

PHARMACOLOGICAL ACTIVITIES OF OCIMUM SANCTUM (TULSI): A REVIEW

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ABSTRACT

In the present review, an attempt has been made to congregate the botanical, phytochemical, ethnomedicinal, pharmacological and toxicological information on *Ocimum sanctum* Linn. (OS, Tulsi), a medicinal herb used in the indigenous system of medicine. OS has been adored in almost all ancient ayurvedic texts for its extraordinary medicinal properties. It is pungent and bitter in taste and hot, light and dry in effect. Its seeds are considered to be cold in effect. The roots, leaves and seeds of Tulsi possess several medicinal properties. Ayurvedic texts categorise OS as stimulant, aromatic and antipyretic. While alleviating kapha and vata, it aggravates pitta. It has a wide range of action on the human body mainly as a cough alleviator, a sweat-inducer and a mitigator of indigestion and anorexia. OS has a variety of biological / pharmacological activities such as antibacterial, antiviral, antifungal, antiprotozoal, antimalarial, anthelmintic, antidiarrhoeal, analgesic, antipyretic, antiinflammatory, antiallergic, antihypertensive, cardioprotective, central nervous system (CNS) depressant, memory enhancer, antihypercholesterolaemic, hepatoprotective, antidiabetic, antiasthmatic, antithyroidic, antioxidant, anticancer, chemopreventive, radioprotective, immunomodulatory, antifertility, antiulcer, antiarthritic, adaptogenic / antistress, anticataract, antileucodermal and anticoagulant activities. This review will definitely help for the researchers as well as clinicians dealing with *O. sanctum* to know its proper usage as this herb is seemed to be highly valuable, possessing many pharmacological / medicinal properties.

KEYWORDS: Chemopreventive, radioprotective, immunomodulatory, antifertility, antiulcer, antiarthritic.

INTRODUCTION

Tulsi is an important symbol of the Hindu religious tradition. Although the word 'Tulsi' gives the connotation of the incomparable one, its other name, Vishnupriya means the one that pleases Lord Vishnu. Found in most of the Indian homes and worshipped, its legend has permeated Indian ethos down the ages. Known in English as Holy Basil and botanically called *Ocimum sanctum*, Tulsi belongs to plant family Lamiaceae. It has made important contribution to the field of science from ancient times as also to modern research due to its large number of medicinal properties. Tulsi has been described as of two types- vanya (wild) and gramya (grown in homes). Although having identical usage, the former has darker leaves. Tulsi is a popular home remedy for many ailments such as wound, bronchitis, liver diseases, catarrhal fever, otalgia, lumbago, hiccough, ophthalmia, gastric disorders, genitourinary disorders, skin diseases, various forms of poisoning and psychosomatic stress disorders.^[1-2] It has also aromatic, stomachic, carminative, demulcent, diaphoretic, diuretic, expectorant, alexiteric, vermifuge and febrifuge properties.^[3] In view of these facts, an

attempt has been made to review on the various pharmacological activities of OS based on the experimental and clinical studies reported in different literatures.

Tulsi grows wild in the tropics and warm regions. The plant is distributed and cultivated throughout India. It is an erect, much branched, fragrant and erected plant attaining a height of about 30-60 cm when mature. Its aromatic leaves are simple, opposite, elliptic, oblong, obtuse or acute with entire or subserrate or dentate margins, growing up to 5 cm long. The Tulsi flowers are small, purplish in elongate racemes in close whorls. The fruits are small and the seeds are reddish-yellow in colour. The plant is bitter and acrid.^[2-3]

Traditional uses: Tulsi is also known as "the elixir of life" since it promotes longevity. Different parts of plant are used in Ayurveda and Siddha Systems of Medicine for prevention and cure of many illnesses and everyday ailments like common cold, headache, cough, flu, earache, fever, colic pain, sore throat, bronchitis, asthma, hepatic diseases, malaria fever, as an antidote for snake

bite and scorpion sting, flatulence, migraine headaches, fatigue, skin diseases, wound, insomnia, arthritis, digestive disorders, night blindness, diarrhea and influenza. The leaves are good for nerves and to sharpen memory. Chewing of Tulsi leaves also cures ulcers and infections of mouth.^[2]

Phytoconstituents: The leaves of OS contain 0.7% volatile oil comprising about 71% eugenol and 20% methyl eugenol. The oil also contains carvacrol and sesquiterpine hydrocarbon caryophyllene. Fresh leaves and stem of OS extract yielded some phenolic compounds (antioxidants) such as cirsilineol, circimaritin, isothymusin, apigenin and rosameric acid, and appreciable quantities of eugenol.^[5]

Two flavonoids, viz., orientin and vicenin from aqueous leaf extract of OS have been isolated.³ Ursolic acid, apigenin, luteolin, apigenin-7-O-glucuronide, luteolin-7-O glucuronide, orientin and molludistin have also been isolated from the leaf extract.⁶ OS also contains a number of sesquiterpenes and monoterpenes viz., bornyl acetate, -elemene, neral, - and -pinenes, camphene, campesterol, cholesterol, stigmasterol and -sitosterol.^[7]

Experimental and clinical studies

All over the world scientific research is getting momentum to evaluate the pharmacological activities, side effects and medicinal uses of OS against different diseases. On the basis of various experimental and clinical researches, the following pharmacological activities or medicinal properties of OS have been reported.

Anticancer activity: The anticancer activity of OS has been proved and cited by several investigators.^[8-11] The alcoholic extract (AIE) of leaves of OS has a modulatory influence on carcinogen metabolizing enzymes such as cytochrome P 450, cytochrome b5, aryl hydrocarbon hydroxylase and glutathione S-transferase (GST), which are important in detoxification of carcinogens and mutagens.^[12] The anticancer activity of OS has been reported against human fibrosarcoma cells culture, wherein AIE of this drug induced cytotoxicity @ 50 g/ml and above.

Morphologically, the cells showed shrunken cytoplasm and condensed nuclei. The DNA was found to be fragmented on observation in agarose gel electrophoresis.^[13] OS significantly decreased the incidence of benzo(a)pyrene induced neoplasia of forestomach of mice and 3'-methyl-4-dimethylaminoazobenzene induced hepatomas in rats.^[14] The AIE of the leaves of OS was shown to have an inhibitory effect on chemically induced skin papillomas in mice.^[15] Topical treatment of Tulsi leaf extract in 7,12dimethylbenz(a)anthracene (DMBA) induced papillomagenesis significantly reduced the tumour incidence, average number of papillomas/mouse and cumulative number of papillomas in mice. Topical

application of the extract significantly elevated reduced GSH content and GST activities.^[16] A similar activity was observed for eugenol, a flavonoid present in many plants, including Tulsi.^[17] Oral treatment of fresh leaves paste of Tulsi may have the ability to prevent the early events of DMBA induced buccal pouch carcinogenesis.^[18] Leaf extract of OS blocks or suppresses the events associated with chemical carcinogenesis by inhibiting metabolic activation of the carcinogen.^[19] The anticancer activity of OS was observed in Swiss albino mice bearing Ehrlich ascites carcinoma (EAC) and S 180 tumours.^[20]

Chemopreventive activity: The chemopreventive effect of OS leaf extract is probably through the induction of hepatic/extrahepatic GST in mice. Elevated levels of reduced GSH in liver, lung and stomach tissues in OS extract supplemented mice were also found.^[21] Significant antiproliferative and chemopreventive activities were observed in mice with high concentration of OS seed oil.^[22] The potential chemopreventive activity of seed oil has been partly attributed to its antioxidant activity.^[23]

Radioprotective activity: The radioprotective effect of OS was firstly reported in the year 1995.^[24] Two isolated flavonoids, viz., orientin and vicenin from OS leaves showed better radioprotective effect as compared with synthetic radioprotectors. They have shown significant protection to the human lymphocytes against the clastogenic effect of radiation at low, non toxic concentrations.^[25] The combination of OS leaf extract with WR-2721 (a synthetic radioprotector) resulting in higher bone marrow cell protection and reduction in the toxicity of WR-2721 at higher doses, suggested that the combination would have promising radioprotection in humans.^[26]

Antioxidant activity: The antioxidant activity of OS has been reported by many workers.^[8-11] The antioxidant properties of flavonoids and their relation to membrane protection have been observed.^[27] Antioxidant activity of the flavonoids (orientin and vicenin) in vivo was expressed in a significant reduction in the radiation induced lipid peroxidation in mouse liver.^[25] OS extract has significant ability to scavenge highly reactive free radicals.^[28] The phenolic compounds, viz., cirsilineol, circimaritin, isothymusin, apigenin and rosmarinic acid, and appreciable quantities of eugenol (a major component of the volatile oil) from OS extract of fresh leaves and stems possessed good antioxidant activity.^[6]

Antihypertensive and cardioprotective activities: The transient cerebral ischemia and long term cerebral hypoperfusion (causing cellular oedema, gliosis and perivascular inflammatory infiltrate) have been prevented by OS.^[28] The OS fixed oil administered intravenously produced hypotensive effect in anaesthetized dog, which seems to be due to its peripheral vasodilatory action. Essential fatty acids like

linoleic and linolenic acids, contained in the OS oil produce series 1 and 3 (PGE1 and PGE3) prostaglandins and inhibit the formation of series 2 prostaglandins (PGE2).^[29] The long term feeding of OS offers significant protection against isoproterenol-induced myocardial necrosis in Wistar rats through enhancement of endogenous antioxidant.^[30]

Antimicrobial activity: AqE of OS showed growth inhibition for *Klesbiella*, *E. coli*, *Proteus* and *Staphylococcus aureus*; while AIE of OS showed growth inhibition for *Vibrio cholerae*.^[31] The AIE of OS was also found to be active against multidrug-resistant strains of *S. aureus* that are also resistant to common beta lactam antibiotics.^[32] Similarly, OS was found to be active against resistant *Neisseria gonorrhoea* strains.^[33] OS fixed oil showed good antibacterial activity against *Bacillus pumilus*, *Pseudomonas aeruginosa* and *S. aureus*. Higher content of linolenic acid in OS fixed oil could contribute towards its antibacterial activity.^[34]

Immunomodulatory activity: Steam distilled extract from the fresh leaves of OS showed modification in humoral immune response in albino rats which could be attributed to such mechanisms as antibody production, release of mediators of hypersensitivity reactions and tissues responses to these mediators in the target organs.^[35] OS seed oil appears to modulate both humoral and cell-mediated immune responsiveness and GABAergic pathways may mediate these immunomodulatory effects.^[36]

Central Nervous System (CNS) depressant activity: The AIE of OS prolonged the time of lost reflex in mice due to pentobarbital (40 mg/kg, ip), decreased the recovery time and severity of electroshock and pentylenetetrazole-induced convulsions. It also decreased apomorphine induced fighting time and ambulation in "open field" trials. At high doses, OS extract increased swimming time suggesting a CNS stimulant and/or antistress activity. The effect was comparable to that of desipramine, an antidepressant drug.^[37] OS fixed oil (2-3 ml/kg, ip) has been reported^[29] to increase pentobarbitone-induced sleeping time in rats. The inhibition of hepatic metabolism of pentobarbitone / renal clearance by fixed oil could be responsible for potentiation of pentobarbitone-induced sleeping time.

Antiinflammatory activity: Methanolic extract (500 mg/kg) and aqueous suspension of OS showed analgesic, antipyretic and antiinflammatory effects in acute (carrageenan-induced pedal oedema) and chronic (croton oil induced granuloma and exudate formation) inflammations in rats.^[38] The fixed oil and linolenic acid possess significant antiinflammatory activity against PGE2, leukotriene and arachidonic acid induced paw oedema in rats by virtue of their capacity to block both the cyclooxygenase and lipoxygenase pathways of arachidonic acid metabolism.^[39]

Analgesic activity: The OS oil was found to be devoid of analgesic activity in experimental pain models (tail flick, tail clip and tail immersion methods). However, it was effective against acetic acid induced writhing method in mice in a dose dependent manner. The writhing inhibiting activity of the oil is suggested to be peripherally mediated due to combined inhibitory effects of prostaglandins, histamine and acetylcholine.^[40]

Antipyretic activity: The antipyretic activity of OS fixed oil was evaluated by testing it against typhoid-paratyphoid A/B vaccine-induced pyrexia in rats. The oil on ip administration considerably reduced the febrile response indicating its antipyretic activity. At a dose of 3 ml/kg, the antipyretic activity of the oil was comparable to aspirin. Further, the fixed oil possessed prostaglandin inhibitory activity and the same could explain its antipyretic activity.^[41]

Memory enhancer activity: The AIE of dried whole plant of OS ameliorated the amnesic effect of scopolamine (0.4 mg/kg) and aging-induced memory deficits in mice. Passive avoidance paradigm served as the exteroceptive behavioural model. OS extract increased step-down latency (SDL) and acetylcholinesterase inhibition significantly. Hence, OS can be employed in the treatment of cognitive disorders such as dementia and Alzheimer's disease.^[42]

Hepatoprotective activity: Oral administration of hydroethanolic extract of OS leaves @ 200 mg/kg in male Wistar albino rats gave protection against liver injury induced by paracetamol.^[43] The cold water extract (3g/100 g, orally for 6 days) of OS was found to be effective against carbon tetrachloride (0.2 ml/100 g, subcutaneously) induced liver damage in albino rats.^[44]

Antifertility activity: Benzene extract of fresh OS leaves in male rats showed decreased total sperm count, sperm motility and weight of testis.^[45] The long term feeding (up to 3 months) of OS leaves (200 and 400 mg/kg) to adult male and female albino rats along with normal diet decreased sperm count, sperm motility and weight of male reproductive organs.^[46]

Antidiabetic activity: Oral administration of OS extract led to marked lowering of blood sugar in normal, glucose fed hyperglycemic and streptozotocin-induced diabetic rats.^[47] A randomized, placebo-controlled, cross over single blind human trial indicated a significant decrease in fasting and postprandial blood glucose levels by 17.6% and 7.3%, respectively. Urine glucose levels showed a similar trend.^[48] Further, OS has aldose reductase activity, which may help in reducing the complications of diabetes such as cataract, retinopathy, etc.^[49]

Antiulcer activity: The fixed oil of OS administered intraperitoneally elicited significant antiulcer activity against aspirin, indomethacin, alcohol (ethanol 50%),

histamine, reserpine, serotonin or stress-induced ulcers in rats.^[41] The fixed oil significantly possessed antiulcer activity due to its lipoxygenase inhibitory, histamine antagonistic and antisecretory effects.^[50]

Antiarthritic activity: The antiarthritic activity of OS fixed oil was evaluated against formaldehyde-induced arthritis in rats. The fixed oil significantly reduced the diameter of inflamed paw. On intraperitoneal administration of the fixed oil daily for 10 days, there was marked improvement in the arthritic conditions in rats. The antiarthritic effect at 3 ml/kg dose was comparable to aspirin @ 100 mg/kg, ip41. The fixed oil inhibited carrageenan and inflammatory mediators (e.g., serotonin, histamine, bradykinin and PGE2) induced inflammation. It is natural that the oil could inhibit any inflammatory response involving these mediators. The result suggests potentially useful antiarthritic activity of the inflammation models, including adjuvant as well as turpentine oil-induced joint oedema in rats.^[51]

Adaptogenic activity/antistress activity: The immunostimulant capacity of OS may be responsible for the adaptogenic action of plant.^[52] The AIE of OS whole plant increased the physical endurance (survival time) of swimming mice, prevented stress induced ulcers and milk induced leucocytosis, respectively in rats and mice, indicating induction of non-specifically increased resistance against a variety of stress induced biological changes by OS in animals.^[53]

Anticataract activity: The AqE of fresh leaves of OS delayed the process of cataractogenesis in experimental models of cataract (galactosemic cataract in rats by 30% galactose and naphthalene cataract in rabbits by 1 g/kg naphthalene). OS 1 and 2 g/kg delayed the onset as well as subsequent maturation of cataract significantly in both the models.^[3]

Anticoagulant activity: The OS fixed oil (3 ml/kg, ip) prolonged blood clotting time and the response was comparable to that obtained with aspirin (100 mg/kg). The effect appears to be due to the antiaggregator action of oil on platelets.^[29]

Toxicity: The median lethal dose (LD50) of OS fixed oil was determined after ip administration in mice. The fixed oil was well tolerated up to 30 ml/kg, while 100% mortality was recorded with a dose of 55 ml/kg. The LD50 of oil was 42.5 ml/kg. There was found no untoward effect on subacute toxicity study of OS fixed oil at a dose of 3 ml/ kg/day, ip for 14 days in rats.^[41]

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