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Therapeutic Potential of *Ocimum sanctum* in Prevention and Treatment of Cancer and Exposure to Radiation: An Overview

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ABSTRACT
Extensive studies, experimental and clinical prove that Tulsi possess anti-stress/adatogenic, antioxidant, immunomodulator and anti-radiation properties which also may help it to play major role in prevention and treatment of cancer. As Tulsi has health benefitting effects by reducing stress and improving both cellular and humoral immunity, its role in prevention and treatment of cancer cases may be a new approach in therapy of cancer and in prevention of ill effects of radiation. Studies in biological models like fibrosarcoma cell culture, papilomas in the skin of albino mice, mice having sarcoma - 180 solid tumors etc. provide proof for its anticancer activity. As it has been shown that Tulsi exhibit anticancer activity in animal models, studies were carried out in human cancer *in vivo* like human cell fibrosarcoma and *in vitro* in human cervical cancer cell line (HeLa) and human laryngeal epithelial carcinoma cell line (HEp-2) and it was found effective. Thus, this review is a concise version of Tulsi's anti-cancer effect. The aim is to stimulate research in this field, prevent and treat human carcinoma by initiating detailed studies in this field. It will be a novel agent, safe and effective for humans suffering with cancer in general and as a specific agent. The research work which is going on this direction is a proof of benefits by reducing toxicity of chemo and radio therapies and providing better and healthier life style by Tulsi. Therefore, it was worthwhile to review its anticancer properties to give an overview of its status to scientist both modern and ancient (Ayurvedic).

Keywords: *Ocimum sanctum*, chemical constituents, anticancer, adaptogen/ antistress, antioxidant, anti-radiation, immunomodulator.

INTRODUCTION

Cancer is a dreaded disease which is best characterized by abnormal cell division and is caused by mutation of genes involved in the control of cell division. Cancer grows out of normal cells in the body. Normal cells multiply when the body needs them, and die when the body doesn't need them. Cancer appears to occur when the growth of cells in the body is out of control and cells divide too quickly. There are various factors involved in the genesis of cancer like toxic chemicals, excessive use of alcohol, exposure to environmental toxins, some poisonous plants like mushrooms and exposure to excessive sunlight, genetic problems, radiation, viruses, etc. However, the cause of many cancers remains unknown. The current standard approach of western medicine for treatment of cancer consists of an attempt to eradicate established tumor with combined treatment such as surgery, chemotherapy and radiation. However, this therapy has failed in many respects. In many cases it makes human life miserable and usually reduces the span of life. The patient remains sick due to toxic effects of radio and chemotherapies as these do not kill only cancer cells but normal cells also and produce low hematological picture and low immune syndromes making the patient prone to opportunistic infections, reduce strength and vitality. The failure of modern therapies has prompted complementary and alternative medicine scientists to investigate the plant derived safe and effective therapeutic agents. The present situation has become too controversial that some oncologists themselves claim that cancer is not a disease, the anaerobic cell growths are meant to absorb the toxins which kill the patients. However, by surgery, chemotherapy and radiotherapy we destroy the protective mechanism and metastasis from one organ to other organ is common. Here Andreas Moritz [1], 2008 in his book "CANCER IS NOT A DISEASE" has quoted experienced Oncologist Professor, Dr. Jones, who says "My studies have proven conclusively those cancer patients who refuse chemotherapy and radiation actually live up to four times longer than treated cases, including untreated breast cancer cases." Further, cancer as disease of toxins usually can happen 4-6 times in an

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individual's life but due to strong immune system everyone does not develop the disease. However, those whose immunity is compromised may develop this disease. In view of the above facts, herbal adaptogens/anti-stress and immunomodulators may be searched as a safe tool in the treatment of malignancy also.

The experimental studies conducted with *Ocimum sanctum* (OS) extract on fibrosarcoma cells in culture have demonstrated that *Ocimum sanctum* exhibits anticancer activity. [2] Most of the modern research on therapeutic uses of Tulsi (*Ocimum sanctum*) has confirmed that Tulsi contains hundreds of phytochemicals which possess antioxidant, adaptogenic and immune-enhancing properties. Tulsi meets the three requirements for an agent to become an adaptogen: being innocuous in nature, promotes physiological functions and induce a state of non-specific increased resistance (SNIR) in the body. Dr. Singh [3] presented its possible clinical benefits at "Continuing Education Program on Herbal Drug Research", INMAS; New Delhi (2005). The anti-radiation effect of Tulsi is particularly relevant to persons exposed to excess radiation such as working with radio- diagnosis and therapy (e.g. nuclear medicine, angiography, operation under X-ray control), receiving radiography for malignomas, working in atomic reactors and other units with exposures to radiation, high altitude solar radiation (e.g. airline personnel), TV and computer screens. Thus, Tulsi uses not only apply as an adaptogen/ antistress agent, but can safely be used in prevention of ill effects of radiation in persons exposed to various radiations [4]. As this herb has health benefitting effects by reducing stress and improving both cellular and humoral immunity, its role in prevention & treatment of cancer cases may be a new approach in therapy of cancer. This review presents studies on biological models and clinical cases for evaluation of the efficacy of OS in prevention and treatment of cancer, also its effects on radiation induced changes.

Botanical classification

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : lamiales
Family : Labiatae
Genus : Ocimum
Species : *sanctum*

Chemical constituents

Several bioactive molecules and nutrients have been found in *O. sanctum* L. The quantity of these constituents depends on the nature of soil, harvesting, processing and storage techniques. Different phytochemicals present in the plant are described below.

Essential oil from leaves [5-29]

α- Thujene, Octane, Nonane, Benzene, (Z)-3-hexanol, Ethyl 2- methyl butyrate, α-pinene, β-pinene, Toluene, citronellal, Camphene, Sabinene, Dimethyl benzene, Myrecene, Ethyl benzene, Limocene, 1,8,-cineole, cis-β-ocimene, p-cymene, Terpiniolene, Allo-oc-imene, Butyl-benzene, α-cubebene, Linalool, Eugenol, Methyl eugenol, β-elemene, (E)-cinnamy, Lactate, Isocaryophyllene, β-caryophyllene, Iso-eugenol, α-guaiene, α-amorphene, α-humulene, γ - humulene, 4,11-seinadiene, α-terpeneol, Isoborneol, Carvacrol, Borneol, germacrene-D, α—selinene, β-selinene, Myrtenylformat, α-murolene, cadinene, δ - Cuparene, Calamene, Geraneol, Nerolidol, Caryophyllene oxide, Iedol, Humulene oxide, α-guaiol, **τ** - cadinol, α- bisbolol, (EZ)-famesol, Cis-sesquisainene hydrate, Elemol, Tetradecanal, Selin-11-en-4-α-ol, 14-hydroxy-α-humulene.

Alcohalic extract of leaves / aerial parts [8, 10-12, 30-31]

Urosolic acid, Apigenin, Luteolin, Apigenin-7-O-glucuronide, Luteolin-7-O-glucuronide, Isorientin, Orientin, Molludistin, Stigmasterol, Triacontanol ferulate, Vicenin-2, Vitexin, Isovitexin, Aesculetin, Aesculin, Chlorgenic acid, Galuteolin, Circineol, Gallic acid, gallic acid methyl ester, Procatechuic acid, Vallinin acid, 4-hydroxybenzoic acid, Caffiec acid, Chlorogenic acid, Phenylpropane glucosides, β-Stigmasterol, urosolic acid.

Fixed Oil from Seeds [32-33]

Palmitric acid, Stearic acid, Linolenic acid, Oleic acid, Sitosterol, Dilinoleno-linolins, Linodilinolin, Hexourenic acid.

Mineral Content/ 100 gram [34-35]

Vit. C (83µg), Carotene (2.5µg), Ca (3.15%), P (0.34%), Cr (2.9µg), Cu (0.4µg), Zn (0.15µg), V (0.54µg), Fe (2.32µg), Ni (0.73µg).

Structure of some important bio-molecules present in *O. sanctum L.* [36]

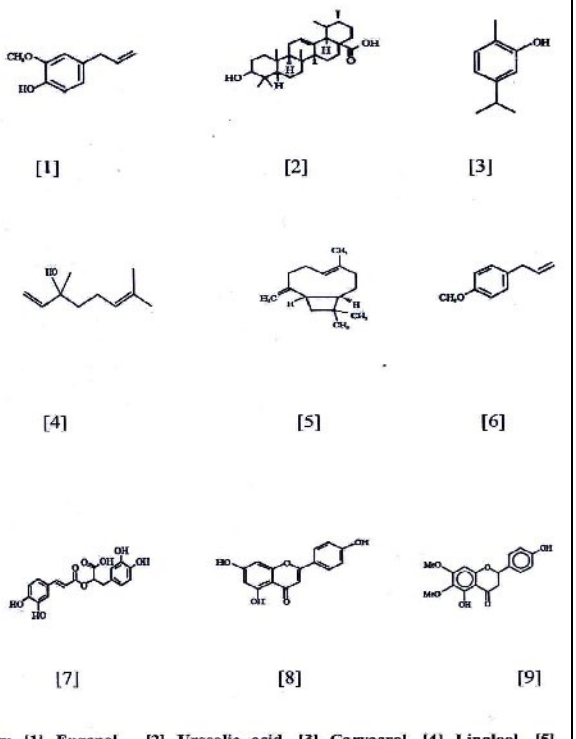

Fig: [1] Eugenol , [2] Urosolic acid, [3] Carvacrol, [4] Linalool, [5] Caryophylline, [6] Estragol, [7] Rosamarinic acid, [8] Apigenin, [9] Cirsimartin.

Anticancer property of *Ocimum sanctum*

The experimental studies carried out on biological models using OS extract on fibrosarcoma cells in culture have demonstrated that *Ocimum sanctum* exhibits anticancer activity. [2] The fresh leaf of the *Ocimum sanctum* has been shown to enhance the immunity *and* also to possess anti-carcinogenic properties in experimental animals. [37] Besides above, *Ocimum sanctum* has also been demonstrated to exhibit rejuvenating properties anti-septic and anti-allergic effects. [38] Tulsi has many beneficial properties with negligible toxicity, and is an ideal antistress/adaptogenic

agent for the promotion of health and the prevention and treatment of disease. Life without health was well described by Herophilies in 300 BC. [39] Methanolic extract of Ocimum verities have been shown to possess cancer preventive activities through reduction of excess amount of nitric oxide. [40] Tulsi has been found to decrease the incidence of benzo (a) pyrine-induced neoplasia and 3-methyl di-methyl amino azobenzene, induced hematomas in experimental animals. [41] Topical treatment with the ethanolic tulsi leave extract has been found to produce significance reduction in the values of tumor incidence (Paplliomas) in the skin of albino mice. [42] A similar activity was observed for eugenol, a flavonoid present in many plants, including Tulsi. [43] Antimetastatic activity has also been observed in ethanol extract of OS through activation of antioxidative enzymes such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) in a concentration dependent manner. [44] Kathirvel P and Ravi S [45] conducted the studies to identify the chemical composition and *in vitro* anticancer activity of the essential oil from Ocimum basilicum Linn. The major constituents were found to be methyl cinnamate (70.1%), linalool (17.5%), β-elemene (2.6%) and camphor (1.52%). The results revealed that this plant may belong to the methyl cinnamate and linalool chemotype. A methyl thiazol tetrazolium assay was used for *in vitro* cytotoxicity screening against the human cervical cancer cell line (HeLa), human laryngeal epithelial carcinoma cell line (HEp-2) and NIH 3T3 mouse embryonic fibroblasts. The IC_{50} values obtained were 90.5 and 96.3µg/ml, respectively, and the results revealed that basil oil has potent cytotoxicity.

The studies conducted to evaluate the chemopreventive potential of the seed oil of *O. sanctum* against subcutaneously injected 20-methylcholanthrene induced-fibrosarcoma tumors in the thigh region of Swiss albino mice revealed that supplementation of maximal tolerated dose (100 µl/kg body weight) of the oil significantly reduced 20-methylcholanthrene induced tumor incidence and tumor volume. Further, the enhanced survival rate and delay in tumor incidence were observed in seed oil supplemented mice. Liver enzymatic (superoxide dismutase, catalase, glutathione-*S*-transferase), non-enzymatic antioxidants (reduced glutathione) and lipid peroxidation end product, malondialdehyde levels were significantly modulated with oil treatment as compared to untreated 20-methylcholanthrene injected mice which suggests that the potential chemopreventive activity of the oil is partly attributable to its antioxidant properties. [46] Eugenol (1-hydroxy-2-methoxy-4-allylbenzene), the active constituent present in *Ocimum sanctum L.*, has been found to be largely responsible for the therapeutic potentials of Tulsi in treatment of various chronic diseases including cancer. **[47]**

Ranga *et al.* [48] observed anticancer and chemo-preventive properties of *Ocimum tanuflorum*. Topical application of *Ocimum* extract has been found to significantly reduce the cumulative number of papillomas in 7, 12-dimethylbenz (a) anthracene-induced skin papillomagenesis in rats and it was found that the ethanolic extract of leaf of ocimum inhibited the proliferation and angiogenesis related protein through the down-modulation of Bcl-2 and Vascular endothelial growth factor (VEGF) expression and over expression of capase-3 during N-methyl-N"-nitro-N-nitrosoguanidine induced gastric cancer bearing rates. [49-50] Similar effects were also noted with reduction in tumor cell size and an increase in lifespan of mice having Sarcoma-180 solid tumors. [51] Similar results were also obtained with OS in Lewis- lung carcinoma in animal models. It has been shown that the active phytochemicals namely urosolic acid and oleanlic acid present in tulsi plants have potential to exhibit anticancer property. [52] The alcoholic extract has also been shown to increase the activities of cytochrome p450, cytochrome b5, aryl hydrocarbon hydroxylase and glutathione S-transferase, which play an important role in the detoxification of carcinogens and mutagens. [49, 53] Furthermore, the anticancer activity of OS has been reported against human fibrosarcoma cells culture. The results of the study demonstrated that morphologically, the cells showed shrunken cytoplasm and condensed nuclei and the DNA was found to be fragmented on observation in agarose gel electrophoresis. [54] Several studies have shown that OS possess prominent anticancer activity. [55-58] The experimental study conducted on animal models have indicated that OS has capability to decrease the incidence of benzo(a)pyrine induced neoplasia of forestomach of mice and 3-methyl-4-dimethylaminoazobenzene induced hepatomas in rats. [59] The alcoholic extract of the leaves of OS was shown to have an inhibitory effect on chemically induced skin papillomas in mice. [60] Oral treatment of fresh leaves paste of Tulsi may have the ability to prevent the early events of 7, 12-Dimethylbenz (a) anthracene (DMBA) induced buccal pouch carcinogenesis. [61] Leaf extract of OS has been found to block or suppress the events associated with chemical carcinogenesis which might be due to inhibition of metabolic activation of the carcinogen. [49] The anticancer activity of OS was observed in Swiss albino mice bearing Ehrlich ascites carcinoma (EAC) and S 180 tumours. [62]

The ethanolic *O. sanctum* leaf extract has been found to inhibit 7, 12-dimethylbenz[a]anthracene (DMBA)-induced genotoxicity and oxidative stress by modulating xenobiotic-metabolizing enzymes, reducing the extent of lipid and protein oxidation and up-regulating antioxidant defenses. [63] Manikandan P *et al.* studied the combinatorial chemopreventive efficacy of *Azadirachta indica* (AI) and *Ocimum sanctum* (OS) against N-methyl-N'-nitro-N-nitrosoguanidine (MNNG)-induced gastric carcinogenesis, based on changes in oxidant-antioxidant status, cell proliferation, apoptosis and angiogenesis in a rat forestomach carcinogenesis model and found that AI and OS combination may be mediated by their antioxidant, antiangiogenic, antiproliferative and apoptosis inducing properties. [64]

The studies have shown that the chemopreventive effect of OS leaf extract might be mediated through the induction of hepatic/extrahepatic GST in mice. [65] Significant antiproliferative and chemopreventive activities were observed in mice with high concentration of OS seed oil. [66] The potential chemopreventive activity of seed oil has been partly attributed to its antioxidant activity. [46]

Adaptogenic/ antistress properties

OS has been found to be a powerful adaptogenic / antistress agent, helpful in preventing and reducing stress: mental, emotional, physical, and environmental stress. [67-80] The immunostimulant capacity of OS may be responsible for the adaptogenic action of plant. [38]

The experimental studies on animal models have shown that *O. sanctum* leaves produced significant increase in the levels of enzymatic (superoxide dismutase) and nonenzymatic (reduced glutathione) antioxidants which suggest that the

potential antistressor activity of *O. sanctum* is partly attributable to its antioxidant properties. [81]

Antiradiation activity

OS has the ability to protect the DNA of the body from dangerous radiation. [3, 82-83] It is significant to mention that the flavonoides namely orientin and vicenin isolated 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. [84] 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. [85]

Bhartiya US *et al.* [86] investigated radio-protective effect of aqueous extract of *O. sanctum* L. (40 mg/kg, for 15 days) in mice exposed to high doses (3.7 MBq) of oral 131 iodine by studying the organ weights, lipid peroxidation and antioxidant defense enzyme in various target organs like liver, kidney, salivary glands and stomach at 24 h after exposure. The results of the studies indicated that the pre treatment with *O. sanctum* L. in radioiodine-exposed group showed significant reduction in lipid peroxidation in both kidney and salivary glands and in liver, reduced glutathione (GSH) levels showed significant reduction after radiation exposure while pretreatment with *O. sanctum* L. exhibited less depletion in GSH level even after 131 iodine exposure. However, no such changes were observed in the stomach. The results indicate the possibility of using aqueous extract of *O. sanctum* L. for ameliorating 131 iodine induced damage to the salivary glands.

Subramanian M *et al.* [87] have observed that two polysaccharides isolated from *O. sanctum* L. have capability to prevent oxidative damage to liposomal lipids and plasmid DNA induced by various oxidants such as iron, 2,2-azobis (2-amidino-propane) dihydrochloride (AAPH) and gamma radiation. Vrinda et al. [88] reported that two water-soluble flavonoids, Orientin (Ot) and Vicenin (Vc), isolated from the leaves of *O. sanctum L.* provide significant protection against radiation, lethality and chromosomal aberration *in vivo*. The effect of aqueous extract (OE) of leaves of *O. sanctum* L. against radiation lethality and chromosome damage was studied by radiation-induced lipid peroxidation in liver and the results have shown that aqueous extract itself increased the GSH and enzymes significantly above normal level, whereas radiation significantly reduced all the values and significantly increased the lipid peroxidation rate, reaching a maximum value at 2 h after exposure (3.5 times of control). [89] In another study, the aqueous extract of OS has been found to reduce the lipid per oxidation and to accelerate recovery to normal levels in experimental animals and Ocimum flavonoids produced promising anti-radiation effects. [90] Ganasoundari *et al.* [91] investigated the radio-protective effect of the leaf extract of O. sanctum L. (OE) in combination with WR-2721 (WR) on mouse bone marrow and observed a significant decrease in aberrant cells as well as different types of aberrations. The antiradiation effect of Tulsi is particularly relevant to person exposed to excess radiation such as working with radio diagnosis and therapy (e.g. nuclear medicine, angiography, operation under X-ray control), receiving radiography for malignomas, working in atomic reactors and other units with exposures to radiation, regularly exposed to high altitude solar radiation (e.g. airline personnel), chronically exposed to TV and computer screens. Thus, Tulsi can safely be used in prevention of ill effects of radiation in persons exposed to various radiations. [4]

Antioxidant Activity

The antioxidant activity of OS has been reported by many workers. [55-58] The antioxidant properties of flavonoids and their relation to membrane protection have been observed. [92] 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. [84] OS extract has significant ability to scavenge highly reactive free radicals. [93] The phenolic compounds, viz., irsilineol, cirsimaritin, 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. [30] The antioxidant capacity of essential oils obtained by steam hydro distillation from *O. sanctum* L. was evaluated using a high-performance liquid chromatography (HPLC) based hypoxanthine/xanthine oxidase and DPPH (1,1-Diphenyl-2-picrylhydrazyl) assays and it has been observed that in hypoxanthine/ xanthine oxidase assay, strong antioxidant capacity was evident from *O. sanctum* L. [94] In another study, the aqueous extract of *O. sanctum* L. was found to significantly increase the activity of anti-oxidant. [95] Oral feeding also provides significant leaver and aortic tissue protection from hypercholestrolemia-induced peroxidative damage. [96]

Immunomodulatory Activity

The studies have demonstrated that OS has potential to modulate the humoral immune responses by acting at various levels in the immune mechanisms such as antibody production, release of mediators of hypersensitivity reactions, and tissue responses to these mediators on the target organs. [97-98] Essential oil of leaves of OS and fixed oil of tulsi seed have been shown to exhibit humoral and cell mediated immune responses in non stressed and stressed animal. [99-100] Mukherjee R *et al.* [101] have found immunotherapeutic potential of aqueous extract of *O. sanctum* L. leaf in bovine sub-clinical mastitis (SCM) which was investigated after intra-mammary infusion of aqueous extract and the results revealed that the aqueous extract of *O. sanctum* L. treatment reduced the total bacterial count and increased neutrophil and lymphocyte counts with enhanced phagocytic activity and phagocytic index. In another study, Mediratta PK *et al.* [100] have investigated the immunomodulatory effect of *O. sanctum* L. seed oil (OSSO) on some immunological parameters in both non-stressed and stressed animals and evaluated that OSSO appears to modulate both humoral and cell-mediated immune responsiveness and these immunomodulatory effects may be mediated by GABAnergic pathway.

Godhwani *et al.*[38] investigated the immunoregulatory profile of methanolic extract and an aqueous suspension of *O. sanctum* L. leaves to antigenic challenge of Salmonella typhosa and sheep erythrocytes by quantifying agglutinating antibodies employing the Widal agglutination and sheep erythrocyte agglutination tests and E-rosette formation in albino rats. The results of the study indicate an immunostimulation of humoral immunogenic response as represented by an increase in antibody titer in both the Widal and sheep erythrocyte agglutination tests as well as by

cellular immunologic response represented by E-rosette formation and lymphocytosis.

DISCUSSION

Cancer continues to be a worldwide killer despite of great advances made in modern system of medicine during the past decades. According to recent statistical data cancer is second most common cause of death after heart disease. [103] Cancer is hyper-proliferative disorder that involves transformation, dysregulation of apoptosis, proliferation, invasion, angiogenesis and metastasis. [104] The process of cancer development (carcinogenesis leading to advanced metastasized cancer) in humans takes many years through initiation, promotion and progression. Oncologists have observed that advanced metastasized cancers are almost impossible to treat. The underlying mechanism leading to cancer development is not exactly known and some oncologists even claim that cancer is not a disease, the anaerobic cell growth are meant to absorb the toxins which kill the patients. However, by surgery, chemotherapy and radiotherapy we destroy the protective mechanism and metastasis from one organ to other organ is common. Here, Andreas Moritz, 2008 in his book "CANCER IS NOT A DISEASE" has quoted experienced oncologist Professor, Dr. Jones who says "My studies have proven conclusively that cancer patient who refuse chemotherapy and radiation actually live up to four times longer than treated cases, including untreated breast cancer cases". [1] There is great potential for the use of medicinal herbs and plant derived products in the fight to prevent onset or delay the progression of the carcinogenic process.

Traditionally, Tusi leaves and decoction have been used as adaptogen helping the body and mind to adopt and cope with a wide range of physical, emotional and chemical stress, it is this property of being anti-oxidant and non specific immune stimulant, which has found a possible application as a radiation protector . Tulsi is a rich store of chemicals like eugenol, carvcnol, methyl eugenol, caryphyllene and flavonoids. Naturally a wide spectrum of therapeutic application has been found over 5000 years. Tulsi needs a comprehensive evaluation for it has immense therapeutic possibilities.

O. sanctum (Tulsi) is a well known plant grown all over India and considered scared by many Indians. Several medicinal properties have been attributed to the plant in the traditional system of medicine. [105-107] Pharmacological studies carried out by various workers [108-112] during the last few decades indicate the presence of anabolic, hypotensive, cardiac depressant, smooth muscle relaxant and anti-fertility properties in this plant. OS is well known for its other biological activities like bronchial asthma, [76, 113-114] antioxidant activities in bronchitis, [115] hypertension, [116] protection against viral encephalitis, [117] anti-ulcer, **[118]** anti-stress/ adaptogenic activity, [119-121] improvement in NIDDM (non-insulin-dependent diabetes mellitus), [122-123] protection against mouth and dental infection, [124] fatigue syndrome, [125-126] protection against tropical pulmonary eosinophilia in children, [127] antimicrobial activity against mycobacterial tuberculosis, [128] hepatoprotective activity. [129-131] The results of the studies mentioned above reflect that OS and its phytochemicals are beneficial in prevention and treatment of different kind of cancer. At clinic of International Institute of Herbal Medicine (IIHM), Lucknow, we are conducting clinical studies to evaluate the efficacy of organic Tulsi (combination of *O. sanctum* & *O. gratissimum*) in prevention and treatment of various type of cancer. It is heartening to mention that *Ocimum sanctum* and *Withania somnifera* in combination with wheat grass are providing better results in cancer patients. [132] Our clinical studies suggest its use as antistress/adaptogenic, antiulcer, liver protective, antiradiation, antidiarrheal, antiasthmatic, anti-inflammatory , antipyretic, antidiabetic, anabolic, anti-aggressive, prevention against viral encephalitis, cell mediated and humoral immune response, antifatigue, anti–AIDS, antibacterial, antitubercular, anticancer, cardiovascular, antifertility, antifilarial, antifungal, etc. [4,133- 134] Dr. Singh is first to conceive the anti-radition effects of Tulsi and initiated studies with Prof. Uma Devi, Kasturba Medical College, Maniphal, Karnataka [135] Later Prof. Uma Devi's research work showed isolated chemicals responsible for anti-radiation effects. However, Dr. Singh's holistic approach allows only whole herb for human use in radiation exposure therapy in humans as isolated chemicals may be potent but are usually toxic to human systems. Recent holocaust of nuclear hazards in Japan and may be at other places demand Tulsi use in protection of humans from the ill effects of radiation. The anti-cancer property of OS might be due to the synergistic interaction of many different active phyto-chemicals present in it and its combined multifactorial properties as described above. Further, Tulsi meets the three requirements for an agent to become an adaptogen: being innocuous in nature, promotes physiological functions and induce a state of non-specific increased resistance (SNIR) in the body. There is a great possibility of Tulsi as a holistic agent in prevention and treatment of the ill effect of nuclear holocaust or accidental exposures such as in recent crisis of nuclear leak in Japan. Although there are great possibilities of such an effect, yet, the herbs should be used in large number of such cases to prove this fact. As using this herb in no way can be harmful as it in any case improves NSIR against any disturbed physiological process. Therefore, OS being powerful immunomodulator, adaptogen/ anti- stress, antioxidant and anti-radiation agent can be used as a novel , safe and effective therapeutic agent in the treatment of human cancer as such or along with radiotherapy and chemotherapy where medicinal herb Ocimum sanctum reduces the ill effects of both and improve life span and life style. [4, 134-134] However, multicentric long term clinical studies are needed on OS to prove our contention. Further, in present time detailed anti-radiation effect of OS needs to be evaluated through in large number of cases exposed or with possibility to expose radiation. It must be studied further in electronic gadget user like X-Rays, MRI, Sonography and others.

REFERENCE

1. Moritz A. Cancer Is Not A Disease, 2nd Edition, Ener-Chi Wellness Press, USA, 2008, pp. 21-23.
2. Karthikeyan K, Gunasekaran P, Ramamurthy N, Govindasamy S. Anticancer Activity of *Ocimum sanctum*. Pharmaceutical Biology 1999; 37 (4):285-290.
3. Singh N. In the Symposium "Continuing Education Programme on Herbal Drug Research" held at Institute of Nuclear Medicine and Allied Sciences, DRDO, Delhi, India on 3-7 October 2005.
4. Singh N, Hoette Y, Miller R. Tulsi 'The Mother Medicine of Nature' 2nd Edition. International Institute of Herbal Medicine, Lucknow, 2010, pp. 28-47.
5. Phillip MP, Damodaran NP. Chemo-types of *Ocimum sanctum* Linn. Indian Perfumer 1985; 29:49-56.

6. Kothari SK, Bhattacharya AK, Ramesh S. Essential oil yield and quality of methyl eugenol rich *O. tenuiflorum* L.F. (syn *Ocimum sanctum L.*) grown in south India as influenced by method of harvest. J Chromatogr A. 2004; 1054:67-72.
7. Lawrence BM, Hogg JW, Terhune SJ, Pichitakul N. Essencial oils and their constituents. The oils of *O. sanctum* and *O. basilicum* from Thailand. Flav Industry 1972; 9:47-49.
8. Sukari MA, Rahmani M, Lee GB. Constituents of stem barks of *Ocimum sanctum*. Fitoterpia 1995; 66: 552-553.
9. Brophy JJ, Goldsack RJ, Clarkson JR. The essential oil of *Ocimum tenuiflorum* L. (Lamiaceae) growing in Nothern Australia. J Essent Oil Res. 1993; 5:459-461.
10. Nguyen H, Lemberkovics E, Tarr K, Mathe IJ, Petri G. A comperative study on formation of flavonoid, tannin, polyphenol contents in ontogenesis of *O. basilicum* L. Acta Agronomica Hungarica 1993; 42:41-50.
11. Skaltsa H, Philians S, Singh M. Phytochemical study of the leaves of *Ocimum sanctum*. Fitoterapia 1987; 8: 286.
12. Norr H, Wanger H. New constituents from *O. sanctum*. Planta Med 1992; 58:574.
13. Ravid Z, Putievsky E, Katzir I, Lewinsohn E. Enantiomeric composition of linalool in the essential oils of Ocimum species and in commercial Basil oils. Flav Frag. 1997; 12: 393-369.
14. Machado MIL, Silva MGV, Matos FJA, Craverio AA, Alencar WJ. Volatile constitution from leaves and inflorescence oil of *Ocimum tenuiflorum* L. F. (syn *Ocimum sanctum L)* grown in Northeastern Brazil. J essent oil Res. 1999; 11: 324-326.
15. Kicel A, Kurowska A, Kalemba D. Composition of the essential oil of *Ocimum sanctum* L. grown in Poland during vegetarian. J Essent Oil Res. 2005; 17:217-219.
16. Mondello L, Zappia G, Cotroneo A, Bonaccorsi L, Chowdhury JU, Yusuf M, Dugo G. Studies on the essential oil bearing plants of Bangladesh. Part 8. Composition of some Ocimum oils, *O. basilicum* L. var. purpurascens; *O. sanctum* L. green; *O. sanctum* L. Purple; *O. americanum* L., citral type; *O. americanum* L., camphor type. Flav Frag J. 2002; 17: 335-340.
17. Vina A, Murillo E. Essential oil composition from twelve varieties of basil (Ocimum spp.) grown in Colombia. J Braz Chem Soc. 2003; 14: 744-749.
18. Mondal S, Mirdha BR, Naik SN, Mahapatra SC. Antimicrobial activities of essential oils obtained from fresh and dried leaves of *O. sanctum* (L) against enteric bacteria and yeast. Editors, AK Yadav. In Proceedings of International Symposium on Medicinal and Nutraceutical Plants. Acta Hort .2007; 756; 267-269.
19. Dey BR, Choudhry M. Effect of plant development stage and some micronutrients on eugenol content in *O. sanctum* L. determination of eugenol by Folin-Ciocalteu reagent. Indian perfumer 1980; 24:199-203.
20. Dey BB, Choudhury MA. Essential oil of *Ocimum sanctum* L. and its antimicrobial activity. Indian Perfumer 1984; 28:82-87.
21. Maheshwari ML, Singh BM, Gupta R, Chien M. Essential oil of sacred Basil (*Ocimum sanctum*). Indian Perfumer. 1987; 31: 137-145.
22. Pareek SK, Maheswari ML, Gupta R. Domestication studies of *O. sanctum* for high oil and eugenol content. Indian pefumer. 1980; 24:93-100.
23. Pareek SK, maheswari ML, Gupta R. Oil content and its composition at different stages of growth in *O. sanctum* Lin. Indian Perfumer 1982; 26: 86-89.
24. Asthana OP, Gupta R. Effects of NP levels on Physiological parameters at growth stages in sacred basil (*Ocimum sanctum* Lin). Indian perfumer 1984; 28: 49-53.
25. Verma PK, Punia MS, Sharma GD, Talwar G. Evaluation of different species of Ocimum for their herb and oil yield under Haryana conditions. Indian Perfumer. 1989; 33: 79-83.
26. Gupta SC. Validation of herbage yield, oil yield and major component of various Ocimum species/ varieties (chemotypes) harvested at different stages of maturity. J Essent oil Res. 1996; 8:275-279.
27. Gupta SC. Population study and improvement of yield charecters in *Ocimum sanctum* Linn. Indian Perfumer. 1999; 36: 289-292.
28. Bhattacharya SK, Kaul PN, Rao BRR. Essential oils of *Ocimum gratissimum* L. and *Ocimum tenuiflorum* (*Ocimum sanctum* L) grown in Andhra Pradesh. Indian Perfumer 1996; 40: 73-75.
29. Raju PM, Ali M, Velasco- Negueruela A, Perez-Alonso MJ. Volatile constituents of the leaves of *Ocimum sanctum* L. J essent Oil Res. 1999; 11: 159-161.
30. Nair AGR, Gunasegaran R. Chemical investigation of certain south Indian Plants. Indian J Chem. 1982; 21 B: 979-980.
31. Skalta H, Tzakou O, Singh M. Polyphenols of *O. sanctum* from suriname. Pharmaceut Biol. 1999; 37:92-94.
32. Nadkarni GB, Patwardhan VA. Fatty oil from the seeds of *O. sanctum* Linn. (Tulsi). Cur Sci. 1952; 91: 68-69.
33. Singh S, Majumdar DK, Yadav MR. Chemical and pharmacological studies of *O. sanctum* fixed oil. Indian J Exp Biol. 1996; 34: 1212-1215.
34. Naredhirakannan RT, Subramanian S, Kandaswamy M. Mineral content of some medicinal plants used in the treatment of diabetes mellitus. Biol Trac Elem Res. 2005; 105:109-116.
35. Anonymous. Wealth of India, Publication and Information Directorate, CSIR, New Delhi, 1991, 7, pp. 79-89.
36. Rahman S, Islam R, Kamruzzaman M, Alam K, Jamal AHM. *Ocimum sanctum* L. A Review of Phytochemical and Pharmacological Profile. American Journal of Drug Discovery and Development 2011; 1-15.
37. Mondal S, Mirdha BR, Mahapatra SC. The Science behind sacredness of Tulsi (*Ocimum sanctum* Linn.). Indian J Physiol Pharmacol. 2009; 53(4): 291-306.
38. Godhwani S, Godhwani JL, Vyas DS. *Ocimum sanctum*-A preliminary study evaluating its immunoregulatory profile in albino rats. Journal of Ethnopharmacology 1988; 24: 193-198.
39. Robbins J. Losing a war we could prevent. In: Diet for a New America. Stillpoint Publishing, Meetinghouse Road Walpole, NH, 248, 1987.
40. Kim OK, Murakami A, Nakamura Y, Ohigashi H. Screening of edible Japanese plants for nitric oxide generation inhibitory activities in RAW 246.7 cells. Cancer let. 1998; 125(1-2):199-207.
41. Aruna K, Sivaramkrishnan VM. Plant products as protective agents against cancer. Ind. J. Exp. Biol. 1990; 28(11):1008-1011.
42. Prashar R, Kumar A, Banerjee S, Rao AR. Chemopreventive action by an extract from *Ocimum sanctum* on mouse skin papillomagenesis and its enhancement of skin glutathione S-transferase activity and acid soluble sulfydril level. Anticancer Drugs 1994; 5(5):567-572.
43. Sukumaran K, Unnikrishnan MC, Kuttan R. Inhibition of tumour promotion in mice by eugenol. Indian J Physiol Pharmacol. 1994; 38:306.
44. Kim SC, Magesh V, Jeong SJ, Lee HJ, Ahn KS, Lee HJ, Lee EO, Kim SH, Lee MH, Kim JH, Kim SH. Ethanol extract of *Ocimum sanctum* extracts anti metastatic activity through inactivation of matrix metalloproteinase-9 and enhancement of anti antioxidant enzyme. Food chem. Toxicol. 2010; 48(6):1478-1482.
45. Kathirvel P, Ravi S. Chemical composition of the essential oil from basil (*Ocimum basilicum* Linn.) and its *in vitro* cytotoxicity against HeLa and HEp-2 human cancer cell lines and NIH 3T3 mouse embryonic fibroblasts. Nat Prod Res. 2011; Sep 22. (Epub ahead of print).
46. Prakash J, Gupta SK. Chemopreventive activity of *Ocimum sanctum* seed oil. J Ethnopharmacol. 2000; 72 (1-2): 29-34.
47. Prakash P, Gupta N. Therapeutic uses of *Ocimum sanctum* Linn (Tulsi) with a note on eugenol and its pharmacological actions: a short review. Indian J Physiol Pharmacol. 2005; 49(2):125-31.
48. Ranga RS, Sowmyalakshmi S, Burikhanov R, Akbarsha MA, Chendil D. A herbal medicine for the treatment of lung cancer. Mol. Cell Biochem. 2005; 280: 125-133.
49. Prashar R, Kumar A, Hewer A, Cole KJ, Davis W, Phillips DH. Inhibition by an extract of *Ocimum sanctum* of DNA-binding activity of 7, 12-dimethylbenz [a] anthracene in rat hepatocytes *in vitro*. Cancer Lett. 1998; 128: 155-160.
50. Manikandan P, Letchoumy PV, Prathiba D, Nagini S. Proliferation, angiogenesis and apoptosis-associated proteins are molecular targets for chemoprevention of MNNG-induced gastric carcinogenesis by ethanolic *Ocimum sanctum* leaf extract. Singapore Med J. 2007; 48: 645-651.
51. Nakamura CV, Ishida K, Faccin LC, Filho BPD, Cortez DAG. *In vitro* activity of essential oil from Ocimum gratissimum L. against four Candida species. Res. Microbiol. 2004; 155: 579-586.
52. Singh V, Amdekar S, Verma O. *Ocimum tanuiflorum* (Tulsi): Bio-pharmacological activities. Pharmacology 2010; 1(10).
53. Govind P, Madhuri S. Medicinal plants: Better remedy for neoplasm. Indian Drug 2006; 43(11): 869-874.
54. Kathiresan K, Guanasekan P, Rammurthy N, Govidswami S. Anticancer activity of *Ocimum sanctum.* Pharmaceutical Biology1999; 37(4):285-290.
55. Madhuri S. Studies on oestrogen induced uterine and ovarian carcinogenesis and effect of ProImmu in rats. Ph.D. thesis, Rani Durgavati Vishwa Vidyalaya, Jabalpur, MP, India: 2008.

56. Madhuri S, Govind P. Effect of ProImmu, a herbal drug on estrogen caused uterine and ovarian cytotoxicity. Biomed. 2010; 5(1):57-62.
57. Govind P. An overview on certain anticancer natural products. J Pharm Res. 2009; 2(12): 1799-1803.
58. Govind P, Madhuri S. Autochthonous herbal products in the treatment of cancer. Phytomedica 2006; 7:99-104.
59. Aruna K, Sivaramakrishnan VM. Anticarcinogenic effects of some Indian plants products. Food ChemToxicol. 1992; 30:953.
60. Devi PU. Radioprotective, anticarcinogenic and antioxidant properties of the Indian holy basil, *Ocimum sanctum* (Tulasi). Indian J Exp Biol. 2001; 39:185-190.
61. Karthikeyan K, Ravichadran P, Govindasamy S. Chemopreventive effect of *Ocimum sanctum* on DMBA-induced hamster buccal pouch carcinogenesis. Oral Oncol. 1999; 35(1): 112-119.
62. Somkuwar AP. Studies on anticancer effects of *Ocimum sanctum* and *Withania somnifera* on experimentally induced cancer in mice. Ph.D. thesis, JNKVV, Jabalpur, MP, India: 2003.
63. Manikandan P, Murugan RS, Abbas H, Abraham SK, Nagini S. *Ocimum sanctum* Linn. (Holy Basil) ethanolic leaf extract protects against 7, 12-dimethylbenz (a) anthracene-induced genotoxicity, oxidative stress, and imbalance in xenobiotic-metabolizing enzymes. J Med Food 2007; 10:495-502.
64. Manikandan P, Vidjaya Letchoumy P, Prathiba D, Nagini S. Combinatorial chemopreventive effect of *Azadirachta indica* and *Ocimum sanctum* on oxidant-antioxidant status, cell proliferation, apoptosis and angiogenesis in a rat forestomach carcinogenesis model. Singapore Med J. 2008; 49 (10): 814.
65. Prashar R, Kumar A. Chemopreventive action of *Ocimum sanctum* on 2, 12- dimethylbenz (a) anthracene (DMBA) induced papillomagenesis in the skin of mice. Int J Pharmacog. 1995; 33: 181.
66. Prakash J, Gupta SK, Singh N, Kochupillai V, Gupta YK. Antiproliferative and chemopreventive activity of *Ocimum sanctum* Linn. Int J Med Biol Environ. 1999; 27:165.
67. Singh N, Gupta ML, Das M, Kohli RP. Preventive effect of some indigenous drugs on stress and aspirin induced gastric ulcer in albino rats. In the Proceeding Decennial Conference. Ind. Pharmacol. Sos, Calcutta 1977, Abstract No. 171.
68. Singh N, Nath R, Kohli RP. Experimental evaluation of adaptogenic properties of *Ocimum sanctum*. In the Proceeding Decennial Conference. Ind. Pharmacol. Sos, Calcutta 1977, Abstract No. 127.
69. Singh SP, Singh N. Experimental Evaluation of Adaptogenic Properties of *Ocimum sanctum*. Ind J Pharmacol. 1978; 10:74.
70. Bhargava KP, Singh N. Anti-stress activity of *Ocimum sanctum* Linn. Indian J Med Res. 1981:73; 443-451.
71. Srivastava AK, Singh N, Bhargava KP. "Pharmacology of Stress" Doctor of Medicine (Thesis MD), Lucknow University, India, 1984.
72. Singh N. A new concept on the possible therapy of stress disease with "adaptogen" (Anti-stress Drugs) of indigenous plant origin. Curr. Med. Prac. 1981; 25: 50-55.
73. Singh SP, Sinha KN, Singh N, Kohli RP. *Innula racemosa* (Pushkarmool), *Terminalia belerica* (Vibhitiki) and *Ocimum sanctum* (Tulsi) - A preliminary clinical trial in asthma patients. Proc. Int Sem Clin Pharmacol. Dev Count. KGMC, Lucknow, India (editors-Saxena RC, Gupta TK and Dixit KS). 1986; 1:18-21.
74. Singh N. A comperative evaluation of the effect of some species of *Ocimum sanctum* on anoxia tolerance in albino rats. 36th Ann. Cong. Med. Plant Res., Gesellschaft Fuer Arzeneipflanzenforschung, Freiburg, 1988, pp.28.
75. Singh N, Mishra N. Experimental Methods- Tools for assessment of anti-stress activity in medicinal plants. J Bio Chem Res. 1993; 12(182):124-127.
76. Dixit KS, Singh SP, Sinha KN, Singh N, Kohli RP. *Inula racemosa* (pushkarmul), *Terminalia belerica* (Vibhitki) and *Ocimum sanctum* (Tulsi) - A preliminary clinical trial in asthma patients. In Proc. Int. Sem. Clin. Pharmacol. Dev. Count. KGMC, Lucknow, India. 1986; 2:22-27.
77. Mishra N, Srivastava AK, Dixit KS, Singh N, Gupta GP. Plant drugs and biochemical changes during stress reaction. Physiology of Human Performance. In Proc. Nat. Symp. Physiol. Hum. Perfor. (editors-Sawhney RC, Sridharan K and Selvamurthy W) Publisher: Defence Institute of Physiology and Allied Science, Defence Research and Development Organization (DRDO), Govt. of India, Delhi, 1987, pp. 104-108.
78. Singh N, Misra N, Srivastava AK, Dixit KS, Gupta GP. Effects of anti-stress plants on biochemical changes during stress reaction. Ind. J. Pharmacol. 1991; 23(3):137-142.
79. Kalsi R, Singh N, Gupta GP. Effects of stress and anti-stress drugs on succinate dehydrogenase enzyme (SDH) in rat brain (A possible role of SDH in stress adaptation phenomenon). Physiology of Human Performance. In Proc. Nat. Symp. Physiol. Hum. Perfor. (editors-Sawhney RC, Sridharan K and Selvamurthy W) Publisher: Defence Institute of Physiology and Allied Science, Defence Research and Development Organization (DRDO), Govt. of India, Delhi, 1987, pp. 114-117.
80. Robbins SR, Angell M, Kumar V. Disease at the Cellular Level: Free radical Mediation of Cell injury. In: basic Pathology. 3rd edn. WS Saunders Company Philadelphia Press. Printed in Japan. Igaku-Shoin/ Saunders international Edition. 1982, pp. 9-13.
81. Jyoti S, Satendra S, Sushma S, Anjana T, Shashi S. Antistressor activity of *Ocimum sanctum* (Tulsi) against experimentally induced oxidative stress in rabbits. Methods Find Exp Clin Pharmacol. 2007; 29(6):411-6.
82. Panda S, Kar A. *O. sanctum* leaf extract in the regulation of thyroid function in the male mouse. Pharmacol Res. 1998, 38(2):107-110.
83. Devi PU, Gonasoundari A. Radioprotective effect of leaf extract of Indian Medicinal Plant *Ocimum sanctum.* Indian J Exp Biol. 1995; 33:205.
84. Devi PU, Gonasoundari A, Vrinda B, Srinivasan KK, Unnikrishanan MK. Radiation protection by the *Ocimum sanctum* flavonoids orientin and vicenin: Mechanism of action. Radiat Res. 2000; 154(4): 455-460.
85. Gonasoundari A, Devi PU, Rao BSS. Enhancement of bone marrow radioprotection and reduction of WR-2721 toxicity by *Ocimum sanctum.* Mutat Res. 1998; 397:303.
86. Bhartiya US, Raut YS, Joseph LJ. Protective effect of Ocimum sanctum L after high-dose 131iodine exposure in mice: An *in-vivo* study. Indian J Exp Biol. 2006; 44:647-52.
87. Subramanian M, Chintalwar GJ, Chattopadhyay S. Antioxidant and radioprotective properties of an *Ocimum sanctum* polysaccharide. Redox Rep. 2005; 10:257-264.
88. Vrinda B, Uma Devi P. Radiation protection of human lymphocyte chromosomes *in-vitro* by orientin and vicenin. Mutat Res. 2001; 498:39-46.
89. Devi PU, Ganasoundari A. Modulation of glutathione and antioxidant enzymes by *Ocimum sanctum* and its role in protection against radiation injury. Indian J Exp Biol. 1999; 37:262-268.
90. Devi PU, Bisht KS, Vinitha M. A comparative study of radioprotection by Ocimum flavonoids and synthetic aminothiol protectors in the mouse. Br J Radiol. 1998; 71:782-4.
91. Ganasoundari A, Devi PU, Rao BS. Enhancement of bone marrow radioprotection and reduction of WR-2721 toxicity by *Ocimum sanctum*. Mutat Res. 1998; 397:303-312.
92. Saija A, Scalese M, Lanza M, Marzillo D, Bonina F, Castelli F. Flavonoids as antioxidant agents: Importance of their interaction with biomembrane. Free Rad Biol Med.1995; 19: 481.
93. Kelm MA, Nair MG, Strasburg GM, DeWitt DL. Antioxidant and cyclooxygenase inhibitory phenolic compounds from *Ocimum sanctum* Linn. Phytomedicine 2000; 7(1):7-13.
94. Trevisan MT, Vasconcelos Silva MG, Pfundstein B, Spiegelhalder B, Owen RW. Characterization of the volatile pattern and antioxidant capacity of essential oils from different species of the genus Ocimum. J Agric Food Chem. 2006; 54:4378-4382.
95. Gupta S, Mediratta PK, Singh S, Sharma KK, Shukla R. Antidiabetic, antihypercholesterolaemic and antioxidant effect of Ocimum sanctum (Linn) seed oil. Indian J Exp Biol. 2006; 44:300-4.
96. Yanpallewar SU, Rai S, Kumar M, Acharya SB. Evaluation of antioxidant and neuroprotective effect of *Ocimum sanctum* on transient cerebral ischemia and long-term cerebral hypoperfusion. Pharmacol Biochem Behav. 2004; 79:155-64.
97. Mediratta PK, Dewan V, Bhattacharya SK, Gupta VS, Maiti PC, Sen P. Effect of *Ocimum sanctum* Linn on humoral immune responses. Indian J Med Res. 1988; 87:384-6.
98. Satayavanti GV, Raina MK, Sharma M. Medical plants of India published by ICMR, New Delhi, 1976.
99. Medrita PK, Dewan V, Bhattacharya SK, Gupta VS, Maiti PC, Sen P. Effect of *Ocimum sanctum* Linn. on humoral immune response. Ind J. Med. Res. 1987, 87:384.
100. Medrita PK, Sharma KK. Effect of essential oil of the leaves and fixed oil of the seeds of *Ocimum sanctum* on immune responses. J Med Aro Plant Sci. 2000; 22:694-700.
101. Mukherjee R, Dash PK, Ram GC. Immunotherapeutic potential of *Ocimum sanctum* (L) in bovine subclinical mastitis. Res Vet Sci. 2005; 79:37-43.

102. Mediratta PK, Sharma KK, Singh S. Evaluation of immunomodulatory potential of *Ocimum sanctum* seed oil and its possible mechanism of action. J Ethnopharmacol. 2002; 80:15-20.
103. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics. CA cancer J Clin. 2007; 57:43-66.
104. Aggarwal BB, Ichikawa H, Garodia P, Weerasinghe P, Sethi G, Bhatt ID, Pandey MK, Shishodia S, Nair MG. From traditional Ayurvedic medicine to modern medicine: identification of therapeutic targets for suppression of inflammation and cancer. Expert Opin Ther Targets. 2006; 10 (1): 87-118.
105. Kirtikar KR, Basu BD. *Ocimum sanctum* in Indian medicinal plants. 1933, 3, pp. 1965.
106. Carak Samhita (1000 B.C.) Chikitsa Sthana Section of Therapeutics, published by Ayurvedic Society of India, 1949; 3: 1278.
107. Nadkarni KM. Indian Materia Medica. Edn 3, Vol. I, Popular Prakashan, Mumbai, 1954, pp. 242-246.
108. Malviya BK, Gupta PL. Growth promoting properties of *Ocimum sanctum*. Indian J Pharmacy 1971; 33:126.
109. Singh TJ, Gupta PD, Khan SY, Misra KC. Preliminary pharmacological investigation of *O. sanctum*. India J Pharmacy 1970; 32: 93.
110. Krishnamurthy TR. Some pharmacological action of an extract of *Ocimum sanctum*. Indian J Physiol Pharmacol. 1959; 3: 92.
111. Vohra SB, Garg SK, Chowdhury RP. Effect of 6 indigenous plants on early pregnancy in albinorats. Indian J Pharmacy. 1968; 30:287.
112. Balta SK, Santhakumari G. The antifertility effect of *O. sanctum* and Hibiscus rasasinensis. Indian J med Res. 1971; 59: 777.
113. Palit G, Singh SP, Singh N, Kohli RP, Bhargava KP. Antiasthamatic potentials of *O. sanctum* and *T. belerica.* In Proc. 14th Convention Indian Coll. Aller. Appl. Immunol., 1980, pp-10.
114. Palit G, Singh SP, Singh N, Kohli RP, Bhargava KP. An experimental evaluation of Antiasthamatic plant drugs from the ancient ayurvedic medicine. Asp. Alter. Appl. Immunol. 1983; 16:36-41.
115. Siurin SA. Effects of essential oil on lipid peroxidation and lipid metabolism in patients with chronic bronchitis, Klin Med (Mosk). 1997; 75(10):43-5.
116. Singh N. A pharmaco-clinical evaluation of some Ayurvedic crude plant drugs as anti-stress agents and their usefulness in some stress diseases of man. Ann Nat Acad Ind Med. 1986; 2(1):14-26.
117. Das SK, Chandra A, Agarwal SS, Singh N. *Ocimum sanctum* (Tulsi) in the treatment of viral encephalitis (a prtelinary clinical trial). The Antiseptic 1983; 1-5.
118. Jalil A. Clinical trial of *O. sanctum (*Tulsi) in peptic ulcerand hyperacidity patients. J Res Ind Med. 1970; 4 (2):238-239.
119. Mediratta PK, Dewan V, Bhattacharya SK, Gupta VS, Malti PC, Sen P. Effect of *O. sanctum* Linn. on humoral immune response. Ind J Med Res. 1987; 87:384.
120. Singh N. A pharmaco- clinical evaluation of some ayurvedic crude plant drugs as anti stress agents and their usefulness in some stress disease of man.Ann. Nat Acad Ind Med. 1986; 2(1):14-26.
121. Singh N, Misra N. Stress disease and their possible remedy by anti-stress drugs (Adaptogens/ Staminators) of plant origin. Physiology of Human Performance. In Proc Nat Symp Physiol Hum Perfor. (Sawhney RC, Sridharan K and Selvamurthy W, eds) Publisher: Defence Institute of Physiology and Allied Science, Defence Research and Development Organization (DRDO), Govt. of India, Delhi, 1987, pp. 89-94.
122. Agarwal P, Rai V, Singh RB. Randomized placebo- controlled single blind trial of holy basil leaves in patients with non insulin-dependent diabetes mellitus. Int J Clin Pharmacol Ther. 1996; 34(9):406-409.
123. Puspangdan P, Sobti SN. Medicinal Properties of Ocimum (Tulsi) species and some recent investigation of their efficacy. Ind. Drugs 1977; 14 (11):207.
124. Patel VK, Bhatt HVK. Folklore therapeutics indigenous plants in periodontal disorder in India (review experimental and clinical approach). Int J Clin Pharmacol Ther Toxicol. 1988; 26 (4):176-184.
125. Adam US. Oceanite: A Maritime Union of India Publication, 1997; 197:37.
126. Singh N, Abbas SS. Effect of *Ocimum sanctum* (Tulsi) in sex-related chronic fatigue syndrome (SRCFS) in young Indians. J. Bio Chem Sci, 1995b, 14:184-187.
127. Sivarajan VV, Balachandran I. Tulsi. In: Ayurvedic Drugs and their Plant Sources. Oxford FBH Publishing Co. Pvt. Ltd., New Delhi, India, 1994, pp. 485- 486.
128. Gupta KC, Vishwanathan. A short note on Antitubercular substance from *Ocimum sanctum.* Antibiotic and Chemotherapy. 1955; 5:33.
129. Singh SP, Singh N. Experimental evaluation of adaptogenic properties of *Ocimum sanctum*. Ind. J. Pharmacol. 1978; 10:74.
130. Bhargava KP, Singh N. Anti-stress activity of *Ocimum sanctum* (Linn.). Ind. J. Med. Res.1981; 73:443-451.
131. Bhargava KP, Singh N. Comparative evaluation of anti-stress activity of *Eleutherococcus senticosus*, *Panax ginseng* and *Ocimum sanctum*. New Data on *Eleutherococcus Moscow (U.S.S.R),* 1984, pp. 181-89.
132. Bhalla M, Singh N. A clinical study of anticancer properties of Organic Ashwagandha, Tulsi and Wheat Grass. In the proceeding of the National Seminar- Brain Storming Session on Integrated Therapeutic Approach in the Management of Cancer, 26-27 march, 2011, Lucknow, pp.35.
133. Singh N, Hoette Y, Miller R. Tulsi 'The Mother Medicine of Nature' Ist Edn, International Institute of Herbal Medicine, Lucknow, 2002, pp. 29-42.
134. Singh N, Gilca M. Herbal Medicine – Science embraces tradition – a new insight into the ancient Ayurveda. Lambert Academic Publishing (Germany), 2010, pp. 315-322.
135. Jogetia GC, Devi PU, Singhatgeri MK, Singh N, Kohli, R.P. Proc. 56th Annual Session of National Academy of Sciences India, 1986, pp.40.