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Review On Nutritional, Medicinal and CNS Activities of Tulsi *(Ocimum. Sanctum)*

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Abstract:

Natural herbs have always been a part of Indian tradition as well as in developing countries around the world. Several studies using herbal extracts have shown significant potential as psychotherapeutics and psychiatric pharmaceuticals. One such herbal drug is Tulsi, which is indigenous to the Indian subcontinent and vastly used in Ayurveda and Siddha medical systems. Invitro studies have been performed to determine the adaptogenic, anti-inflammatory, cardioprotective, anti-microbial and immunomodulatory effects though clinical efficacy and safety studies are still underway. An extensive literature review was performed to identify the possible effects of Tulsi on the CNS. Recent research has been carried out on Tulsi for its CNS effects including anti-stress, anti-Alzheimer, anti-depressant, anti-anxiety, anti-epileptic, anti-oxidant activity. Databases included in this article involved articles from books, theses, electronic databases Google Scholar, Medline, PubMed, Science Direct, and Indian Medical databases from the past five years of research. All the studies have reported favourable outcomes with very few adverse effects reports. Further studies are yet to be carried out to determine its exact mechanisms, dosage forms and to identify which type of population is more likely to avail the therapeutic benefits of Tulsi. This review has identified and compiled the traditional herbal approach of utilizing Tulsi in CNS disorders.

Keywords: Tulsi, CNS disorder, In-vitro, adverse effects, mechanisms

INTRODUCTION:

The Tulsi plant belongs to small family ***Lamiaceae*** and the botanical name is ***Ocimum sanctum*** [1,2]. Tulsi is also called ''Queen of herb'', the one which possesses a large number of medicinal properties in herbal drugs[3]. There are two types of Tulsi – Green (Ram Tulsi) and Black (Krishna Tulsi) and both are having nearly the same characteristics[4,5]. Different kinds of species are enclosed in the Genus *Ocimum*, for instance, *Ocimum Sanctum*, *Ocimum. canum* (Dulal Tulsi), *Ocimum. kilimandschricum*, *Ocimum gratissimum* (Ram Tulsi) *Ocimum. americanum*, *Ocimum. Camphora*, *Ocimum. bascilicum* (Ban Tulsi) and *Ocimum. micranthu*[6, 7]. Tulsi is an excellent herbal medicine, which has been used for five thousand years as it produces an immediate effect on most of the diseases in India. Some of the active constituents of Tulsi gives quick relief, while other active constituents of Tulsi takes a certain time to heal the diseases. It also relaxes the body and boosts up the energy in the body[8]. Tulsi slows down the activity of enzyme, Acetylcholinesterase because it develops a fault against the acetylcholine neurotransmitter. Acetylcholine is liable for memory, sustaining sleep, promoting Rapid Eye Movement sleep (REM). Therefore, Tulsi has the ability to increase the level of acetylcholine neurotransmission to develop memory and cognitive function in the brain[7].

O. bascilicum minimizes the inflammation, reduces the noxious effect of free radicals and also protects the nerves and tissues; hence it is recognized as a good anti-inflammatory and antioxidant drug. They enhance the elimination of the mucous layer and phlegm from the bronchial tube[9]. As mentioned above, this herbal drug possesses a greater extent of medicinal properties against various diseases for example Asthma, bacterial and viral infection, cancer, convulsions, hyperlipidemia, CVS disorder, hypertension, stress, anxiety, depression, Alzheimer's diseases, and hepatotoxicity etc.[4,5]. Furthermore, Tulsi leaves show protective action for coughs, bronchitis, skin diseases, diarrhea, cholera, influenza and malaria and therapeutic action of Tulsi seeds for curing ulcers, emesis, tiredness and it achieves as an overall tonic. Tulsi (*Ocimum tenuiflorum*) extract is also utilizing for synthesizing Ag nanoparticles with glucose as a capping agent[10, 11].

ORIGIN, DISTRIBUTION, AND MORPHOLOGY:

Structural description of Ocimum sanctum

O.sanctum is straight, a branched shrub that develops up to 30- 60cm in height. The morphology of Tulsi has distinguished as its height is about 30-60cm with the structure of branched fragmented shrub. Their leaves are arranged in the plain, odoriferous, branched, incompatible, thick, and oval-shaped, moreover, they are arranged with dentate margins. Flowers are purple in color and are elongated. Fruits are moderate and seeds are radish yellow in colour[12, 13 6, 12]. After the rainy season it will be seeded and harvested[14 13].

Horticulture

Holy basil raises in equatorial along with warm regions and it is circulated as well as cultivated throughout the country, especially in India. The ancient Ayurveda literature says that it is cultivated nearly 1800m over the sea level and usually grows in moist soil[6,13]. It initiates from the Himalayas to Andaman and Nicobar islands, but it is broadly distributed in few sectors of Asia including Africa [14]. Predominantly, OS develops in moist soil and based upon the pattern of soil and differences in the rainfall, size form and therapeutic property of the plant are considered[15].

Chemical properties

The Ocimum sanctum leaf contains essential or volatile oil, which carries phenols, terpenes, and aldehydes and

hence it has a particular aromatic odor. The fixed oil is extracted from seeds, which is the composition of fatty acids. Likewise, Alkaloids, saponins, tannins, and glycosides are involved in the plant and leaves contain ascorbic acid and carotene too. Because of edaphic and geographic factors, the chemical constituents get varied[1].

Phytoconstituents

0.7% of volatile oil which is present in Ocimum sanctum leaves carriescarvacrol and sesquiterpene hydrocarbon caryophyllene which consists of around 71% eugenol and 20% methyl eugenol. Few phenolic compounds like, rosameric acid,circimaritin, cirsilineol, isothymusin apigenin andappreciable quantities of eugenol are obtained through the fresh leaves alwith aitha stem of *Ocimum sanctum*. As well as Ursolic acid, apigenin-7-O-glucuronide, apigenin, orientin, luteolin-7-O glucuronide, luteolin and molludistin are isolated along with that orientin and vicenin flavonoids are also isolated. This plant also holds a certain amount of monoterpenes and sesquiterpenes such as-elements, neral, - and-pinenes, sitosterol, bornyl acetate, camphene,cholesterol, campesterol, stigmasterol[16,17].

MEDICINAL AND PHARMACOLOGICAL PROPERTIES:

Anti-stress activity:

Stress is a very common disorder, where most of the individuals are suffering frequently[28]. It is described as psychological, physiological, and behavioral responses by individuals when they receive a deficiency in equilibrium between their inadequacies and their ability to quench those inadequacies[29]. Stress reacts due to the lack of amount of neurotransmitters such as dopamine, norepinephrine, and serotonin[30]. The previous studies say that Ocimum sanctum leaves produce protective action against the stress activity by enhancing the serotonin level in the brain[30]. Tulsi is an effective herb and gives a calming effect, especially when it takes twice a day[30,31]. Both acute and chronic noise stress, which is stimulated by the plasma level of stress hormone cortisone prevented by the extraction of Tulsi leaves[28]. And this effect is confirmed by performing the animal experiment or by animal research. When stress occurs at a high level, it gives noxious effect to the body and raises a variety of disorders such as psychiatric disorder, immune suppression, peptic ulcer, and hypertension and ulcerative colitis; hence it is very necessary to be cured. Stress can affect physical or physiological. Tulsi improves memory power and also improves survival time during anoxic stress, meanwhile reduces hypoxia too[28, 32, 33].

There are different kinds of stress like:

Toxicant stress: chemicals, heavy metals, and radiation.

Due to the experimental studies, it has been proved Tulsi has the ability to prevent the toxicant effects, which causes genetic, immune and cellular damage[34]. Tulsi protects against numerous industrial chemicals, pharmaceutical drugs, heavy metals and also protects against the toxic effects of radiation[34]. Holy basil removes the free radicals and decreases the oxidative cellular and chromosomal damage enhanced through radiation[35-38]. Followed by there will be decreases of organ damage and increases post-radiation survival in experimental animals[39-41].

Physical stress: physical stress arises from the toxic effect of chemicals and radiation and it extends to extreme noise, physical effort, and severe cold along with enhancing physiological and metabolic stress. Tulsi produces an effect like improving aerobic metabolism, decreases harmful oxidative stress and maintains the physiological biochemical parameters affected by physical stres[34, 42-44]. Some of the previous data has shown that oxidative stress can cause cell and tissue injury[45].

Mental stress: Mental stress causes not only by toxicity, infections, modern living but also with a high level of physiological stress that occurred with high demands and fast pace of modern life. Tulsi moves out the toxicity from the body's cells and organs and normalizes to a peaceful mind[34, 46-49].

Anti- Alzheimer's activity:

Alzheimer's disease is a neurodegenerative disease, which mainly causes behavioral changes, cognitive impairment, and mood swings[50]. Usually, dementia is involved in AD, around 70% of industrialized countries suffering from dementia and approximately 17 to 25 million people are affected worldwide[51-53]. There is no treatment to cure AD completely; it reduces some of the symptoms of AD and restoration of cholinergic function[54-56]. Memantine and Donepezil drugs increase the cognitive impairment in AD patients and as per the review literature no memory improvement after attempting two clinical trials[57-59]. Hence nootropic herbal drugs can enhance the anti-Alzheimer's activity with another anti AD drug[60-62].

Meanwhile, oxidative stress is also another main content which is involved in the AD by stimulation of neuronal death[63-65]. Most of the nootropic drugs possess an antioxidant effect against Alzheimer's disease[66,67].

OS contains antioxidant activity; especially eugenol is the main constituent and also some of the other secondary constituents like fixed oils and flavones which have pharmacological properties[68-78]. Eugenol is a major active constituent of *O. bascilicum*, which is liable for the therapeutic property of Tulsi[79-81]. Moreover, the standardized extract of OS has been statistically relieved the chronic hypoperfusion – enhanced cognitive impairment and ischemia reperfusion-enhanced oxidative stress in rodents[82,83].

Holy basil has memory-enhancing power and antioxidant property in the models of cerebro-degenrative diseases. As mentioned above, AD is also connected with cognitive impairment and oxidative stress. That is why by using neurotoxins such as Ibotenic acid and colchicine models, the outcome of OS in AD was assessed. Ibotenic acid is a structural analog of glutamate, which leads to neuronal necrosis through excitotoxicity exhilarating glutamate receptors. When the drug ibotenic acid is injected, that causes a shortage of spatial learning and memory. This is estimated by using the Morris water maze. Furthermore, colchicine also causes memory impairment through

demolishing granule cells in the dentate gyrus of the hippocampus[84].

Thus when holy basil is administered, it induces acetylcholine (ACh) neurotransmission which is liable for memory power by inhibiting the enzyme known as *acetyl cholinesterase* that destroys acetylcholine in the brain. As a result, Tulsi improves memory and cognitive function by raising the obtainable of acetylcholine in the brain[85].

Anti-depressant activity:

Depression is affecting approximately 121 million people throughout the globe. It deals with the mood swings, acquiring suicidal thoughts, less concentration on personalized work[86,87]. It occurs due to the inadequacy of the monoamines phase such as dopaminergic, norepinephrine and serotonin level in brain[88,89]. Hence herbal drug called OS contains anti-depressant activity [89]. The mechanism of action of antidepressants is not yet resolved entirely, as still, research is going over it. Because available literature says that many parts of plants, phytochemicals are involved in the mechanism of action of anti-depressant, such as root extracts, ethanolic extract of leaves of OS and ursolic acid, eugenol, apigenin, luteolin, apigenin 7-glucuronide, luteolin-7-O-glucuronide, orientin, mollusdistin and two flavonoids, orientin and vicenin140 and cures the depression[86,90].Moreover, leaves ethanolic extract of OS implicated as decreasing in the duration of immobility through the dopamine 2 receptor agonist and ursolic acid which is mainly identified to induce the phase of dopamine, nor epinephrine, and serotonin in the brain [91-93].

Anti-anxiety activity:

Anxiety is one of the disorders which belong to the psychiatric morbidities. It is commonly characterized by dreadful, sentimental behavior but it becomes the reason for the CVS and psychiatric complications. There are some allopathic antianxiety drugs that reduce anxiety disorder but it produces certain side effects. Therefore, herbal drugs are used to treat this disorder and to minimize the side effects as well as it may prevent the chronic effect of the allopathic drugs. This achieves due to to the presence of a large number of secondary metabolites which enhances the medicinal property of the drug. As per the literature, the Ethanolic extract of *O. bascilicum* possesses a medicinal effect against anxiety disorder[94].

It has been proved in an animal experiment is that the time spent as well as the number of entries to the bright chamber is drastically induced after the administration of Holy basil Ethanolic extract [94-96].

Antiepileptic activity:

The word seizure is expressed as the discharging of neurons in the brain which causes[97]. Repeatedly arrival of seizure is known as epilepsy, which is the second major chronic neurological disease worldwide following stroke[98,99]. Approximately 40 to 60/1,000,000 people are suffering from this disease per annum[98,100]. Around 60-70% of the population showed a positive reaction against seizures by consuming antiepileptic drugs, meanwhile closely 30% of the population showed no significant reaction to the treatment[98, 101]. However, it is essential to investigate the better antiepileptic property drugs along with minimum side effects[98, 102]. Since this disorder takes place with three important mechanisms of action such as:

1. Imbalance between excitatory and inhibitory neurotransmitters i.e., GABA and glutamate neurotransmitters.
2. Opening of voltage dependent sodium channels.
3. Activation of the NMDA receptor followed by raises the influx of calcium ions[97].

The Ethanolic extract of leaves of Holy basil helps to reduce the symptoms of epilepsy by improving neuronal functions of the brain[97]. Primarily, OS extract blocks voltage-gated Na^+ channels and also acts by blocking N-methyl-D-aspartate receptors which diminish the T-type Ca^{2+}current in the thalamus. Moreover, the drug influences the agonistic power of gamma-aminobutyric acid ($GABA_A$[103]. Additionally, OS extends the phenobarbitone enhanced sleeping time[103]. As per the existing databases, Ethanol and chloroform extractives of stem, leaf and stem calli of Holy basil holding defensive action against tonic hind limb extension(THLE), followed by all these positive reactions against disease proves that drug has effective antiepileptic property[104].

Antioxidant activity:

The antioxidant activities were compared to standard antioxidant ascorbic acid. Antioxidants are nothing but refusing the generation of oxidizing chain reactions which leads to suppresses the oxidation of other molecules[105, 106 107]. Oxidation is necessary for several living organisms for the production of energy to fuel biological processes[108]. Free radicals possess one or more unpaired electrons that react with another molecule by taking or giving electrons which will lead to the causation of several diseases[109]. These are unstable and highly reactive substances that cause' irreversible damage to cells[110]. As per the previous data, due to the presence of free radicals inside the body manifesting the cellular changes and development of various disorders. Though this could be managed by the antioxidants from many herbal medicinal plants[111]. Approximately 80% of the world population depend up on the medicinal plants to enhance their health care needs[112]. The membrane lipids, proteins, DNA and carbohydrates are mainly required for life; these may destruct from the reactive oxygen species. Due to this reason, the occurrence of various disorders such as liver cirrhosis, atherosclerosis, cancer, and diabetes, etc. Hence, Antioxidants prevents destruction from reactive oxygen species to the human body[113]. OS has the ability to fight against the free radicals which destroys the liver microsomes and also enhances the superoxide dismutase property as well as suppresses the lipid peroxidat[105, 114]. Mostly, the standard antioxidant ascorbic acid was used to compare the antioxidant activities[115]. In some of the studies, a qualitative preliminary phytochemical analysis was carried out for the identification of phenols, alkaloids, flavonoids, steroids, tannins[116].

The antioxidant activities were compared to standard antioxidant ascorbic acid. OS constituent's flavonoids contain membrane protective activity as such decreases in the radiation-induced lipid peroxidation in the liver. Active constituents such as phenolic compounds and Eugenol of OS extract of fresh leaves and stems having excellent antioxidant attributes[108]. Available literature says that dietary antioxidants have better therapeutic properties against the various diseases[105].

Table 1: the chemical substance involved in Holy Basil

1.	Alcoholic Extract[18]	Aesculin, Vitexin, Caffeic acid, Circineol, Gallic Acid, Galuteolin, Isorientin, Isovitexin, Luteolin, Orientin, Apgenin, Stigmsterol, Chlorgenic Acid, Urosolic acid, Vallinin, Viceni, , Molludistin, Aesculectin, Procatechuic acid.	Leaves / Areal Parts
2.	Mineral Contents [19]	Vitamin C, Zinc, Vitamin A, Phosphours Calcium, Copper, Iron Chromium.	Whole Plant
3.	Essential oil[20,21,22]	Aromadendrene oxide, D-Limonene, Benzaldehyde, Eicosane, Borneol, Cubenol, Bornyl acetate, Eucalyptol, Camphor, Caryophyllene oxide, cis-αTerpineol,, Cardinene,, Eugenol, Farnesene, Farnesol, Furaldehyde, Germacrene, Heptanol, Humulene, Selinene, Limonene, α-Thujene, β-Guaiene n-butylbenzoate, Ocimene, Oleic acid, Sabinene, Phytol, Veridifloro, α-Camphene, αMyrcene, α-Pinene, β-Pinene, methyl chavicol β-Gurjunene, and linalool.	Leaves
4.	Fixed oil [23]	Linoleic acid, Oleic acid, Linolenic acid, Palmitric acid, Stearic acid.	Seeds

Table 2: NUTRITIONAL VALUE [24,25, 31]

Principle	**Nutrient value**	**Percentage of RDA**
Energy	23 Kcal	1%
Cholesterol	0 mg	0%
Protein	3.15 g	6%
Carbohydrates	2.65 g	2%
Total Fat	0.64 g	2%
Dietary Fibre	1.60 g	4%
Phytonutrients		
Crypto-xanthin-ß	46 µg	--
Lutein-zeaxanthin	5650 µg	--
Carotene-ß	3142 µg	--

Table 3: Extract and segment of the Tulsi Plant Utilized to treat certain diseases[26,27]

SL.No.	**Diseases to be treated**	**Extract used**	**Part used**
1.	stress	Ethanolic	The whole plant(dried)
2.	Hepatotoxicity	Ethanolic/aqueous	The whole plant (aerial)
3.	Fungal infection	Methanolic/Ethanolic	Leaves
4.	Inflammation	Methanolic/aqueous	Leaves
5.	Diabetes	Ethanolic/aqueous	Leaves
6.	Cancer disease	Ethanolic	Root
7.	Microbial infections	Ethanolic	Leaves
8.	Psychotic disorder	Methanolic/ leaves paste	Leaves
9.	Infertility ovulation disorder	Benzene	Leaves
10.	Ulcerative	Ethanolic/aqueous	Leaves

CONCLUSION:

Tulsi has been widely used and accepted worldwide for its numerous benefits and reduction of adverse effects of synthetic drugs. This review emphasis the various CNS activities which are not explored extensively. This might aid researchers working in this particular herbal drug to identify newer avenues in CNS research and elucidate the possible mechanisms of actions and therapeutic outcomes.

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