

# Rapid Literature Review: Tulsi (Ocimum Sanctum) on Chronic Stress and Mood Regulation

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**Abstract-** *Ocimum sanctum*, commonly known as Tulsi and also known as Holy Basil. It is highly esteemed herb in Ayurvedic medicine. It is an aromatic perennial plant in the family Lamiaceae. Tulsi is mainly used for cough, cold, help in digestive system, stress relief and also It shows various activities like antioxidant, anti-inflammatory, immunomodulatory antimicrobial and widely act as potent adaptogen. Tulsi supports body strength and reduces impact of physical chemicals and mental stress. It works by mechanism of neurotransmitters like dopamine, GABA, and serotonin which are involved in mood regulation, depression and anxiety. Main chemical constituents are eugenol, carvacrol, rosmarinic acid, Oleanolic acid, and linalool etc. Clinical and preclinical studies shows that tulsi reduces stress, anxiety and depression. And also helps in regulating stress hormones like cortisol. Further investigation is required to validate long term efficacy.

**Index Terms-** Adaptogen, Anxiety, Chronic stress, Cortisol, Depression, Eugenol, HPA axis, Mood regulation, Neurotransmitters, *Ocimum sanctum*, Phytochemicals, Tulsi

## INTRODUCTION

Tulsi is also known as *Ocimum sanctum*. Tulasi in Sanskrit or Tulsi in Hindi (Holy Basil in English) is an Aromatic plant in Ayurveda belonging to the Lamiaceae family. Tulsi has been used in Ayurveda over 3000 years to treat various health problems.[1] Tulsi is cultivated in tropical and subtropical region of southeast Asia. And also grow in some parts of Africa.[2] Tulsi is considered as an adaptogenic herb, adaptogens help the body adapt to stress.[3] Tulsi contains different chemical constituents such as Rosmarinic acid, Eugenol, Carvacrol, Linalool, Oleanolic acid,  $\beta$ -caryophyllene etc. [2] Tulsi is also used for antimicrobial, antioxidant, antistress, antiasthmatic, anti-inflammatory activity. According to previous reference of Richard 2016: A study explored the effect of *Ocimum sanctum* on rats exposed CVC model. In these rats are treated with (200mg/kg) for 16 days showed reduced stress symptoms, less weight loss and decrease adrenal gland weight and cortisol level.[4] Stress can cause

many changes in mind like anxiety, depression, loss of appetite, change in immune system and activated hypothalamic pituitary adrenal axis which leads to high level of corticosterone.[5] It was explained that *Ocimum sanctum* would reduce stress, improved sleep, and reduce physiological factor reduced by MAST.[6] Further studies shows that *Ocimum sanctum* affects the biological markers such as cortisol level, adrenal gland weight, neurotransmitters, heart rate and BP. In animal model *Ocimum sanctum* impacts psychological factors such as forced swim test, mood symptoms. The review is important for chronic stress and mood regulations because it provide scientific supports and stress related disorders anxiety, depression and this problem is globally file. Hence needed to validate its effectiveness. The review supports development of evidence, plant base therapies and contribute to MOA in managing mental health. This review shows the systematically examine and synthesize the existing literature on the role of Tulsi in managing chronic stress and mood disorders. It explores traditional uses, bioactive compounds, mechanistic pathophysiology, preclinical and clinical evidence, safety data, and future research directions.

## PHYTOCHEMISTRY (BIOACTIVE COMPOUNDS)

The plant shows various Therapeutic properties due to presence of active chemical constituents or phytochemicals.[7] It contains essential oils, flavonoids, triterpenoids, phenolic compounds which are useful in management of antioxidant, anti-inflammatory and stress related activity.

*Ocimum sanctum* contains 0.7% volatile oil with 71% eugenol and 20% methyl eugenol. Also contains carvacrol, sesquiterpene hydrocarbon  $\beta$ -caryophyllene.[8]

Eugenol is major phenolic compound has been shown significant anxiolytic, antioxidant and modulate HPA axis and reduce cortisol level.[9] [10]

Ursolic acid, apigenin, lutealin, apigenin-7-o-glucuronide, leutoline-7-o-glucuronide, orientin have also been isolated. [11] it contributes adaptogenic properties and protecting against stress induced neuronal damage. [12], [13]

Rosmarinic acid has been isolated from aerial parts of plants. [14,15] suggested to be biological marker for standardization [16] potent antioxidant, plays important role in mood regulation by inhibiting MAO.[17] apigenin and luteolin modulate GABA and serotonergic system and shows antidepressant and anti-anxiety activity.[18]

Other constituents like ocimunosides A and B shows significant anti-stress activity by lowering corticosterone level.[19] This species of *Ocimum* also contains a variety of sesquiterpenes and monoterpenes; barnyl acetate, piperenes (both alpha and beta), [7] Beta carophyllene also supports mood regulation with monomeric receptor.[20]

#### TRADITIONAL USE

Tulsi is dark or shyama Tulsi (o-sanctum). Tulsi plant used by all the cultures since Long. India is the richest, oldest and diverse cultural traditions related with use of Tulsi. [21] The plant is useful in various kinds of traditional medicine such as Ayurveda, sidha And unani and it is used to treat various diseases or disorders such as bronchitis, Gastric, malaria fever, cardiac and genitourinary disorders, rheumatism, anxiety, Cough, asthma, diarrhea, fever, dysentery, indigestion, ringworm and skin disorders. [22, 16] Leaf extract of *Ocimum sanctum* with hot water is commonly used to relieve muscular Pain, joint pain and headache in south India, particularly at Thoothukludy, Muduvaithaneda. Thirunvetvelly and kannyakumari region. An adaptogenic properties of Tulsi depends upon the immune stimulant capacity of Tulsi. [23, 24] Tulsi leaves used for purification of drinking water, memory sharpening, good for nerves.[25] Tulsi can increase the capacity to survive adapt to changing environment and reduce Negative physical and psychological effects of stress. Intake of 12 leaves of Tulsi twice Day prevents stress. Purifies the blood and prevents several common psychological Disorders. [24,25] *Ocimum sanctum* used in various purposes such as leaves, flowers, stem, roots, seed Etc. Are known to potential pharmacological activity such anti stress, anxiety and Depression. [26] Tulsi has been used to calm the nerves and balance emotional disturbances (fear, Sadness).

Sattva the Ayurvedic quality and purity and balance in the mind and Emotions. [27] Fresh leaves kadha during time of emotional distress, fatigue and commonly used to Improve sleep, mental clarity. Purify environment and mind.[13]

#### ADAPTOGENIC PROPERTIES

Though stress is often perceived as relating to mental and emotional well-being, stress Can occur any time the body or mind is pushed beyond its “normal” measures, or any Time the body or its processes are imbalanced. Athletes create physical stress when engaging in activities such as running, sprinting, weight training, etc. Physical and Mental stress can result when sickness, such as a cold or flu, occurs. Bacteria can Interfere with the skin or oral tissue, causing stress to the tissues. Improperly Functioning adrenal glands can affect excretion of cortisol, pushing several processes Within the body beyond normal function. [28]

The term “adaptogens” refers to herbs and herbal products used to normalize body Functions and strengthen systems compromised by stress. Basically, adaptogens help the body adapt to stress.[28] Tulsi improves stress tolerance, decrease anxiety and enhance cognitive performance of healthy individuals. [9] Adaptogenic property of Tulsi supports is Ayurvedic classification as a ‘rasayana’ herb for promoting mental clarity, emotional stability and resilience against stress.[9] *Ocimum sanctum* (Tulsi) is considered a potent adaptogen, helping the body resist Various physical, chemical, and biological stressors while maintaining homeostasis. [19] Its adaptogenic activity is linked to bioactive compounds such as eugenol, ursolic acid, Rosmarinic acid, apigenin, and ocimunosides A and B, which modulate the Hypothalamic–pituitary–adrenal (HPA) axis, normalize cortisol secretion, and enhance Antioxidant defense systems [29] Preclinical studies explain that Tulsi reduces oxidative stress and inflammation Associated with chronic stress.

#### PATHOPHYSIOLOGY OF CHRONIC STRESS

Stress is a condition or feeling experienced when a person Perceives that “demands exceed the personal and social Resources the individual is able to mobilize.” (attributed to Richard S.Lazarus) “Stress is not what happens to you, but how you react to what happens!

“...we define stress as environmental conditions that require behavioral adjustment” (Benson, H. The Relaxation Response, 2000, pg. 41). Thus, change, good or bad, can induce a stress response.

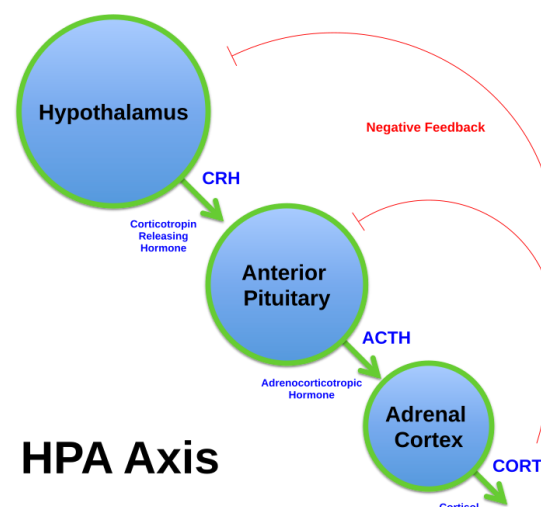
**Pathophysiology:** Chronic stress arises due to activation of the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic-adrenomedullary (SAM) system, resulting in sustained release of Glucocorticoids and catecholamines. [30, 31] In case of Acute Stress, activation is adaptive which prepare body for fight or flight. When stress is chronic, there is sustained hypercortisolemia and catecholamine release, which disrupt negative feedback mechanisms and impair glucocorticoid receptor sensitivity in the hypothalamus and pituitary. [32, 33]

**1. Neuroendocrine Dysregulation:** Chronic activation of the HPA axis leads to structural and functional brain changes. High glucocorticoid leads to dendritic atrophy and reduced neurogenesis in the Hippocampus. Hypertrophy of the amygdala and atrophy of the prefrontal cortex. Dysregulation of neurotransmitters — including serotonin, dopamine, noradrenaline, And GABA — contributes to depression, anxiety, and cognitive decline. chronic stress Also alters CRH (corticotropin-releasing hormone) and AVP (arginine vasopressin) Signaling, both of which potentiate ACTH release and further stimulate cortisol Production. [30]

**2. Immune and Inflammatory Pathways:** Long-term elevation of glucocorticoids and catecholamines shifts immune function toward a pro-inflammatory state, with increased levels of IL 6, TNF- $\alpha$ , and CRP. [33] chronic exposure suppresses adaptive immunity, reduces natural killer (NK) cell activity, and impairs wound healing. This immune dysregulation links chronic stress to higher susceptibility to infections, and systemic inflammation that explores mood disorders. [34]

**3. Clinical Implications:** The neuroendocrine dysregulation, immune imbalance, oxidative stress, and metabolic Disruption explains the wide-ranging effects of chronic stress — from psychiatric Conditions like depression and anxiety to somatic disorders such as cardiovascular disease, diabetes, and neurodegeneration. This complex pathophysiology multimodal Interventions that can modulate HPA axis activity, restore

neurotransmitter balance, suppress inflammation, and enhance cellular resilience — mechanisms in which Ocimum sanctum has shown adaptogenic potential.



## HPA Axis

Fig 1: In chronic stress, the hypothalamus (via CRH and AVP) activates the pituitary and Adrenal glands persistently, resulting in prolonged cortisol exposure and impaired Negative feedback control. This contributes to receptor resistance and elevated basal Cortisol level

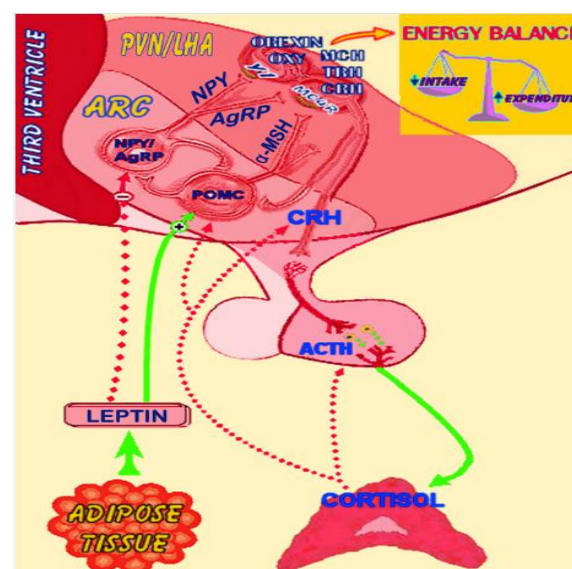


Fig 2: HPA axis regulation under chronic stress, showcasing how the hypothalamus Releases CRH and AVP, which stimulate ACTH release from the pituitary—this in turn Drives cortisol production in the adrenal cortex

## PRECLINICAL (ANIMAL STUDIES) ON STRESS

Multiple animal studies have demonstrated the adaptogenic, anxiolytic, and anti-stress Properties of *Ocimum sanctum* in experimentally induced stress models.

1. Restraint Stress Models: In chronic restraint stress models, ethanolic and aqueous extracts of *O. sanctum* Significantly reduced stress-induced ulceration, adrenal gland hypertrophy, and plasma Corticosterone levels in rats. these effects are attributed to its modulation of the Hypothalamic–pituitary–adrenal (HPA) axis and enhancement of antioxidant enzyme Activity.[29]

2. A preclinical study in Wistar rats found that *Ocimum sanctum* (Tulsi) extract, given Orally (50–]200 mg/kg) during 16 days of chronic variable stress, improved body weight Gain, reduced immobility in the forced swim test, and normalized adrenal weight and Cortisol levels.[4]

3. *Ocimum sanctum* (Tulsi) tested in rats and mice exposed to restraint stress. Forced Swim Test (FST) & Rotarod Test which result in Tulsi significantly reduced stress-induced Immobility and improved motor performance, but effects were less potent the Mechanisms via HPA axis modulation, antioxidant action, and dopaminergic effects.[5]

4. Evaluated antistress activity of *Ocimum sanctum* in albino rats which shows Significant adaptogenic effects under stress conditions. In which Immobilization and Cold stress models are used.[35]

5. Preliminary study on immunoregulatory profile in albino rats. Tulsi leaf extracts Modulated immune responses in stressed animals. [36]

6. Assessed immunomodulatory potential of *Ocimum sanctum* seed oil enhanced both Humoral and cell-mediated immunity in animal models, possibly via modulation of Stress-related immune suppression.[37]

7. Immunotherapeutic potential in bovine subclinical mastitis Relevant as a veterinary Model showing immune enhancement under inflammatory stress.[38]

8. Cold-Restraint Stress: Cold-restraint stress, which induces gastric ulceration and oxidative damage, was Attenuated by pretreatment with *O. Sanctum* extract in Wistar rats, reducing ulcer index and lipid peroxidation while increasing glutathione levels. [39]

## PRECLINICAL STUDIES ON BRAIN CHEMISTRY (ANXIETY, DEPRESSION)

1. Male Swiss albino mice subjected to unpredictable chronic mild stress which Reduce depression and anxiety like symptoms by using sucrose preference test And for behavior despair used tail suspension test, Forced swim test and also Used open field test for grooming behavior. Active constituent (luteolin, apigenin) Are contribute to the antidepressant and anxiolytic potential. OS-B effect block By inhibitors serotonin and catecholamines. [40]

2. Chronic Variable Stress (CVS) in Wistar rats which increases immobility time by using forced Swim Test and tulsi extract reduce immobility time which shows antidepressant effect. COMT inhibition supporting mood regulation. HPA axis activity and catecholamine metabolism, stress-related changes linked to anxiety and depression.[4]

3. Inhalation of *Ocimum sanctum* and *Ocimum basilicum* essential oils for 21 Days. Male Wistar rats were injected intracerebroventricularly with amyloid beta (1–42) including anxiety- and depression-like behaviors. In which Elevated Plus-Maze (EPM) and Forced Swimming Test (FST) is used to measure depression, Anxiety and behavioral. And linalool is considered for anxiolytic and Antidepressant activity.[41]

4. To evaluate ethanol leaf extract of *Ocimum sanctum* (OS) in Swiss albino mice for both antidepressant and anxiolytic effects, with relevance to mixed anxiety–depressive disorder (MADD). Male Swiss albino mice (20–25 g) for depression Tail Suspension Test (TST), Forced Swim Test (FST) and for anxiety Light-Dark test, Elevated Plus Maze (EPM), Holeboard test. Imipramine (antidepressant), Diazepam (anxiolytic) this reference drugs are used. And antistress effects affect brain chemistry.[42]

## HUMAN STUDIES ON STRESS REDUCTION

1. Clinical trial with 158 participants effect of Tulsi reduces stress and related Symptoms such as fatigue, sleep related problems. Also reduces depression Anxiety. The results from this trial suggest that 8 weeks of supplementation with An *Ocimum tenuiflorum* extract (Holixer™) may reduce objective and subjective Measures of stress, and improve subjective measures of sleep quality.[6]

2. Randomized, double-blind, placebo-controlled trial. Ocimum tenuiflorum Extract (Holixer™), 250 mg/day for 8 weeks. Perceived Stress Scale (PSS), Athens Insomnia Scale (AIS), Hair cortisol levels are measured in this study. [43]

3. Hospital-based clinical trial. 35 subjects (21 male, 14 female) in which Ocimum Sanctum extract capsules, 500mg twice daily for 60 days. Outcomes measured at baseline, day 30, and 60. While produce antistress, Anxiolytic and Antidepressant activity and it is safe herbal alternative for benzodiazepines. [19]

4. 44 healthy male volunteers (18–30 years). At AIIMS, New Delhi, India. It is a Double-blind, randomized, placebo-controlled trial in which ethanolic leaf Extract of Ocimum sanctum (EtOS) is used for 30 days of dose 300 mg/day. Which improves stress related psychological measures and enhance cognitive Performance in volunteers. [44]

5. 158 adults two groups OciBest group (n=76) Placebo group (n=82) at extract of Ocimum tenuiflorum 1200 mg/day (400 mg capsule × 3 daily) for 6 weeks which Significantly reduces stress related symptoms and mood regulation and safe for short term used. [45]

#### HUMAN STUDIES ON ANXIETY AND DEPRESSION

1. In previous papers Ocimum sanctum leaf extract, 500 mg twice daily, for 60 days is used in which 35 patients with GAD. It is controlled trial program which shows Significant reduction in stress and depression scores compared to baselines. Clinical trial suggests Ocimum sanctum has anti-anxiety and mild Antidepressant effects, especially in GAD patients. [19]

2. It is a Double blind, placebo-controlled. Ocimum sanctum extract, 1200 mg/day, For 6 weeks. Total no of participants 71 with stress-related symptoms. The Study shows the Symptomatic improvement in stress, mood, and sleep based on Self-reported examine. Higher doses over 6–8 weeks shows the significant Benefits for anxiety and depression. [45]

3. The studies identified in this review could be classified according to three Main clinical domains including metabolic disorders (15 studies), neurocognitive or mood conditions (4 studies), and immunity and Infections (5 studies), which are all

extremely relevant to the growing World-wide epidemic of lifestyle-related chronic disease. [46]

#### DOSAGE AND FORMULATION USED

In Humans studies Tulsi has been administered primarily in standardized formulation Such as capsule, tea and tinctures and we can also use tablet and syrups in future Studies. All studies consistently report good safety and tolerability, with no serious Adverse events.

Ocimum tenuiflorum Extract (Holixer™), 250 mg/day for 8 weeks used Perceived Stress Scale (PSS), Athens Insomnia Scale (AIS), Hair cortisol levels are Measured in this study. [43] Ocimum Sanctum extract capsules, 500mg twice daily for 60 days. Outcomes Measured At baseline, While produce antistress, Anxiolytic and Antidepressant Activity. [19]

Similarly, the Holixer™ hydroalcoholic extract of Tulsi leaves and aerial parts, standardized to its bioactive chemicals was administered at a lower dose of 250 mg/day For eight weeks, resulting in reductions in perceived stress, improved mood, and better Sleep outcomes relative to placebo. [6]

#### SAFETY, TOXICITY AND ADVERSE EFFECTS

Tulsi is considered as safe but few adverse effects are reported. Long term Consumption and use during pregnancy are limited. Acute and chronic toxicity studies At high dose. In previous research papers some adverse effects are reported. Such as High doses in animals have shown possible antifertility effects so avoid during Pregnancy. [47] Anticoagulant interaction, Pregnancy & Lactation. Tulsi lowers blood Glucose and enhance antidiabetic effect. [48]

Tulsi has safety margin in both preclinical and clinical studies. It is safe for short term Use but only rare adverse effects are reported such as gastrointestinal side effect.

In preclinical studies Repeated administration of standardized extracts was well Tolerated, with no histopathological changes in the liver, kidney, or reproductive organs. But very high doses have been associated with mild hepatotoxic changes.

#### BIOLOGICAL MARKERS

Preclinical Biomarkers: Multi targeted effect in biochemical and neurochemical markers. Supporting Its adaptogenic, antioxidant. Wide range of biological markers Such as Neuroendocrine markers, Oxidative stress markers, Immunological markers, Neurotransmitter levels. White blood cell count, neutrophil–lymphocyte ratio, and cytokines (IL-6, TNF- $\alpha$ ) are used under Tulsi treatment, suggesting immunomodulatory Activity. For Immunological markers. In brain serotonin (5-HT), dopamine (DA), and GABA are maintained Neurotransmitters levels. Tulsi enhances antioxidant enzymes while lowering lipid peroxidation Superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and Malondialdehyde (MDA) are various Oxidative markers. Plasma corticosterone levels are commonly measured to assess HPA axis Activity. And reduce stress level. [9 29, 39]

Clinical Biomarkers: Tulsi supplementation reduced cortisol levels in stressed individuals. Various Clinical studies shows that Tulsi reduces fasting glucose, triglycerides, and LDL cholesterol, which affects stress metabolic interactions. Tulsi's ability to modulate HPA axis function, oxidative balance, and inflammation, supporting its adaptogenic properties. [9,29,39]

#### FUTURE RESEARCH DIRECTION

Future studies include, mechanistic studies, standardized formulations, well designed Clinical trials, long term safety terms, stress management considering genetics, lifestyle Factors which affects adaptogenic property also we can studies about comparative and combinations studies.

#### RESULT AND DISCUSSION

This review shows that significant adaptogenic, anxiolytic and mood Regulating activity. Various preclinical and clinical studies are mentioned in This studies which shows or reduced stress, cortisol levels and various Stress related symptoms. *Ocimum sanctum* also shows mood regulating Properties. Tulsi also shows multi targeted mechanism of action like neurotransmitters Level, cortisol level, immunomodulatory activity and HPA axis. The results shows that Tulsi is safe and effective adaptogen for chronic Stress and mood regulation. Tulsi extracts in the various doses reduces Perceived stress, anxiety symptoms, and cortisol levels, while improving Mood and cognitive function. Various

biological markers also described in this study. More clinical trials are needed for long term used.

#### CONCLUSION

The overall review shows potential to reduce chronic stress and related symptoms, Anxiety, and mood regulations along with effects of biological markers. Overall tulsi is Safe herbal extract for stress management. Long term safety terms and larger Randomized controlled trials are needed.

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