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EVALUATING THE CLINICAL EFFECTIVENESS AND SAFETY OF TULSI: A COMPREHENSIVE REVIEW

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ABSTRACT

Tulsi, or holy basil, is a venerated medicinal herb that has profound historical significance in Ayurvedic medicine. This study consolidates data from more than one hundred investigations on the pharmacological advantages of Tulsi, emphasizing its adaptogenic, anti-inflammatory, and immunomodulatory characteristics, among others. Despite considerable in vitro and animal studies indicating its therapeutic potential, there is a significant deficiency of complete human clinical trials assessing the safety and efficacy of Tulsi as a singular therapy. This paper seeks to critically evaluate these human clinical trials to offer an educated view of the therapeutic efficacy and safety of Tulsi.

KEYWORDS: Pharmacological, Immunomodulatory, Adaptogenic.

INTRODUCTION

Tulsi in Hindi or Tulasi in Sanskrit (holy basil in English) is a highly esteemed culinary and medicinal fragrant plant belonging to the Lamiaceae family. It is native to the Indian subcontinent and has been utilized in Ayurvedic treatment for over 3000 years. In the Ayurvedic system, Tulsi is frequently referred to as an "Elixir of Life" due to its therapeutic properties and its efficacy in addressing several prevalent health issues. Tulsi leaf extracts are documented in the Indian Materia Medica for treating bronchitis, rheumatism, and pyrexia.[1] Additional documented therapeutic applications encompass the management of epilepsy, asthma or dyspnea, hiccups, cough, dermatological and hematological disorders, parasite infections, neuralgia, headaches, wounds, and inflammation[2] and oral conditions.[3] The juice extracted from the leaves has been utilized as a remedy for earache[4], The tea infusion has been utilized for the treatment of stomach and hepatic problems.[5] The roots and stems

were historically employed to remedy insect and snake bites, as well as malaria.[5]

Three varieties of tulsi are frequently delineated. Ocimum tenuiflorum (or Ocimum sanctum L.) comprises two botanically and phytochemically different cultivars: Rama or Sri tulsi (green leaves) and Krishna or Shyama tulsi (purplish leaves)[6,7], Ocimum gratissimum is a third kind of tulsi, referred to as Vana or wild/forest tulsi, characterized by its dark green leaves.[8,9] The many forms of tulsi have significant variety in shape and phytochemical composition, including secondary metabolites; nonetheless, they may be differentiated from other Ocimum species by their yellow pollen and elevated eugenol content[10], and smaller chromosome number.[11] Despite being distinct species with Ocimum tenuiflorum having six times less DNA than Ocimum gratissimum[11], they are traditionally employed identically to address comparable diseases.[5] This review consistently used the term tulsi to denote both Ocimum tenuiflorum and Ocimum gratissimum.

Tulsi has been extensively studied, with over one hundred papers in the past decade addressing its pharmacological properties and many medicinal uses. Numerous in vitro and animal investigations demonstrate that tulsi leaf has significant pharmacological properties, including adaptogenic effects[12,14], metabolic[15,17], immunomodulatory[18,20], anticancer[21,23], anti-Inflammatory[24,25], antioxidant[26,27], hepatoprotective[28,29], radioprotective[30,31], antimicrobial[32,35], and antidiabetic effects[36,38] that have been extensively reviewed previously.[39,45]

Preclinical studies have demonstrated that tulsi increases swimming survival times in mice and prevents stress-induced ulcers in rats[46] exhibiting antistress effects akin to those of antidepressant medications.[47] Similarly, recent studies report leaf extracts from ethanolic and aqueous tulsi to protect rats from stress-induced cardiovascular changes.[47,49] Research utilizing animal models has demonstrated that tulsi leaf extract has anticonvulsant and anxiolytic properties.[50,51] Numerous animal studies published over the last fifty years indicate that the consumption of tulsi leaves improves glucose and lipid profiles in both normal and diabetes-induced animal models.[36,38,52–58] The intramammary infusion of Tulsi aqueous leaf extract has demonstrated a potential impact in enhancing the immunological response in bovine animals.[59]

Alongside the comprehensive literature detailing in vitro and animal experiments, investigations into the use of tulsi within a polyherbal formulation in people have been

extensively evaluated. Currently, there are no comprehensive evaluations assessing the therapeutic effectiveness and safety of tulsi as a standalone herbal intervention in humans. This study aimed to describe and critically evaluate human clinical studies of tulsi to assess its clinical effectiveness and safety based on existing data.[60]

Approximately 160 species within the genus Ocimum, such as Ocimum sanctum, Ocimum americanum, Ocimum basilicum (Ban Tulsi), Ocimum camphor, Ocimum canum (Dulal Tulsi), Ocimum gratissimum (Ram Tulsi), Ocimum kilimandscharicum, Ocimum micranthum, and Ocimum tenuiflorum (Krishna Tulsi), are extensively distributed across the warm regions of the globe and possess recognized medicinal properties.[62–65]

Sanctum is a fragrant herb and an invasive weed. It is an upright, extensively branched perennial or biennial subshrub, measuring 30–75 cm in height, characterized by hairy stems and simple, opposite, aromatic green leaves. The leaves are ovate, oblong, obtuse, or acute, measuring up to 5 cm in length, and are typically somewhat serrated. Flowers are little and purple-hued, arranged in elongated racemes with closely spaced whorls. The fruits are little, and the seeds have a reddish-yellow hue.[66] The plant is cultivated across India, from the Himalayas (up to 1800 meters above sea level) to the Andaman and Nicobar Islands.[67] It propagates by seeds and may be cultivated effortlessly across diverse soils and weather conditions.

Sanctum is renowned for its remarkable therapeutic properties in ancient folklore and several indigenous medical systems, including Ayurveda, Unani, Siddha, Greek, and Roman practices.[64,69] Distinguished for its powerful fragrance and astringent flavor. In Ayurveda, Sanctum is referred to as 'the elixir of life' and is said to enhance longevity. Sanctum is conventionally used in several forms, including cold or hot infusions of dried leaves (herbal tea), dry powder, fresh leaves, alcoholic tinctures, and oil (ghee) preparations, as well as compositions including stem, root, and seeds, utilized both systemically and topically.[70] As per the Indian Materia Medica, which encompasses the Ayurvedic and Unani medical traditions. Sanctum possesses numerous medicinal properties, including antipyretic, antiseptic, antiemetic, alexipharmic, carminative, diaphoretic, demulcent, expectorant, and stimulant effects. Consequently, it has been advocated for the treatment of various ailments, such as malaria fever, bronchitis, catarrh, gastric and genitourinary disorders, rheumatism, and dermatological conditions.[71] The leaves of the sanctum are utilized for throat and chest disorders, as well as for alleviating colds, coughs, and indigestion. The juice extracted from

fresh leaves, blossoms, and thin roots serves as an antidote for snake bites and scorpion stings.[72] The leaves are utilized as a seasoning in salads and various culinary applications. The essential oil derived from the leaves is utilized to relieve joint discomfort and possesses significant insecticidal and larvicidal properties. The seeds possess anticoagulant qualities and are beneficial for both constipation and diarrhea.[73] Consequently, every component of the plant possesses medicinal properties and is utilized for the treatment of many ailments grounded in traditional knowledge.[68]

Recent scientific investigations have demonstrated that various components of sanctum, including leaves, stem, root, flowers, and seed, exhibit a multitude of biological and pharmacological activities, such as antioxidant, anti-inflammatory, antiallergic, immunomodulatory, anticoagulant, antimicrobial, antistress, antiulcer, wound-healing, anticataract, analgesic, antipyretic, antihypertensive, antidiabetic, antifertility, central nervous system depressant, cardioprotective, gastroprotective, hepatoprotective, renoprotective, radioprotective, chemopreventive, and anticancer properties.[61,66,68,70,73–76] Despite several recent studies providing a comprehensive summary of the pharmacological characteristics of sanctum, the application of this herb for chemoprevention or treatment of oncological disorders has not been thoroughly and critically examined in the literature. This essay seeks to deliver, for the first time, a thorough and critical examination of current anticancer and cancer prevention research on sanctum.

Ocimum sanctum and cancer

This section emphasizes research that illustrates the impact of sanctum extracts and phytoconstituents in preclinical in vitro and in vivo cancer models, as well as in clinical contexts.

In-vitro studies

The use of an ethanolic extract of sanctum leaves to HFS-1080 human fibrosarcoma cells demonstrated cytotoxicity at a dosage of 50 mg/ml. Mechanistic investigations have identified induced apoptosis ask, indicating reduction or downregulation; m, indicating rise or overexpression.

Reduced intracellular glutathione (GSH) and elevated amounts of lipid peroxidation products.[77] 6-alkylamines are powerful mutagenic, carcinogenic, and cytotoxic molecular lesions caused by both exogenous and endogenous alkylating agents. Enhanced clearance of

these lesions by the augmentation of methylguanine–DNA methyltransferase (MGMT) activity appears to be an effective chemopreventive approach. Both ethanolic and aqueous extracts of sanctum leave dose-dependently increased amounts of MGMT mRNA and protein, as well as its demethylation activity in HT29 human colon cancer cells. The activity and protein expression of glutathione S-transferase-pi (GSTP1) were elevated after treatment with each extract.[78] These findings highlight the potential of using sanctum to mitigate alkylation- induced carcinogenesis. Magesh et al.[79] examined the anticancer efficacy of an ethanolic extract of sanctum leaves on A549 human non-small-cell lung carcinoma cells. The extract demonstrated cytotoxicity, elevated the sub-G1 population, and generated apoptotic bodies. Furthermore, the extract-cleaved poly (ADP-ribose) polymerase (PARP) liberated cytochrome c into the cytosol, activated caspase-9 and caspase-3 proteins, elevated the ratio of pro- apoptotic protein Bax to anti-apoptotic protein Bcl-2 and concurrently inhibited the phosphorylation of AKT and extracellular signal-regulated kinase (ERK). A subsequent study by the same researchers utilizing mouse Lewis lung carcinoma cells demonstrated that the extract markedly inhibited tumor cell adhesion and invasion, along with the activity of matrix metalloproteinase-9 (MMP-9), but not MMP-2, underscoring the critical role of MMP-9 in the antimetastatic efficacy of sanctum. The anticancer activity of vicenin-2, an active component of the sanctum, has been evaluated against several human prostate cancer cell lines, including LNCaP (androgen-dependent), PC-3, and DU-145 (androgen-independent).[80]

Morphology

Distribution	Grow up to 30 - 60 cm in height.
Territory	Found throughout the Indis.
Habit	Annual herb.
Mool	Thiny, wired, branches, hairs, soft, color black to brown from external or dull and violet internal.
Tana	Stiff, greenly, wooded, branches are hairy, external color pinkish-brown to black, internal color dull yellowish, fracture: stringy and slightly aromatic odor.
Patra	Leaves are 2.5 to 5cm long 1.6 to 3.2 cm wide, elliptically egg-shaped, dumb or acute apex, and hairy on both sides. The petiole is thin and hairy; the odor is aromatic.
Chaal	Color: Greyish brown from the outside and pale pink from the inside, longitudinal cracks are present.
Pushpa	Purplish or crimson-colored, calyx elliptical or campanulated 3-4 mm blipped, odor is aromatic, taste is pungent.
Phal	Four nutlets, each containing one seed, membranous, color is dull brown or reddish with small black patches, odor is aromatic, taste is pungent.
Beej	The shape is oval, the color is brown, mucilaginous when soaked in water, the odorless, taste is pungent.

Extract and the Part of Tulsi Plant Used For Pharmacological Activities

Therapeutic activity	Extract used	Part used
Anti-stress	Ethanolic	Whole plant (dried)
Anti-inflammatory	Methanolic/aqueous	Leaves
Anti-fungal	Methanolic/aqueous	Leaves
Anti-fertility	Benzene	Leaves
Hepatoprotective	Ethanolic/aqueous	Whole plant (aerial)
Anti-diabetic	Ethanolic/aqueous	Leaves
Anti-ulcer	Ethanolic/aqueous	Leaves
Anti-microbial	Ethanolic	Leaves
Anti-psychotic	Methanolic/ leaves paste	Leaves
Anti-cancer	Ethanolic	Root

CONCLUSION

In conclusion, Tulsi, or holy basil, is a revered plant with a rich history of medicinal and culinary use on the Indian subcontinent. It has been employed in Ayurvedic medicine for over 3000 years and is recognized for its medicinal properties in treating various health concerns. Tulsi has been thoroughly examined, revealing many pharmacological qualities such as adaptogenic, immunomodulatory, antioxidant, and antibacterial activities. Recent studies indicate that Tulsi possesses antistress, anticonvulsant, and anxiolytic qualities, along with potential advantages in enhancing glycemic and lipid profiles.

Numerous kinds of Tulsi exist, each exhibiting distinct phytochemical compositions and morphological characteristics, however all are historically employed to treat analogous ailments. Moreover, additional species in the Ocimum genus, including Ocimum sanctum, are acknowledged for their therapeutic virtues and have been employed in many medical systems throughout for millennia. Sanctum possesses a diverse array of therapeutic characteristics, including antipyretic, anti-inflammatory, expectorant, and stimulating actions. It has been utilized to address different conditions, including malaria, rheumatism, and gastrointestinal issues.

Recent scientific studies have demonstrated that constituents of Tulsi and Sanctum possess various biological and pharmacological actions, including anticancer effects. Research indicates that extracts from these plants can trigger apoptosis in cancer cells, diminish intracellular glutathione levels, and augment the activity of certain enzymes associated with chemoprevention. Preclinical studies indicate that Tulsi extracts exhibit cytotoxic effects on cancer cells and may impede tumor cell adhesion and invasion. The active constituents of Tulsi and Sanctum have demonstrated potential in suppressing the proliferation and spread of several

cancer cell lines.

Tulsi and Sanctum possess a longstanding history of traditional application and have significant potential in contemporary scientific study about their therapeutic attributes, particularly as anticancer agents. Additional study is required to comprehensively elucidate the mechanisms of action and prospective therapeutic implications of these plants in cancer therapy and prevention.

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