

Pharmacological screening of neurocognitive activity found in different plants and its comparison with tea: A descriptive review

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ABSTRACT

Neurocognitive functions are cognitive functions closely linked to the function of particular areas, neural pathways, or cortical networks in the brain substrate layers of neurological matrix at the cellular molecular level. A neurocognitive deficit is a reduction or impairment of cognitive function in the mental/ brain areas, but particularly when physical changes can be seen to have occurred in the brain, such as after neurological illness, mental illness, drug use, or brain injury. Tea is one of the most ancient and popular therapeutic beverages consumed around the world and reported to contain thousands of bioactive ingredients such as polyphenols, catechins, caffeine, amino acids etc. which plays a key role in prevention and treatment of many diseases. Consistent with abundant research on the benefits of caffeine, the performance benefits of tea were identified in a number of studies, with particularly consistent evidence for improved attention. Tea consumption also consistently improved self-reported alertness and arousal, whereas effects on pleasure or relaxation were less consistent. This review summarizes the research on the effects of tea and its ingredients like L-theanine, caffeine etc. on attention and behaviour in experimental animal. These data were compared with the reported plant extracts having neurocognitive effect already shown in experimental animals. Suitable experimental neuro-behavioural animal models mainly elevated plus maze test, zero maze test, open field test etc. were considered to be the basis of this comparative study. From the findings of the review it was revealed out that Tea has shown to be a better alternative in the therapy of neurocognition.

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1. Introduction

1.1. What is Cognition?

Cognition is "the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses". It encompasses processes such as knowledge, attention, memory and working memory, judgment and evaluation, reasoning and "computation", problem solving and decision making, comprehension and production of language. Human cognition is conscious and unconscious, concrete or abstract, as well as intuitive and conceptual. Cognitive processes use existing knowledge and generate new knowledge. Cognition has a physical basis in the brain with over 100 billion nerve cells in a healthy human brain. Each of these can have up to 10,000 connections with other nerve cells called neurons. All of this makes it an incredibly complicated organ.

1.2 What role does cognition have?

Cognition fundamentally controls our thoughts and behaviours and these are regulated by discrete brain circuits which are underpinned by a number of neurotransmitter systems. There are a number of brain chemicals which play major roles in regulating cognitive processes; including dopamine, noradrenaline (norepinephrine), serotonin, acetylcholine, glutamate and GABA (Mestry et al., 2016) In order to better understand what drives certain behaviours, in both healthy and disease states, it is important to consider cognition and the underlying neurobiology that underpins these behaviours. Our distinct cognitive functions arise because of processes occurring within certain parts of our brain, but only some of these, end up entering our conscious awareness (Joseph et al., 2015).

1.3. What Causes A Cognitive Disorder?

Like most mental disorders, cognitive disorders are caused by a variety of factors. Some are due to hormonal imbalances in the womb, others to genetic predisposition and still others to environmental factors. Common environmental causes of cognitive disorders include a lack of proper nutrients and interaction during vulnerable stages of cognitive development, particularly during infancy. Other common causes of cognitive disorder include substance abuse and physical injury (Dade et al., 2016).

1.4. What Are The Signs of Cognitive Disorder?

Cognitive disorder signs vary according to the particular disorder, but some common signs and symptoms overlap in most disorders. Some of the most common signs of cognitive disorder include:

- *Confusion*: The state of being bewildered or unclear in one's mind about something.
- *Poor motor coordination*: coordination problems, poor balance
- *Loss of short-term or long-term memory*: impaired ability to form new episodic memories.
- *Identity confusion*: failure to achieve ego identity during adolescence
- *Impaired judgment*: failure of judgement or rational choice

Some cognitive disorders develop in stages and symptoms increase in severity the further the disease progresses. They may have rare moments of clarity, but life is generally lived in a state of confusion (Shah et al., 2013).

1.5. Types of Cognitive Disorder

Neurocognitive disorders (NCDs), also known as cognitive disorders, are a category of mental health disorders that primarily affect cognitive abilities including learning, memory, perception, and problem solving (Simpson, 2014). The Cognitive disorders are categorised as-

1. Alzheimer's disease
2. Creutzfeldt-Jakob disease
3. Dementia with Lewy bodies
4. Frontotemporal dementia
5. Parkinson's disease
6. Huntington's disease
7. Mixed dementia
8. Normal pressure hydrocephalus.
9. Wernicke - Korsakoff syndrome.

1.6. Herbal Therapy of Cognition

Cognition and memory are two of the most vital processes carried out in the brain (Fernandes, 2014). To carry out our daily activities, to be able to learn and earn a livelihood one has to have a normal memory and cognitive function. Several factors such as age, mental stress, history of anxiety or depression, coping abilities etc decide the severity of the diseases and its outcome. There are some medicines for treating such problems, but these drugs are not always useful. However, you can help these drugs.

1.6.1. Vinpocetine (*Catharanthus roseus*)

This is a nutritional supplement made from the herb periwinkle. It has been found to be quite useful in improving memory and cognitive functions. In laboratory experiments this herbal product has shown that it can dilate blood vessels, enhance blood circulation in the brain and improve its oxygen utilization. It also makes red blood cells more elastic. It is now proved that vinpocetine can increase the blood flow to the brain. Owing to this and the fact that red blood cells become more pliable the flow of oxygen to the brain increases by an appreciable amount. This increases the energy produced in the brain cells.

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1.6.2. Sage (*Salvia officinalis*)

This is a herb of the mint family. It is said to act on the cortex of the brain. It can help you to cope with mental exhaustion and improve concentration. Sage is known as a memory enhancer. It also protects the brain against some chemical processes which cause memory loss as experienced in people suffering from dementia or alzheimers. It protects acetylcholine, the brain messenger. This chemical is also necessary in production of new brain cells.

1.6.3. Basil (*Ocimum basilum*)

Basil leaves are known to help in coping with mental fatigue, improve focus, enhance clarity of thought, and control emotions. Two to three leaves of basil plant taken daily can be quite beneficial for memory and cognitive problems.

1.6.4. Rosemary (*Rosemarinus officinalis*)

This herb supports the nervous system, the circulatory system in the brain, and helps in improvement of memory. The effect on memory is supposed to be due to the boost in blood flow to the brain.

1.6.5. Gotu Kola (*Centella asiatica*)

This herb has been used in India traditionally for thousands of years specifically to improve brain function. It improves blood circulation in the brain. Improved blood circulation brings more oxygen to the brain which enhances the production of acetylcholine and helps in increasing memory.

1.6.6. Ginkgo Biloba (*Ginkgo biloba*)

This may well be the best herb ever found for memory enhancement. In clinical studies this herb has even been seen to reduce the intensity of alzheimers and dementia. The work-

Table 1: Neurocognitive activity of various plants extracts with comparison to tea extracts using Elevated plus maze Test method.

Test	Extracts	Treatment/ Doses (mg/kg)	Data (Sec± SEM)	Animal	Reference
Elevated Plus Maze Test	<i>Camellia sinensis</i>	350	15.4 ± 1.4	Rat	Mancinia et al., 2017.
	Scopolamine	15	19.25 ± 2.16		
	<i>Catharanthus roseus</i>	350	16.50±2.5	Rat	Cai et al., 2012.
	Scopolamine	15	19.10±1.10		
	<i>Salvia officinalis</i>	350	14.00±5.94	Rat	Lopresti, 2017.
	Scopolamine	15	18.33±8.20		
	<i>Ocimum basilum</i>	300	14.91±3.1	Rat	Sen, 1993.
	Diazepam	1.5	16.36±1.5		
	<i>Rosmarinus officinalis</i>	350	15.76±8.3	Rat	Calabrese et al., 2008
	Scopolamine	15	12.46±2.3		
	<i>Centella asiatica</i>	350	17.34±9.4	Rat	Tiwari et al., 2011
	Diazepam	1.5	19.12±3.2		
	<i>Ginko biloba</i>	300	20.5±2.47	Rat	Gaby, 1996
	Scopolamine	15	17.66±2.01		
	<i>Vitis vinifera</i>	300	14.57±5.11	Rat	Dhingra & Kumar, 2012
	Diazepam	2	15.41±4.14		
	<i>Bacopa monnieri</i>	350	13.45±3.24	Rat	Al-Snafi, 2013
	Diazepam	1.5	15.21±4.14		

-ing of this herb is similar to gotu kola. It increases the cerebral blood flow specifically in the areas of cerebellum. It enhances availability of oxygen in the whole of vascular system including the brain.

1.6.7. Grape Vine (*Vitis vinifera*)

When the brain cells are under attack from free radicals you need antioxidants to protect the tender cells. Grape vine is a herb whose seeds are high-grade antioxidants.

1.6.8. Brahmi (*Bacopa monnieri*)

The alcoholic extract of *Bacopa monnieri* improved acquisition, consolidation, and retention of memory in a foot shock-motivated brightness-discrimination test and a conditioned-avoidance test in rats. Bacosides A and B (a mixture of two saponins) may be responsible for its promoting effect on learning and memory.

1.7. Tea and Attention

According to the American Psychological Association, attention is “a state of focused awareness on a subset of the available perceptual information.” Attention allows the brain to effectively deal with the vast amount of input that is continuously received through its sensory (eg, vision, hearing) and cognitive (eg, memory) processes and to focus on what is relevant. As such, attention is an important prerequisite for many cognitive processes, including memory and reasoning. Attention can be measured objectively as performance on attention tests, usually in terms of speed of response and number of correct responses, or subjectively as self-reported alertness, usually by means of a visual analog rating scale (Eino & Martens, 2013).

1.7.1. Effects of Tea Ingredients on Attention

Tea contains a large number of bioactive compounds, yet its attention benefits have generally been attributed to 2 of its components: caffeine and theanine. Typically, a cup of tea contains 35–61 mg caffeine and 4.5–22.5 mg theanine. Other ingredients in tea, such as the green tea polyphenol, epigallo-

-catechin-3gallate (EGCG), have been ascribed certain neuroprotective effects, but acute effects on performance measures have not been found (Juneja et al., 1999).

Caffeine is known to affect neurotransmission in general by antagonizing (ie, competing with) adenosine receptors. When adenosine binds to its receptors in the brain, primarily A1 and A2a receptors, neural activity slows down. However, when caffeine binds instead to these receptors it causes a general increase in neurotransmission. As such, caffeine attenuates the inhibitory effects of adenosine in the brain. As an adenosine antagonist, caffeine also affects the dopaminergic system, which is involved in arousal and higher-order attentional processes (Nobre et al., 2013).

1.8. Tea and Mood

The influence of food and beverage consumption on mood has been (and still is) widely researched. Mood refers to a state of mind ranging from increased happiness, contentment, relaxation, alertness and energy, and relief of depression and anxiety to feelings of guilt and failure. The consumption of tea, both black and green, has been associated with relaxation and refreshment and feelings of satisfaction. These putative benefits may be the result of the interaction of a number of elements, including the hot temperature at which tea is consumed, its sensory properties and its active ingredients, which exert effects at different times during and after tea consumption. In the studies summarized below, the effects of tea or tea ingredients on mood have been investigated by using various validated scales with self-reports. These include facets of mood related to arousal and relaxation, as well as aspects related to the pleasantness of mood. In addition, particular changes in mood related to arousal and alertness can also be determined with physiologic measures, for example, blood pressure and skin conductance (Appleton & Rogers, 2004; Graham, 1992).

1.8.1. Effects of Tea Ingredients on Mood

Caffeine is well known for its effects on feelings of arousal

Table 2: Neurocognitive activity of various plants extracts with comparison to tea extracts using Zero Maze method.

Test	Extracts	Treatment/ Doses (mg/kg)	Data (Sec ± SEM)	Animal	Reference
Zero Maze Test	<i>Camellia sinensis</i>	100	12.72 ± 3.6	Mice	Mancinia et al., 2017
	Diazepam	1	13.62±2.4		
	<i>Catharanthus roseus</i>	150	14.00±7.29	Mice	Cai et al., 2012
	Diazepam		12±2.45		
	<i>Salvia officinalis</i>	150	18.17±9.93	Mice	Lopresti, 2017
	Diazepam	1	15.92±6.85		
	<i>Ocimum basilum</i>	200	17.17±3.64	Mice	Sen, 1993
	Diazepam	1.5	16.33±3.24		
	<i>Rosmarinus officinalis</i>	150	14.42±7.13	Mice	Calabrese et al., 2008
	Scopolamine	20	16.42±3.24		
	<i>Centella asiatica</i>	150	19.33±2.55	Mice	Tiwari et al., 2011
	Diazepam	1	14.66±5.27		
	<i>Ginko biloba</i>	200	12.78±1.10	Mice	Gaby, 1996.
Diazepam	1.5	16.29±1.23			
<i>Vitis vinifera</i>	200	15.7±5.4	Mice	Dhingra & Kumar, 2012	
Scopolamine	15	18.6±2.5			
<i>Bacopa monnieri</i>	150	12.45±4.57	Mice	Al-Snafi et al., 2013	
Diazepam	1.5	14.21±5.23			

Table 3: Neurocognitive activity of various plants extracts with comparison to tea extracts using Open Field method.

Test	Extracts	Treatment/ Doses (mg/kg)	Data (Sec ± SEM)	Animal	Reference
Open field test	<i>Camellia sinensis</i>	300	48.82 ± 4.64	Mice	Mancinia et al., 2017
	Piracetam	2	59.6 ± 5.62		
	<i>Catharanthus roseus</i>	300	64.14±5.7	Mice	Cai et al., 2012
	Piracetam	2	72.12±6.9		
	<i>Salvia officinalis</i>	250	58.44±6.49	Mice	Lopresti, 2017
	Aniracetam	2.5	56.87±5.41		
	<i>Ocimum basilum</i>	300	98.4±9.84	Mice	Sen, 1993
	Diazepam	1.5	84.21±6.62		
	<i>Rosmarinus officinalis</i>	300	82.17±3.17	Mice	Calabrese, 2008
	Piracetam	20	73.33±3.24		
	<i>Centella asiatica</i>	250	87.42±7.15	Mice	Tiwari et al., 2011
	Diazepam	1.5	71.28±3.47		
	<i>Ginko biloba</i>	300	64.33±3.52	Mice	Gaby, 1996
scopolamine	10	65.46±6.27			
<i>Vitis vinifera</i>	300	87.31±5.83	Mice	Dhingra & Kumar, 2012	
Diazepam	1.5	63.12±5.72			
<i>Bacopa monnieri</i>	250	41.45±7.31	Mice	Al-Snaf, 2013	
Piracetam	2	65.21±4.14			

energy, and alertness even at doses as low as 50 mg, which is comparable to the amount of caffeine in a cup of tea. In addition, a number of studies also found improved hedonic tone, happiness and calmness, and contentment after caffeine consumption. The number of studies on the effects of theanine in relation to mood is limited (Nehlig, 2010).

1.9. Pharmacological screening method of cognition

Pharmacological methods are the types of method that are used in experimental animal to determine the various types of pharmacological activity. The pharmacological method used

in determining neurocognitive activity are categorised as-

1.9.1. Zero Maze Test

Zero maze for testing anxiety like behaviours. The zero maze is elevated approximately 18 inch above the floor, and it consists of two open and two closed areas. Mice are permitted free exploration of the maze for 5 min. Illumination of the maze is critical and should be between 40 to 60 lux. Anxious mice remain in the closed areas and do not venture onto the open areas of the maze. The percent time spent in the open areas is taken as an index of anxiety in the mouse (Shepherd et al., 1992).

1.9.2. Sucrose solution Consumption Test

The test was done according to the method recorded in the document in a quiet room 72 hrs before each open-field test. Before the test, the rats were trained to adapt to drinking water that was supplemented with sugar. Two bottles were placed in every cage. In the first 24 hrs both bottles were filled with 1% sucrose solution, and over the next 24 hrs, one of the bottles was filled with 1% sucrose solution, and the other was filled with pure water. Then the basic energy expenditure test and water consumption test were measured after 24 hrs of food and water deprivation. Meanwhile, the rats were given 2 bottles of liquid that had first been weighed. One of the bottles was filled with 1% sucrose solution, and the other with pure water. At 60 min later, both bottles were weighed. Then the total liquid consumed and the percentage sucrose consumed were calculated (Henningsen et al., 2009)

1.9.3. Open Field Test

The open maintained field test (OFT) is an experiment used to assay general locomotor activity levels and anxiety in rodents in scientific research and willingness to explore in rodents. However, the extent to which behaviour in the open field measures anxiety is controversial (Stanford, 2007).

1.9.4. Elevated Plus Maze Test

The test apparatus consisted of two enclosed arms (length 30 cm × width 5 cm × height 15 cm), two open arms (length 30 cm × width 5 cm), and a central platform (5 cm × 5 cm). The maze was elevated 45 cm above the floor level. Mice were placed individually into the center of the maze, facing one of the open arms. The number of open arms entries and the time spent in the enclosed and open arms were recorded for 5 min with a video camera. Increased activity in the open arms was indicative of less anxiety. Entry into an arm was defined when mice placed all four feet into the arm. The maze was cleaned with 10% ethanol solution after each test (Boccia, 1998).

1.9.5. Fear Conditioning Test

Fear conditioning, a fearful experience establishes a memory that can result in long-term behavioural changes. On the first day, mice are placed into a chamber and conditioned with a tone paired with foot shock. On the second day, the mice are returned to the chamber, and the incidences of freezing are examined in the absence of tone and foot shock (context test). Alternatively, the mice can be placed in a novel chamber, and freezing behaviour is noted following the presentation of the tone without foot shock (cued test). In both tests, immobility or freezing behaviour is scored (Pezze, 2004).

2. Comparative study of Neurocognitive activity between different plant extracts and tea extracts by using suitable animal model

Comparative study is a study in which a participant is randomly assigned to one of two or more different treatment groups for purposes of comparing the effects of the treatments. In this study the different plant extracts and standard cognition enhancing drugs with different doses (mg/kg) are treated in animals such as rat /mice which give optimum and different neurocognitive activities as data

(sec ± SEM) indicates immobility time which are compare with data of tea (*Camellia sinensis*) by different pharmacological screening methods such as Elevated plus maze test, Zero maze test and Open field test. Which are described as follows in **table no 1,2 & 3**.

3. Discussion

In the comparative study various pharmacological screening method are used mainly elevated plus maze test, zero maze test and open field test are used for determining the neurocognitive activity in experimental animal.

In elevated plus maze test *Camellia sinensis* and *Bacopa monnieri* showed the effective result than the *Catharanthus roseus*, *Salvia officinalis*, *Ocimum bacillum*, *Rosemarinus officinalis*, *Centella asiatica*, *Ginko biloba*, and *Vitis vinifera*. *Camellia sinensis* and *Bacopa monieri* was found to be in range (12-15) and in the other plants it was found in the range of (17-20).

In zero maze test use of *Camellia sinensis* and *Bacopa monnieri* showed the effective result in comparison with *Catharanthus roseus*, *Salvia officinalis*, *Ocimum bacillum*, *Rosemarinus officinalis*, *Centella asiatica*, *Ginko biloba*, and *Vitis vinifera*. *Camellia sinensis* and *Bacopa monieri* was found to be in range of units (12.4-12.8) and in the other plants it was found in the range of units (13-20).

In open field test *Camellia sinensis*, *Catharantus roseus* and *Bocopa monnieri* showed the excellent result in albino mice in comparison with *Salvia officinalis*, *Ocimum bacillum*, *Rosemarinus officinalis*, *Centella asiatica*, *Ginko biloba*, and *Vitis vinifera*. *Camellia sinensis*, *Catharantus roseus* and *Bacopa monieri* was found to be in range (41-48) and in the other plants it was found in the range of units (55-98).

4. Conclusion:

In this review work related to the comparative observation on neurocognition, effect of tea (*Camellia sinensis*) and other natural cognitive enhancing agent were compared in respect to different pharmacological screening animal models. It was found that tea have significant neurocognitive activity. Therefore, tea can be used as an easily available alternative in cognitive enhancement therapy in future. It may be a replacement for other neurocognitive agent in the treatment of cognition deficient disease like dementia and Alzheimer's disease. May be use as beverage supplement with conventional therapy and can reduce or minimise the side effects by reducing the dose of conventional drug in neurocognitive disorder.

Conflict of Interest

The authors report no conflict of interest.

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