria*.

Conclusion

Depression is a major issue which is found to be increasing among total individual of the world. This disease gradually reduce our mental ability and focus on any work. Today many herbal treatments were used for reduced the depression. In this study with some suitable pharmacological screening methods are use to evaluate antidepressant activity of various plants perform by various researchers. Different extracts of plants are comparing with tea by pharmacological screening methods to determine antidepressant activity. This conclusive study shows tea having some chemical constituents which have promising antidepressant activity. Tea (*Camellia sinensis*) reported for having higher antidepressant activity than various plants, which have shown significant results in different experimental work on depression. Tea having lower toxicity than any other antidepressant plants as found in the literature review of this work. After completion of this review work we can conclude that tea may be applied as natural adjuvant in depression. Further research work can only establish this hypothesis fruitfully and may be establish a new approaches treatment in depression.

Conflict of Interest

No conflict of interest.

Reference

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