

Holy basil: A potential herbal source for therapeutic applications

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Abstract

Human dependence on plants, especially for medicinal purpose can be dated back to centuries and this reliance continues till date for various reasons such as minimal cost and easy availability in nature. *Ocimum sanctum*, commonly known as 'Holy basil' is a sacred plant with immense medicinal significance. The present review aims to summarize the holy basil research works and its therapeutic potentials. Juice extracted from the holy basil is used to cure a wide array of ailments such as cold, headache, fevers, eye and mouth disorders and holds anti-stress activity. It controls the blood cholesterol levels, thereby aids in curing cardiac disorders. Also, the plant extracts were proven to possess anti-oxidant, anti-helminthic, anti-inflammatory, anti-diabetic and anti-microbial activities. Specifically, the holy basil extracts possess anti-cancerous properties besides radioprotective properties. In addition, *Ocimum sanctum* products are also helpful to maintain immune levels. Hence, the wide spectrum of medicinal benefits and the consistent increase in demand for plant-based medicines, we have been encouraged to discover further therapeutic values of the sacred holy basil.

Key words: Holy basil, Anti-inflammatory, Anti-cancer, Anti-diabetic, Anti-oxidant, Anti-microbial

Introduction

Since time immemorial plants were given utmost importance in the field of medicine besides serving basic necessities such as food, shelter and clothing (1). The reliance continues till date for several reasons such as minimal cost, easy availability in nature and short life span of synthetic drugs. Scholars of all ages gathered huge knowledge on medicinal plants through trial and error methods which is in practice till date (2, 3). Specifically, they worked on medicinal plants and mentioned their nomenclature, healing properties and provided complex description of the interpretation of medicines. The knowledge of medicinal plants and their therapeutic properties urges the isolation of certain industrial chemicals which are useful to cure various diseases (4). The world health organization (W.H.O) estimates that a large number of people especially in developing countries still rely on traditional plant-derived drugs since they are more economical (5). In contrast, only 1% of phytochemical composition has been investigated amongst a global luxurious gene pool of plant kingdom particularly using leaves, stem, root, flowers and seeds of medicinal plants (2). Several plants are yet to be investigated for their chemical composition and medicinal properties. Generally, medicinal herbs are subjected to

rigorous chemical analysis and the bioactive components found are isolated depending on their composition. Later these compounds are evaluated through pharmacological methods using appropriate procedures, thereby increasing the utility and efficiency of these drugs (6). The pharmacological properties of medicinal plants vary with the composition of metabolites which are unique to individual species. Long back, Wink (7) reported that the feasibility of research extension in medicinal plants is possible through identifying the active principles of secondary metabolites. Parallel to the allopathic drug system, usage of about 2000 or more diversified medicinal plant species in ayurvedic and unani system of medicine has been recorded (8, 9). In addition, the plant medicines need not be sold in the form of powders, instead direct crude extracts of roots, stems and leaves are the best alternatives. Number of indigenous drug industries were established recently which supply either readymade medicines for direct use or partially processed raw material for the preparation of prescriptions (10).

Ocimum sanctum Linn. (syn. *Ocimum tenuiflorum*) commonly known as 'Holy basil' or 'Tulsi' belongs to the family Lamiaceae, which possess a number of therapeutic compounds (4). Holy basil is found in most parts of tropical and semitropical regions in the world. In India, holy basil is grown in all areas due to its countless medicinal benefits as well as its integration into the daily lives of the people, especially its use in religious ceremonies that made it sacred (6). Apart from Indian system, it is a vibrant medicinal plant in other systems of medicine in most of the countries (9, 11). Normally, the solvents used to extract the holy basil are ethanol, methanol, benzene etc. (12). Also, extracts of holy basil (EHB) are used either alone or in combination with other herbal plants to cure various diseases (13). Apart from medicinal purpose, the powdered holy basil is used to make aromatic beverages along with other herbal products in certain countries (14). The genus *Ocimum* has a number of species depending on the region it grows and possess

comparable chemical composition (15, 16). More than 150 *Ocimum* species with numerous cultivars are distributed in different regions and grow up to 6000 feet above sea level (3, 16, 17). Some of the known important species of *Ocimum* includes *O. americanum*, *O. angustifolium*, *O. basilicum*, *O. carnosum*, *O. gratissimum*, *O. minimum*, *O. serratum* etc. Holy basil is used since thousands of years for its healing properties and is often called the queen of herbs as mentioned in *Charaka Samhita* written by a legend in the field of Indian medicine (14). In the present review, several medicinal properties of holy basil are discussed in detail using different case studies.

Bioactive therapeutic components of holy basil:

Holy basil is one of the most reliable resources in the area of medical science since ancient times. Although number of compounds are isolated and characterized, however further investigations are necessary to investigate remaining compounds of holy basil and related *Ocimum* species (11, 12, 17, 18). One of the active constituents of *O. sanctum* is eugenol (2-methoxy-4-(2-propenyl) phenol), an allylbenzene class of volatile compound which is a major part in its essential oil (4). Holy basil is reported to possess ursolic acid (1*S*, 2*R*, 4*aS*, 6*aR*, 6*aS*, 6*bR*, 8*aR*, 10*S*, 12*aR*, 14*bS*)-10-hydroxy-1,2, 6*a*, 6*b*, 9, 9, 12*a*-heptamethyl-2, 3, 4, 5, 6, 6*a*, 7, 8, 8*a*, 10, 11, 12, 13, 14*b*-tetradecahydro-1*H*-picene-4*a*-carboxylic acid) and monoterpenoid phenol namely carvacrol (5-isopropyl 2-methyl phenol), as important medicinal components (Fig. 1). In addition, holy basil possess rosmarinic acid ((2*R*)-3-(3,4-dihydroxyphenyl)-2-[[{(2*E*)-3-(3, 4-dihydroxyphenyl) prop-2-enoyl] oxy} propanoic acid), linalool (3,7-dimethylocta-1,6-dien-3-ol), caryophyllene (1*R*,4*E*,9*S*)-4,11,11-trimethyl-8-methylidenebicyclo [7.2.0] undec-4-ene, terpinene-4-ol, (+) α cadinene, 3-careen, eugenol methyl ester and alpha humulene (14).

It also possess important flavonoids such as apigenin (4',5,7-trihydroxyflavone), orientin, vicenin-2, luteolin and other phytoconstituents

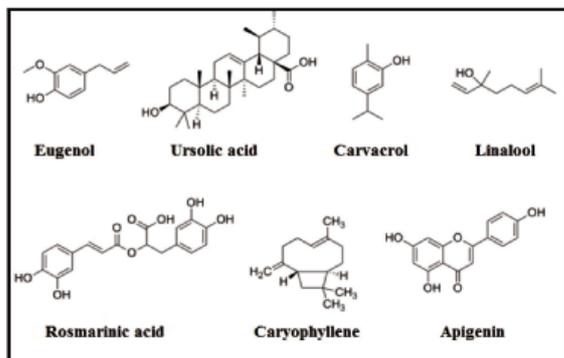


Fig. 1: Some of the therapeutic components of *Ocimum*

including cirsimaritin, á pinene, cervacrol, methylchavicol, isothymusin, isothymon, palmitric acid, vallinin, galic acid, ocimumoside A, ocimumoside B and ocimarin (9, 11, 12, 18). Different chemical compounds mentioned above exhibited mild to severe action against various diseases.

Functions of chemical components and pharmacological uses: In ancient days, without

knowing much phytochemistry, extract of holy basil was used to treat a number of diseases based on the success rate, which was mentioned in ayurveda and naturopathy (4, 6). Initially, holy basil has been used in the treatment of headache (14, 15). Later, by identifying the therapeutic compounds through advanced technology, it was established as a powerful medicinal plant. Extracts of holy basil prepared with various solvents are used to cure several diseases including common colds, cough, headache, mouth and eye disorders, diabetic, heart disorders, cancer, inflammation, other microbial diseases and different fevers as mentioned in Figure 2 (9).

Due to the presence of eugenol and linoleic acid in leaf extracts, holy basil is an excellent remedy for cough, cold and various fevers including malaria and dengue (6, 19). Similarly due to the presence of eugenol, EHB is also used to cure bronchitis. Leaf powder of Tulsi mixed with sandalwood paste is an excellent remedy against heat, headache and allied diseases (4). Holy basil is used to treat regular illnesses, fungal and

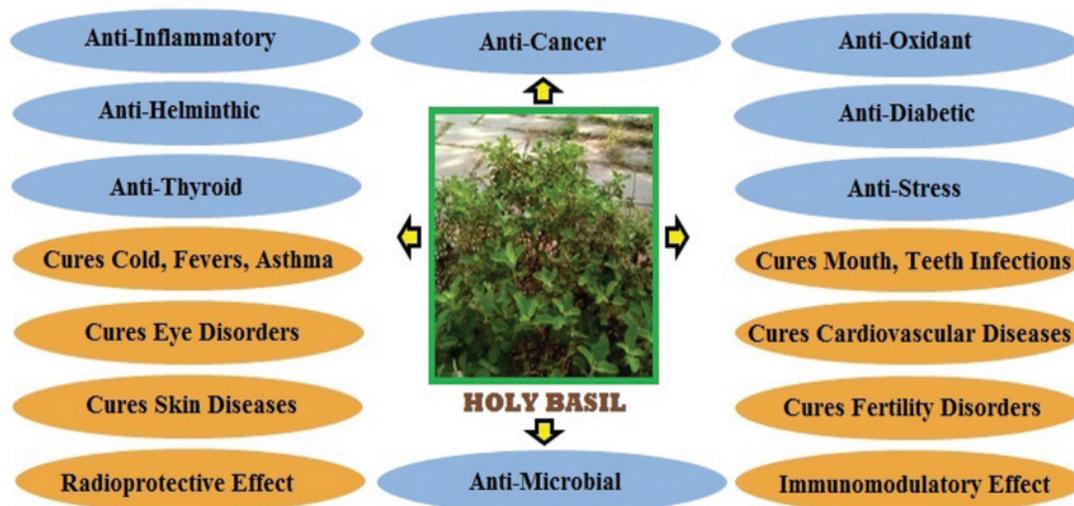


Fig. 2. Medicinal properties of holy basil. Tulsi is majorly used as anti-cancer, anti-inflammatory, anti-oxidant, anthelmintic, anti-diabetic, anti-microbial as well as other medicinal activities.

bacterial infections because of essential oil (20, 21). Also, Tulsi is used to repel insects in stored grains by mixing dried leaves due to the presence of volatile oil (22). In addition, the extract of this plant is used as repellent to control mosquitoes that often act as vectors in spreading different fever causing pathogens (23, 24). Due to the presence of ocimumosides A and B, holy basil is one of the best anti-stress agents (18). Ursolic acid, a pentacyclic triterpene acid is used to stabilize the body from certain pains and is also helpful in recovering from stress (13, 25). According to several studies, chewing holy basil leaves leads to notable changes in salivary pH and enhances the bicarbonate concentration in salivation due to the presence of essential oil, terpenes, terpenoids which includes eugenol, ursolic acid, carvacrol etc. (26). Holy basil's essential oil possess eugenol, caryophyllene and linalool that plays a key role in curing certain diseases including anti-microbial activities (6, 9). Moreover, major components of holy basil are responsible for preventing dental

problems (27, 28, 29). These compounds also improves the metabolic function, levels of immunity, lowers the stress, holds anti-oxidant property by reducing liver lipid synthesis, enhances insulin secretion and reduces inflammation (4, 6, 9, 25, 30). Singh (16) also noticed that the anti-inflammation property of Tulsi due to the presence of chemical compounds such as eugenol, apigenin, rosmarinic acid, cirsimaritin etc. Phytochemicals of holy basil alters the metabolic function, cures obesity related problems and exhibits anti-oxidant property due to the presence of eugenol, isothymusin, isothymonin, rosmarinic acid etc. (31). Mainly the presence of linoleic acid in holy basil is extremely beneficial to treat certain diseases including inflammation and inhibited various cancer cell lines proliferation (16, 32). Ursolic acid down regulates the proliferation and arrested cell cycle at G1 and G0 phases which induces apoptosis in cancer cells and suppresses the activities of nuclear factor (NF)-8B activation (9, 33). Moreover eugenol, ursolic acid, linoleic

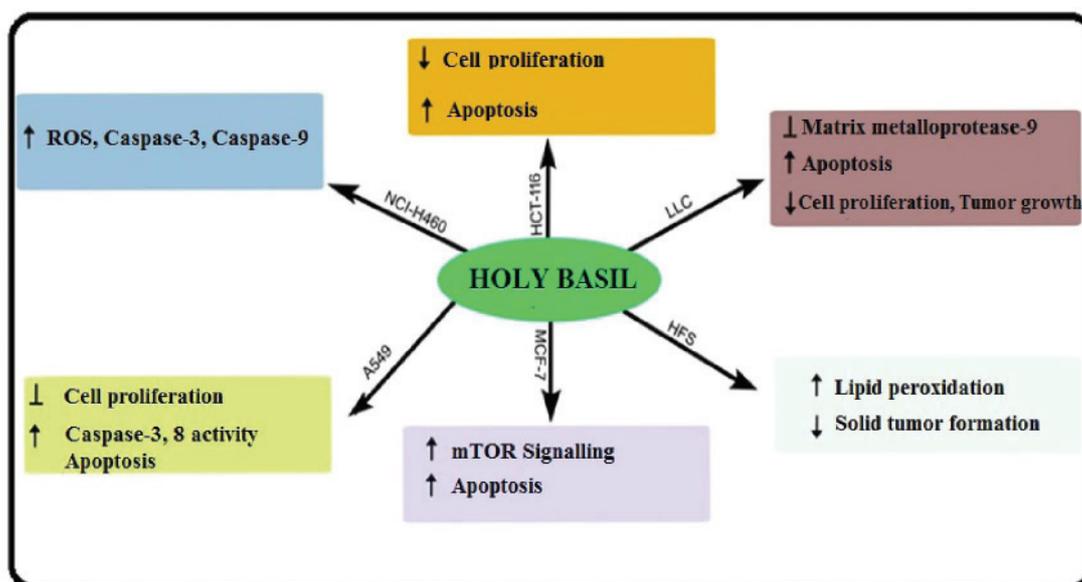


Fig. 3: Holy basil effect on various cancer cells: Holy Basil inhibits proliferation of different cancer cell lines and induces apoptosis by enhancing the ROS and Caspase 3,8 activity and down regulates tumor formation on human fibrocarcinoma and Lewis lung carcinoma models.

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acid, betulinic acid, (-)-rabbosin, vicenin-2, orientin etc., were actively involved in anti-cancerous activities (11, 12, 34).

Therapeutic properties of holy basil: The present work offers detailed information on potential therapeutic values of the holy basil. The phytochemical analysis and pharmacological investigations of *O. sanctum* has helped in the treatment of cold, fever and various respiratory ailments such as bronchitis, asthma, influenza and cough (35). Anti-dengue and anti-typhoid activities of Tulsi were recently demonstrated by Tang et al (19) and Mandal et al. (23). Leaf extracts of holy basil elevates the salivary pH and curbs the acidic environment in mouth and stomach thereby, beating ulcers (4, 36). Phytoconstituents of holy basil also prevents dental issues such as caries, plaque, bad breath etc., by mainly targeting *Streptococcus mutans* (*S. mutans*) which are responsible for tooth decay (27, 28, 37). In Ayurvedic medicine, an important poly herbal eye drop extract is prepared with *Ocimum*, *Caesalpinia*, *Jasminum* and *Cynodon* for the treatment of eye disorders and conjunctival congestion in rats as well as other animals. Holy basil is used to prepare eye drops along with Triphala, which is useful to cure cataract, glaucoma, chronic conjunctivitis and other eye-related diseases (11, 35). Further, essential oil obtained from distillation of *O. sanctum* leaves is used extensively in the pharmaceutical industry majorly in skin cream preparation (38). Tabassum and Hamdani (39) prepared a moisturizer to cure acne (skin disease) using ethanolic extract of holy basil (EEOS) as one of the ingredients along with *Andrographis paniculata*, *Glycyrrhiza glabra*, *Azadirachta indica* and green tea extracts. Due to the presence of rich anti-oxidants, ethanolic and aqueous extract of holy basil fastens wound healing in rat skin (40). Gupta et al. (18) isolated ocimunosides A and B from the leaves of holy basil, which are implicated as anti-stress agents. Treatment with Tulsi leaves in albino rats with oxidative stress showed increased superoxide dismutase and reduced glutathione indicating its anti-stressor activity (41).

Myocardial infarction (MI), also known as heart attack is one of the primary reasons for fatality due to the shortage of blood flow to heart and its muscles. Effect of hydroalcoholic extract of holy basil at different doses was investigated against isoproterenol-induced myocardial infarction in rats and found significantly reduced levels of glutathione (GSH), superoxide dismutase (SOD) and lactate dehydrogenase (LDH). The extract also inhibited lipid peroxidation with the maximum cardioprotective effect at 50mg/kg dose (42). Recently, Kavitha et al. (43) proved the relation between inflammation and myocardial infarction using Tulsi extract. Blood clotting within vessels is one of the main diseases, which leads to blood flow issues. Extract of Tulsi exhibits thrombolytic potential along with curcuma, azadirachta and anacardium (44). It was studied that extract of *O. sanctum* leaves exhibited the reversible anti-fertility effect due to the presence of key components such as eugenol (45, 46). Albino rats treated with *holy basil* extract (250 mg/kg body weight) exhibited decreased total sperm count and sperm motility as well as an increase in abnormal sperms. Withdrawal of treatment led to regaining of normal conditions within two weeks (46).

The anthelmintic or anti-parasitic activity of the essential oil of holy basil was evaluated by model *Caenorhabditis elegance* and proved that eugenol is the predominant component in putative anti-helminthic principle (47, 48). Crude aqueous and hydroalcoholic extract of *O. sanctum* showed anthelmintic activity against ovine gastrointestinal nematodes in sheep and no deleterious effect was found indicating that holy basil is safe to use (49). Various extracts of holy basil exhibited anti-inflammatory activity in different animal models (50). Eugenol, cirsilineol, cirsimaritin, apigenin and rosmarinic acid are the main compounds involved in anti-inflammatory activity (9, 35). An ethyl acetate root extract of *O. sanctum* was proved to be the best anti-inflammatory agent in carrageenan-induced paw edema model (51).

Anti-diabetic and anti-hyperlipidemic effects of hydroalcoholic extracts of holy basil have

been evaluated using diabetic rats induced by streptozotocin (STZ) and nicotinamide (52). This experiment predicts the biological activities of holy basil constituents and significantly exhibits the anti-diabetic effect compared to standard drug glibenclamide. In diabetic induced rats, oral administration of extract of Tulsi decreased the blood sugar content. Further, effects of holy basil on aldose reductase activity could help in reducing the complications of diabetes such as cataract, retinopathy etc. (53). Hypoglycemic condition was noticed when normal rats were fed with fructose and later treated with extracts of holy basil for 30 days (54). It was noticed that leaves of Tulsi reduced glucose and cortisol in serum of corticosteroid-induced diabetes mellitus. Gholap and Kar (55) unravel the possible mechanism of glucose-lowering activity of *O. sanctum* in male mice. In another study, Chattopadhyay [56] also observed the reduction of blood sugar levels with oral administration of extract of Tulsi in streptozotocin-induced diabetic rats.

Cancer is one of the most life threatening diseases across the world for several reasons. Statistically, it was estimated that about 1,665,540 new cases of cancer were expected to be diagnosed by the American Cancer Society 2019 (57). Various groups of drugs work in different ways to fight against cancer cells and shrink tumors (58). Apart from synthetic drugs, herbs and sea weeds are also useful for cancer remedy (59). The findings of Kim et al. (60) exhibited that ethanolic extract of *O. sanctum* inactivates matrix metalloprotease-9, stimulated anti-oxidant enzymes, inhibited proliferation of Lewis lung carcinoma (LLC) cells and reduced the volume of tumors in mice. Sridevi et al. (32) also reported that alcoholic root extract of Tulsi inhibited cell proliferation and induced apoptosis through enhancing intracellular reactive oxygen species (ROS) in human non-small cell lung carcinoma cell line (NCI-H460). Recently, Utispan et al. (61) proved the anti-invasive effect of ethanolic leaf extracts of holy basil on head and neck squamous cell carcinoma (HNSCC) cell line by attenuating

matrix metalloproteinase (MMP) activity. *In vitro* anti-cancer activity of holy basil has been demonstrated using human fibrosarcoma (HFS) cells. The ethanolic extract of *O. sanctum* influences lipid peroxidation and decrease the rate of solid tumor formation in tumor-bearing mice (62). Extract of holy basil enhanced anti-tumor activity through down regulating apoptosis regulator BAX and enhancing caspase-3 and cytochrome c which in turn induces apoptosis in forestomach of N-methyl N'-nitro-N-nitrosoguanidine (MNNG)-induced gastric carcinogenesis model (63). *Ocimum sanctum* inhibits proliferation of non-small cell lung carcinoma A549 and induces apoptosis by activating caspase-3 (64). Extract of Tulsi reduces the damage of DNA in normal cells and induces apoptosis in SiHa cancer cells (65). Ehrlich ascites carcinoma (EAC) mice treated with leaf extract of holy basil decreased the haemoglobin content and increased the WBC (white blood cells), which implicit that this sacred plant has high anti-neoplastic activity (66). Ethanol and acetone leaf extracts of *O. sanctum* inhibits the growth of A549 lung cancer cell line but aqueous extract does not show any anti-cancer activity (67). Flegkas et al. (68) isolated rabdosiin (terpenoid) from *O. sanctum* leaves, which induced apoptosis in HCT-116, MCF-7 and SKBR3. It also exhibited reduced cytotoxicity to normal human peripheral blood mononuclear cells. However, orientin from holy basil is non cytotoxic to human cancer cells HepG2 (69). Major cultivars of *O. sanctum* including 'rama' and 'krishna' induced apoptosis in mouth epidermal carcinoma cells (KB) (70). These results indicate that most of the holy basil possess anti-tumor properties. Figure 3 represents the anti-cancerous activity of *O. sanctum* in detail.

Thyroid diseases are generally diagnosed using radioactive iodine therapy that causes structural and functional damage to the salivary glands as a result of lipid peroxidation by reactive oxygen species (71). Aqueous extract of *O. sanctum* and its components such as orientin and vicenin significantly decreased the lipid

peroxidation, leading to membrane protection of salivary glands, thereby reducing the incidence of thyroid cancer (72). Thus, holy basil can be used as potential candidate for radioprotection against iodine induced salivary gland damage (73).

Several laboratory studies proved that *O. sanctum* protects the body against damage caused by toxic chemicals by increasing the level of anti-oxidant enzyme activities (74). These extracts initiate the anti-oxidant enzymes which protect organelles and radical membranes that are caused due to lack of oxygen and other toxic substances (75). The phytochemicals in Tulsi extract are rich in anti-oxidants, which can be used as an effective preservative in the food industry. In cadmium treated albino rats, oral administration of hydroalcoholic extract of *O. sanctum* protect cadmium damage by decreasing lipid peroxidation and by up regulating the superoxide dismutase, catalase and glutathione peroxidase activities (76). In sodium fluoride treated rats, chemical compound such as carvacrol of holy basil protect the liver tissue from fluoride toxicity and also modulates the anti-oxidant enzymes (77). Hydroalcoholic extract of *O. sanctum* down regulates the lipid peroxidation and inhibits DNA damage and reactive oxygen species generated by mitochondrial membrane in SH-SY5Y human neuronal cells (78).

Phytochemicals of holy basil have been evaluated for its radioprotective effects using different models (14, 79). Leaves of *O. sanctum* consist certain compounds such as cirsilineol, isothymusin, apigenin, rosmarinic acid, eugenol etc. were exhibited the diverse pharmacological effects, including radioprotective activity (80). In tumor-bearing animals, holy basil and other plant flavonoids were shown to have a protective effect towards normal tissue during radiation, thereby permitting the application of higher dose of radiation in order to control severe tumors (81, 82).

Ocimum sanctum acts as an important immunomodulator and exhibits great impact on human health (83). The immune system is a complex network of organs, tissues, cell types

and proteins that orchestrate collectively to protect the host from bacterial, fungal, viral and other parasitic infections as well as from tumor growth (84). Immunomodulator (biological and chemical agent) can interfere and alter the functioning pattern of immune response either through immunopotential, immunosuppression or immunological tolerance. Leaf extract of Tulsi increases the production of antibody by stimulating the humoral immune response (85, 86). Vaghasiya et al. (87) compared the alcoholic and aqueous extracts of holy basil in immune modulatory activity. It was reported that the oral administration of aqueous extract of *O. sanctum* in wistar albino rats stimulates the antibody production as compared to untreated samples and also enhanced the production of white blood cells, red blood cells and hemoglobin (88).

Benzene and methanolic extracts of holy basil combined with ampicillin inhibits the *E. coli*, *P. aeruginosa* and *S. aureus* cultures when compared to ampicillin alone (89). Similarly, alcoholic, aqueous and chloroform extracts of *O. sanctum* leaves exhibit adverse effects on *E. coli*, *S. aureus*, *P. aeruginosa* and *S. typhimurium*. Compounds of the holy basil are known to inhibit the growth of both gram-positive and gram-negative bacteria (21). Fixed oil of *O. sanctum* demonstrates anti-bacterial effect towards *B. pumilus*, *S. aureus* and *P. aeruginosa* (90). Also, aqueous extract of holy basil showed a high zone of inhibition towards *E. coli*, *Klebsiella* and *S. aureus* when compared to ethanolic extract (91). Methanolic extract of Tulsi leaves damages the growth of *V. cholerae* cells and show MBC (minimal bactericidal concentration) at 0.5-3.0 mg/ml concentration (92). Apart from above mentioned medicinal properties, ethanolic extract of Tulsi exhibited normal wound healing and dexamethasone-depressed healing properties in albino rats (93). The extract significantly stimulated the wound breaking strength, made wound epithelialize faster as compared to the control. In addition, dried powder or fresh leaf extracts of Tulsi are often consumed in various forms such as herbal

tea, which reduces the formation of stones in the kidney (3).

Need of biotechnological tools to enhance the use of holy basil: Conservation of ancient natural treasure such as holy basil and the capability to utilize it in a sustainable manner are essential for the well being and continued survival of humans (94). There are a number of constraints for systematic collection of elite *Ocimum* and its cultivars, which include variations in edaphic and climatic factors, low percentage of seed set and seasonal dormancy (4, 6). Moreover, future work on Tulsi may require more finesse to exploit additional medicinal benefits (9). The application of biotechnological techniques such as *in vitro* propagation and genetic engineering could prove to be a great benefit for low cost production of these plants with additional secondary metabolites (95). Advantage of these techniques lead to overcome seasonal dormancy. *In vitro* clonal propagation of holy basil enables large scale production of therapeutically high value taxa for commercialization and sustainable utilization in the industrial sector. In addition, it would be more beneficial if tablets could be prepared with powdered holy basil for commercial purpose.

Conclusion

Ocimum sanctum generally known as holy basil holds a set of potential phytochemicals, which possess high therapeutic properties for various diseases including cancer. Extracts of *Ocimum* have certain specificity in the treatment of cold, cough, various kinds of fevers including malaria, dengue and respiratory ailments such as bronchitis, asthma, influenza that spread extensively during particular seasons. Extracts of holy basil also work as an anti-inflammatory, anti-cancer, anti-thyroid, anti-diabetic, anti-oxidant, anti-microbial agent and is also involved in anthelmintic activities. Tulsi juice has the capacity to cure mouth and teeth infections, eye disorders as well as heart and vascular disorders. It also possesses radioprotective property and can balance the immunity levels in the human body.

Hence, studies on this sacred plant can be warranted as extremely beneficial for the human community in the field of medicine. Because of anti-viral property, Tulsi extract may be helpful to cure different viral diseases which need to confirm in near future. Likely, this review reports the therapeutic properties of holy basil in detail.

Conflict of interest

The authors declared that they have no conflict of interest.

Acknowledgements

The authors are thankful to Dr. K. Paramesh and Dr. D. Varaprasad, Yogi Vemana University, India for their technical help.

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