
OCIMUM SANCTUM : An Updated Review

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ABSTRACT

Ocimum sanctum (OS) Linn (family: Labiatae) is known for its medicinal values in various traditional medicines in India and other Asian nations. Different parts of this plant have been claimed to be valuable in a wide spectrum of diseases. Leaves of OS are used in cold, cough, fever, respiratory disorders, as a tonic rejuvenator and in non-healing ulcers. Recently it has been shown that OS has antistress, antioxidant, immuno-modulatory, radioprotective, analgesic, antipyretic, antiinflammatory, anticarcinogenic, antifertility and abortifacient properties. This review describes phytochemical, pharmacognostical, pharmacological properties and clinical studies conducted on OS.

Keywords: OS; antioxidant; immunomodulator; adaptogen; anti-inflammatory.

INTRODUCTION

In recent years, scientific interest in many aspects of complementary medicine particularly in medicinal plants has increased considerably. “Chinese herbal medicines” and their Japanese counterpart “Kampo” have the largest tradition for which the most extensive data are available. In Ayurveda (an ancient system of Indian medicine), the parts of plants which are extensively used include leaves, stem, roots, seeds, flower tops and decoction of roots etc.

Ocimum sanctum (OS), holy basil or tulsi a herbal plant of family Labiatae is known for its medicinal value in various traditional medicines in India and other Asian nations particularly Ayurveda and Unani medicine. The leaves of OS are used in cold, cough, fever, respiratory disorders and non-healing ulcers etc. It has been reported that OS has antistress, antilucrerogetic, radioprotective, analgesic, antiinflammatory, nootropic, antifertility and abortifacient properties. The ethanol extract of OS leaves was found to prevent the reduction in adrenergic neurotransmitters in rat brain exposed to swimming, gravitational and restrained stress. OS has been used as tonic, rejuvenator or vitalizer to induce longevity and a disease free state. It has been proposed that it has an immunostimulant action which might be due to its adaptogenic action. Different parts of the plant have been claimed to exhibit several medicinal properties. Dried whole plant is used as a stomachic and expectorant. Leaves ground with water are applied on boils. Infusion of the leaves and roots is given in malaria, in the gastric disorders of children and in hepatic infections. The juice of the fresh leaves and slender roots is used as an antidote in snake bite and scorpion sting. The seeds are mucilaginous, demulcent in nature and are given in disorders of genitourinary system. All the parts of plant are being used without any side effects. Four varieties of Ocimum (OS, Ocimum amaricanum, Ocimum basilicum and Ocimum gratissimum) are used in traditional medicine, this review describes properties and uses of OS as ascribed in traditional medicine, phytochemical, pharmacognostical, pharmacological and clinical studies.

PHYTOCHEMICAL STUDIES

Gas liquid chromatography

Gas liquid chromatography of the essential oil of OS revealed the presence of eugenol (70%) as major constituent. Other components identified were nerol, eugenol, methyl ether, caryophyllene, terpinene, 4-ol, decylaldehyde, α-selinene, α-pinene, α-pinene, caphor and carvacrol. The leaves have also been reported to yield ursolic acid, apigenin, luteolin, apigenin-7-o-glucuronide, luteolin, 7-o-glucuronide, orientin and mrolludistin. In another study, the essential oil from different parts of OS has revealed that the leaf contained the highest percentage of oil followed by inflorescence and stem but the roots were devoid of essential oil. The oil yielded eugenol, methyl eugenol, caryophyllene and some other identified compounds. OS (old) leaves contained 3.15% calcium and 0.34% phosphorus, along with 4.97% insoluble oxalate. Roots of OS contain α-sitosterol and α triterpenes. The whole plant is reported to contain ascorbic acid, carotene, alkaloids, glycosides, sponins and tannins. Seed oils contain sitosterol, palmitic, stearic, oleic, linoleic and linolenic acids.

PHARMACOCGONOSTIC STUDIES

Various species of Ocimum were studied in detail by Gupta (1967) who reported important pharmacognostical features differentiating the leaves of OS, Ocimum americanum, Ocimum gratissimum Linn and Ocimum killimandscharicum Guerke. Morphologically, the leaf of OS is elliptic, oblong, obtuse

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or acute, subserrate or entire, pubescent and minutely gland dotted. The leaf powder is characterized by dull green or brown colour, faintly smelling like cloves and 2 types of trichomes, covering type up to 12 cells which are simple, uniseriate, unbranched and warty, while the glandular trichomes are sessile or uni-stalked, small, pear headed or globular shaped and 1-8 celled. The sessile glands are more in number. The stomata are present on both the surfaces of leaf epidermal cells, fibres are non-lignified, acutely pointed, vessels having pits of spiral and annular type are present (Gupta 1967)\(^\text{18}\). The comparative morphology of the seeds (Nutlets) of various *Ocimum* species raised in Nainital has been described by Srivastava et al.\(^\text{19}\) OS nutlets are subglobose in shape, being the smoothest of all the species. The colour varies from pale brown to dark brown with slight blackish marking on the external surface.\(^\text{19}\)

**PHARMACOLOGICAL STUDIES**

**Effects on Central Nervous System/Behavioural Effects**

Crude aqueous extract of OS has been shown to potentiate hexobarbitone induced hypnosis in mice.\(^\text{20}\) OS extract significantly decreased immobility time and the extent of the decrease was comparable to that found for imipramine but much less than that for d-amphetamine. This effect was blocked by haloperidol and sulpiride in *Ocimum* pretreated rats.\(^\text{21}\) Bromocryptine also lowered immobility time and when given with OS the effect was potentiated. OS extract decreased the immobility time in the forced swimming test compared to the control group of mice. Five days pretreatment with OS extract significantly potentiated pentobarbitone induced loss of righting reflex in mice.\(^\text{21}\) Pretreatment with OS extract increased apomorphine induced ambulation, circulatory movements, self grooming and paper biting events, while lowering the frequency and severity of fighting episodes and rearing.\(^\text{21}\) OS extract appeared to protect the animals for maximal electroshock induced convulsions in rats. The extract also protected rats from pentylenetetrazole induced clonic convulsions. Onset of convulsions was delayed and there was less mortality.\(^\text{21}\) OS treated mice were protected from amphetamine toxicity when compared to control. In open field test *Ocimum* treated mice showed a significant decrease in ambulation response but with no alteration in the stereotypic behaviour (rearing and preening). Pemminatte et al 2006 demonstrated that ethanolic extract of OS leaf (1.75, 4.25 & 8.5 mg/kg) antagonized haloperidol (1 mg/kg) induced catalepsy in mice, dose dependently. These workers suggested that OS could be used to prevent drug induced extrapyramidal side effects. OS treatment significantly prevented hypoperfusion induced functional and structural disturbances.\(^\text{22}\) Raghavendra et al\(^\text{23}\) reported that OS exhibited anxiolytic activity in an open field test. In an elevated plus maze test OS significantly alleviated ibotenic acid and choline induced anxiety and depression in the Porolt’s swim test.

**Antistress activity**

OS and few other plants are found to offer protection (adaptogenic property) against a variety of biological, physical and chemical stressors. The mechanism involved is the modulation in human immune responses by acting at various levels in immune mechanism such as antibody production, release of modulators of hypersensitivity reactions and tissue responses to these mediators on the target organs.\(^\text{24-26}\) Ethanol extract of OS has shown good antistress property in acute and chronic stress and noise induced stress.\(^\text{27,28}\) The ethanolic extract of OS leaves was found to prevent the reduction in adrenergic neurotransmission in the brain of rat exposed to swimming stress, and gravitational stress.\(^\text{2}\) OS leaf extract can reverse stress induced dendritic deficiency in the hippocampal neuron. Hence treatment with OS can help stressed animals to restore impaired learning and memory.\(^\text{29}\) Essential oil from leaves and seeds of OS showed antistress effects in rats exposed to restrained stress.\(^\text{9}\) Chronic stress is known to cause memory impairment.\(^\text{30}\) Neural basis for this impairment is neuronal injury due to excitotoxicity, alterations in neurotransmitters, increased glucocorticoids and oxidative stress.\(^\text{31}\) Treatment of stressed animals with ethanolic extract of OS has been shown to prevent the changes in plasma corticosterone induced by both acute and chronic noise stress, indicating antistress properties of OS plant. Antistress activity of OS fresh leaves (2gm per day for 3 days) has also been demonstrated by Sethi et al\(^\text{32}\) in sodium nitrite induced anaeamic hypoxia in rabbits. Studies with ursolic acid, a major constituent of OS has been shown that it protects hippocampal neurons from kainic acid injury.\(^\text{33}\)

**Learning and Memory**

Joshi and Parle\(^\text{34}\) demonstrated nootropic and antiammesic properties of OS in mice. Aqueous extract of whole plant of OS ameliorated the amnesic effect of scopolamine (0.4 mg/kg), diazepam (1 mg/kg) and aging induced memory deficits in mice. These workers suggested that beneficial effects of OS extract in the treatment of cognitive disorders such as dementia and alzheimer’s disease. Kumar et al\(^\text{33}\) demonstrated memory enhancing effects of OS plant in restraint stress induced memory impaired rats, using morriss water maze and passive avoidance task. Raghavendra et al\(^\text{23}\) demonstrated in Morris Water Maze test, OS pretreatment improved reference memory, working memory and spatial learning. Both ibotenic acid and colchicine induced deficits in active avoidance learning and retention of learned behaviour, which were significantly reversed by OS, ibotenic acid and
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Colchicine induced increased lipid peroxidase activity, which was significantly reversed by OS, and stabilized the rise in superoxide dismutase activity but it had no effect on acetylcholinesterase activity. These workers suggested that OS might be effective in clinical Alzheimer’s disease by virtue of its cognition enhancement, antidepressant and antianxiety properties.

### Antioxidant effect

Most of the disorders e.g. inflammation or pyrexia are caused by oxidative stress. Linolenic acid (an w-3-fatty acid) present in OS seed oil could act as a reducing agent/antioxidant and thereby could be responsible for the biological activity of the oil. Gupta et al demonstrated antioxidant properties of OS seed oil. Increased lipid peroxidase activity reported to reversed by OS treatment (as seen from reductions in malanondialdehyde level) and stabilized the rise in superoxide dismutase activity. Dietary supplementation of tulsi leaves (2g/day for 30 days ) has been shown to decrease MDA levels (42.4%) in rabbits. All these effects confirmed antioxidant activity of OS.

### Immunomodulatory effects

OS modulates the humoral immune responses by acting at various levels of the immune mechanisms such as antibody production, release of mediators of hypersensitivity reactions and tissue response to these mediators on the target organs. Effects of OS seed oil on some immunological parameters have been studied. A significant increase in antisheep red blood cells (RBC) antibody titre and a decrease in percentage histamine release from peritoneal mast cells of sensitive rats (humoral immune response) and decrease in foot pad thickness and percentage leucocyte migration inhibition (cell mediated immune response, was observed with OS seed oil (3 ml/kg, ip). Thus OS seed oil appears to modulate both humoral and cell mediated immune responsiveness and GABA ergic pathways may mediate these immunomodulatory effects. Godhwani et al demonstrated immuno-stimulant property of OS methanolic extract and aqueous suspension in rats.

### Chemopreventive/anticarcinogenic effects

OS protects against radiation lethality and bone marrow damage in mouse and has strong radical scavenging activity in vitro. Uma Devi & Ganasoundri reported that pretreatment with OS extract checked the radiation induced depletion of glutathione (GSH) and reduced the radiation induced lipid peroxidation in the liver of mouse. Prakash & Gupta reported chemopreventive activity of OS seed oil (100µl/kg, SC) in Swiss albino mice as evident from reduced 20-methylcholanthrene induced tumor incidence and tumor volume. Aqueous extract of OS used for ameliorating 131 iodine induced damage to the salivary gland. OS plant extract has been shown to protect against chemically induced oral cancer and the development of skin papillomas in rodents. Two flavonoids (orientin & vicenin), isolated from leaves of OS provide radioprotection when given before whole body exposure to gamma radiation. Potential chemopreventive activity of OS oil which is partly attributed to its antioxidant properties polyunsaturated fatty acids like linoleic and linolenic acid could be responsible for antioxidant effect.

Plant products are likely to suppress carcinogenesis and can act protective agent against cancer. OS leaves increased carcinogen-detoxifying enzyme glutathione-S-transferase (GST) activity by more than 70% in stomach, liver, esophagus of Swiss mice. Antiproliferative activity of seed oil of OS against the La cell in culture has been reported. Aruna & Siva Rama Krishnan demonstrated that OS significantly decreased the incidence of both benzo (a) pyrene (B(a)P) induced neoplasia and 3-methyl-4-dimethyl aminoazobenzene induced hepatoma in rats. Local application of fresh leave aqueous extract and ethanolic extract and oral administration of these extracts reduced the incidence of papillomas and squamous cell carcinoma of buccal pouch mucosa in experimental animals. Researchers have shown that OS suppresses the events associated with carcinogenesis by inhibiting the metabolic activation of carcinogens.

### Analgesic, antipyretic and anti-inflammatory activity

Analgesic activity of OS fixed oil was evaluated using tail flick, tail clip and tail immersion into hot water. The oil (3 ml/kg, ip) showed significant analgesic activity compared to morphine. OS fixed oil (3 ml/kg, ip and po) also significantly inhibited acet acid induced writhing. Analgesic activity of oil appears to be peripherally mediated and could result from the combined inhibitory effects on prostaglandins, histamine and acetylsalicylic acid also demonstrated inhibition of acetic acid induced writing in rat by using triglyceride fraction of OS seed oil.

Antipyretic activity of OS fixed oil was evaluated by testing it against typhoid-paratyphoid A/B vaccine induced pyrexia in rats. The oil (3 ml/kg, ip) administration considerably reduced the febrile response in rats indicating its antipyretic activity. Antipyreric effect of OS oil was comparable to aspirin. Antipyreric effect of OS oil could be due to its prostaglandin inhibitory activity.

The fixed oil of OS was found to possess significant anti-inflammatory activity against carrageenan and different other mediators induced paw edema in rats. Linolenic acid present in OS oil possess significant anti-inflammatory activity which has capability to block both the cyclo-oxygenase and lipo-oxygenase pathway of arachidonate metabolism. OS fixed oil also exhibited significant anti-inflammatory property against prostaglandin (PGE2) and histamine.
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**Antiarthritic activity**

Freund’s adjuvant induced arthritis model in rats was used to study the effect of OS fixed oil. OS fixed oil (3 ml/kg, ip) showed significant edema inhibition comparable to aspirin (100 mg/kg). Significant decrease in inflammation and arthritic nodes was also observed.

**Antiulcer activity**

Antiulcerogenic properties of OS after ip administration has been demonstrated in albino rats. Antiulcerogenic effect of OS was studied in pyloric ligated and aspirin treated rats. Extract of OS leaves reduced the ulcer index, free and total acidity on acute and chronic administration. OS extract increased mucous secretion. The fixed oil of OS was found to possess significant antiulcer activity against aspirin, indomethacin, alcohol, histamine, reserpine, serotonin and stress induced ulceration in experimental animal models.

**Anticataract activity**

Aqueous extract of OS leaves possess potential anticataract activity against selenite induced experimental cataractogenesis. OS fresh leaves (crushed) 1 & 2 g/kg, orally has been shown to delay the process of cataractogenesis in rats induced by 30% galactose and naphthalene.

**Effect on female reproductive system**

OS causes gross, histological and biochemical changes in male reproductive organs of experimental animals, which are responsible for its antifertility effects. Khanna et al have shown significant decrease in sperm count, motility as well as decrease in weight of testis, epididymis, seminal vesicles and ventral prostate after long term feeding of OS leaves. These workers suggested that decreased levels of testosterone directly or indirectly was responsible for decreased mating behaviour in rats. Similar findings have been reported by Seth & coworkers. Kasinathan et al demonstrated some histopathological and biochemical changes after high dose of OS leaves. They have shown adherence of spermatogonial cells in tubular lumen, poorly developed spermatid bundles with scattered sperms in tubular lumen and degenerated interstitial cells. They suggested that infertility in male rats seems to be due to impairment of spermatogenesis as well as due to physical changes such as decrease in pH of seminal vesicles. High levels of reducing substances (fructose, ergothioneine and glutathione) were estimated from tissue homogenates of testis and seminal vesicles. When concentration of these substances are increased, hypertonic environment is created which affect sperm motility adversely. Kantak and Gogte have reported decrease in sexual behavioural score in male rats who were fed with OS fresh leaves extract 200 & 400 mg/kg for 15 days. Raghunandan et al demonstrated in rabbits who were fed OS fresh leaves (1g/kg for 1 month) a degeneration of spermatogenic element and reduction in activity of GTP, a marker of sartoli cell function. They have shown degeneration of seminiferous epithelium and sartoli cells as well as reduced Leydig cell count and less number of spermatozoa.

**Effect on male reproductive system**

The leaves of OS has antizygotic, antiimplantation and early aborti facient effect in women and in the experimental animals. Long term use of OS leaves disrupts the estrous cycle and estrous stage is prolonged. Histologically it causes foldings in lumen lining of uterus with congestion and edema with increased vascularity of all the uterine walls. Number of glands increased markedly in the endometrium. Ovaries become devoid of primary and secondary follicles and
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show some large graffian follicles. Haemorrhagic corpus luteum is also seen in ovary. OS leave feeding also inhibits ovarian hormones in the rats. Early abortifacient effect of OS leave feeding was reported. Batla & coworkers\(^8\) were unable to see abortifacient effect, however, they confirmed antifertility effect of OS by showing 80% reduction in implantation site on 10\(^{th}\) day of pregnancy. Vohra et al demonstrated the absence of pregnancy in OS fed rabbits which were allowed to mate immediately after stoppage of feeding OS leaves. Some workers reported formation of vaginal plug in animals.\(^7\)

Sardessai et al\(^5\) measured the reproductive behaviour in terms of Lordosis Quotient (LQ). Lordosis behaviour is a sequence of sensorimotor reflexes and dopamine system in striatum and forebrain and is believed to inhibit the LQ. LQ was markedly decreased after administration of OS leaf extract to female rat which was postulated as the inhibition of the effect of ovarian hormone on dopamine system. Khanna et al\(^6\) demonstrated significant decrease in mating behaviour both in male and female rats, fed with OS leaves, this effect is suggested to be mediated via disturbances in LHRH surge.

**Biochemical effects**

OS leaves exhibited antithyroidic and antioxidative properties.\(^7\) OS leaf extract (0.5 g/kg for 15 days) significantly decreased serum T\(_4\) concentration, hepatic lipid peroxidation and glucose-6, phosphatase activity while activities of endogenous antioxidant enzyme superoxide dismutase (SOD) and catalase were increased.\(^2\) Researches in modern medicine have shown that administration of fresh leaves of OS has resulted in significant lowering in serum total cholesterol, triglyceride, phospholipids, LDL cholesterol levels and significant increase in HDL-cholesterol and total faecal sterol contents.\(^3\) A significant decrease in blood sugar levels after OS extracts has been shown by various workers.\(^4,7\) Sarkar & Pant\(^5\) reported that both OS leaves and seed powder significantly reduce fasting blood sugar levels in rabbit. Leaves were more effective than seed powder. Chattopadhyay\(^7\) reported that oral administration of alcoholic extract of leaves of OS led to marked lowering of blood sugar level in normal, glucose fed hyperglycemic and streptozotocin induced diabetic rats. Rai et al\(^5\) demonstrated hypoglycemic and hypolipidemic effect of OS leaf powder (fed as 1% level for 1 month) in diabetic rats. Sethi et al\(^5\) reported hypoglycemic effect after dietary supplementation of OS fresh leaves (2 g/kg, for 30 days) in rabbits. Agarwal et al\(^6\) reported results of a randomized placebo, controlled single blind trial with OS leaves in patients with NIDDM. Administration of OS leaf powder resulted in a significant decrease in fasting and postprandial blood glucose levels. The lower values of glucose represented reductions of 17.6% and 7.3% in the levels of fasting and postprandial blood glucose respectively. Mean total cholesterol level showed mild reduction during OS treatment period. Administration of 1 and 2 g OS fresh leaves (mixed with feed) and seed powder (1 & 2 g each day) in rabbits for 4 weeks exhibited significant decrease in the serum uric acid level with an increase in urinary uric acid excretion. Therefore, OS leaves and seeds exerts significant hypouricemic and uricosuric effect in rabbit.\(^8\) Ahmed et al\(^5\) showed that OS leaf extract temporarily inhibit the hypothalamic pituitary axis and thus can be utilized as a safe contraceptive.

**Antibacterial activity**

OS fixed oil showed good antibacterial activity against Staphylococcus aureus, Bacillus pumilus and Pseudomonas aerugonosa.\(^5\) Antibacterial activity of ether extract of OS leaves against E. coli, Staphylococcus aureus and mycobacterium tuberculosis has been reported.\(^6\) Geeta et al\(^5\) reported inhibition of Klebsiella, E. coli, Proteus and Staphylococcus after treatment with OS aqueous extract. Alcoholic extract inhibited Vibro cholerae and enteric pathogens. Singh et al\(^5\) reported antibacterial activity of essential oils from OS leaves against E. coli, Shigella, Salmonella typhi and Candida albicans. Ophthacare eye drop, a polyherbal preparation containing OS has been shown to be effective in acute conjunctivitis.\(^5\)

OS fixed oil showed potent antihelmintic activity in the caenor habditis elegans model.\(^6\) Essential oils of OS have also showed antifungal activity against Aspergillus niger, Rhizopus stolonifera, and Penicillium digitatum.\(^6\)

**Antiviral effect**

Crude OS leaf extract totally inhibited the infectivity of the papaya leaf reduction virus.\(^5\) The juice of OS showed potent antiviral activity against top necrosis virus of pea. The extract also reduced the infectivity of bean mosaic virus.\(^6\)

**Miscellaneous effects**

Aqueous and methanolic extracts of OS exhibited antilusive effect by central action probably mediated via both opioid system and GABA-ergic mechanisms.\(^9\) Oral administration of OS extract provided protection against mercuric chloride (HgCl\(_2\)) induced toxicity in Swiss albino mice.\(^5\) Aqueous extract of OS possessed significant wound healing and antioxidant properties which may be useful in the management of abnormal healing such as keloid and hypertrophic scars.\(^5\) Anticholinergic effect of the OS oil against acetylcholine induced contraction of rat ileum has been reported.\(^4\) Leaves and seeds of Tulsi are reported to possess diuretic and laxative properties as well.
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CLINICAL STUDIES
A commercial Ayurvedic preparation with four ingredients (OS, Allium sativum, Piper nigrum and Curcuma longa) has been claimed to have potent antimalarial activity. In a controlled clinical study undertaken on 53 patients of malaria (49 with Plasmodium vivax and 4 of P. falciparum) in rural area in south India. It is reported that the drug did not reveal any antiparasitaemic effect during one week period of observation, although there was relief in clinical symptoms in 52% of P. vivax patients and all 4 patients of P. falciparum malaria. In another trial of a preparation having Tulsi as a constituent on 32 patients of viral hepatitis, course of illness was shortened significantly in drug treated group, the clinical symptoms and biochemical parameters showing a beneficial change.

In a preliminary clinical trial on 16 patients suffering from viral encephalitis, the aqueous extract of OS has been reported to lead to a higher survival rate of patients. The incidence of residual neurological deficit in a period of one month was reported to be low in the extract treated patients.

Ophthacare eye drops contain herbs (Carum copticum, Terminalia bellirica, Emblica officinalis, Curcuma longa, OS, Rosa damascene and Cinnamomum camphora). Ophthacare was given 1-2 drops in each eye every hour for 1-2 weeks, on completion of study 40 patients reported that they were completely symptom free from acute conjunctivitis.

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