Phytochemistry, Pharmacology, and Applications of *Ocimum sanctum* (Tulsi)

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Abstract

Ocimum sanctum, an aromatic and medicinal herb, has gained a special importance for its pharmacological potential since time immemorial. The meaning of tulsi in Sanskrit is "Matchless" and called as queen of all the herbs. *O. sanctum* is well known for its religious, spiritual, and cultural sanctity. OS tastes pungent and bitter. Its effect is hot, light, and dry. The root, leaves, and seed of OS possess several medicinal values. Cultivation of tulsi is widely done for its uses in pharmaceutical industry, perfumery, cosmetics industry, and indigenous systems of medicine. Treatment of the several ailments has been successfully performed from the time of Ayurveda. Ayurveda classifies OS as stimulant, aromatic, and antipyretic herbs; it shows activity by alleviating kapha and vata while aggravating pitta. The special attention has been given to essential oils along with herbal extract in scientific research due to their extraordinary potential in pharmacology, aromatic flavors, and extensive traditional practice. These phytochemicals are discovered from a different class of plant secondary metabolites, namely, phenolic compounds, flavonoids, phenylpropanoids, coumarins, tannins, terpenoids, essential oils, fixed oils, and steroids as well as some vitamins and minerals. A plethora of pharmacological activities such as anticancer, antioxidant, anti-inflammatory, anti-stress, free radical scavenger, anti-diabetic, antileishmanicidal, central nervous system (CNS) depressant,

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anticoagulant, ulcer protective, antifungal, hepatoprotective, antihypertensive, cardioprotective, antiasthmatic, immunomodulatory, antifertility, antiulcer, antiviral, and antimicrobial activity have been reported for OS. The different study suggests OS have no toxic effect in humans; peoples are using its leaf and stem from traditional periods of time, so OS is safe for the treatment of diseases directly as herbal medicine or as a nutraceutical for prevention of diseases. The information and data regarding traditional uses, major chemical constituents, pharmacological potentials, clinical study, and marketed formulation of tulsi have been well explored and noted in this chapter.

Keywords

Ocimum sanctum · Medicinal herb · Phytochemistry · Pharmacological potential · Anti-cancer

Abbreviations

3-MeDAB	3′-Methyl-4-dimethylaminoazo- benzene
ABTs	2,2′-Azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) radical
ADR	Adverse drug reaction
AHH	Aryl hydrocarbon hydroxylase
ALP	Alkaline phosphate
ALT	Aminotransferase
API	Active pharmaceutical ingredients
AQOS	Aqueous extract of *Ocimum sanctum*
AST	Aspartate amino transferase
BCL-2	B-cell lymphoma 2
CAT	Catalase
CCL4	Tetrachloromethane
CD	Cluster of differentiation
CDK4	Cell division protein kinase 4
CK	Creatine kinase
c-Myc	Avian myelocytomatosis virus oncogene cellular homolog
COX	Cyclooxygenase
CYT-c	Cytochrome *c*
DM	Diabetes mellitus
DMBA	7,12-Dimethylbenz (a) anthracene
DPPH	2,2-Diphenyl-1-picrylhydrazyl.
ED_{50}	Effective dose
FBS	Fasting blood sugar level
GAD	Glutamic acid decarboxylase
GGT	Gamma-glutamyl transferase
GK	Glucokinase
GSH	*Glutathione*

GSH-Px	Glutathione peroxidase
GST	Glutathione S-transferases
GSTP1	Glutathione S-transferase pi gene
HbA1C	Hemoglobin A1c
HK	Hexokinase
hTERT	Human telomerase reverse transcriptase.
IL-1β	Interleukin 1 beta
IP	Intra-peritoneal
K_2O	Potassium oxide
LOOH	Lipid hydroperoxide or peroxide
LOX	Lipoxygenase
LPO	Lipid peroxidation
MDA	Malondialdehyde
MFC	Minimum fungicidal concentration
MGMT	Methylguanine-DNA methyltransferase
MIC	Minimum inhibitory concentration
MMP-9	Matrix metallopeptidase 9
MNNG	*N*-Methyl-*N*′-nitro-*N*-nitrosoguanidine
N	Nitrogen
NCCLS	National Committee for Clinical Laboratory Standards
NSAIDs	Non-steroidal anti-inflammatory drugs
ODC	Ornithine decarboxylase
OS	*Ocimum sanctum*
P_2O_5	Phosphorus pentoxide
pAKT	Phosphorylated-serine473-AKT
PARP	Poly (ADP-ribose) polymerase
PC	Pyruvate carboxylase
PCNA	Proliferating cell nuclear antigen
PERK	PKR-like endoplasmic reticulum kinase
PFK	Phosphofructokinase
PGE	Prostaglandin
PP2BS	Post-prandial blood sugar
pRb	Retinoblastoma protein
RDA	Recommended dietary allowance
ROS	Reduced oxide species
SDH	Succinate dehydrogenase
SOD	Superoxide dismutase
T2DM	Type 2 diabetes mellitus
TBARs	Thiobarbituric acid reactive substances
u-EGF	Epidermal growth factor family gene
USDA	United States Department of Agriculture
UTI	Urinary tract infection
UV	Ultraviolets
WHO	World Health Organization

4.1 Introduction

Having an extensive use from prehistoric time, aromatic and medicinal plants have gained attention of researchers and scientists to cure aliments. Edible plants are accepted as a potent biochemists and major sources of phytomedicine since time immemorial (Ross and Kasum 2002; Narendhirakannan and Hannah 2013). Aromatic plants with medicinal potential are increasingly used in several aromatherapy, medicinal market, perfumery, food applications, and cosmetics (Awuchi 2019). The API of most of the drugs discovered these days are found to be isolated from plant source (Mehndiratta et al. 2011). The special attention has been given to essential oils along with herbal extract in scientific research due to their extraordinary potential in pharmacology, aromatic flavors, and extensive traditional practice. A survey of WHO revealed that more than 80% patients in India, Burma, and Bangladesh are treated by traditional system of medicine using crude drug. The holy basil "tulsi" is well known for its religious and spiritual holiness. It is regarded as queen of herbs and comes under the family Labiatae (Raseetha Vani et al. 2009; Naibaho et al. 2013). The Sanskrit meaning of tulsi is "Matchless" and is very specially treated in Hindu culture (Kayastha 2014). A great importance is given to tulsi in the traditional system of medicine such as Ayurveda, Unani, and Siddha (Vogel 1997; Khurana et al. 2016). The phytochemical potential of tulsi is also mentioned in Greek and Romanian system of medicine. It is believed to have originated in India although the geographical distribution of holy basil is tropical Asia, northern and eastern part of Africa, Taiwan, Hainan Island, and certain parts of China. *Ocimum sanctum* is a plant with multiple health benefits. Tulsi is one of the most important sources of medicine. The essential oil and secondary metabolite constituents of tulsi impart extensive pharmacological potential and are suggested to be used for treatment of diarrhea, malaria, ulcer, dysentery, skin diseases, bronchitis, bronchial asthma, eye infections, chronic fever (Prakash and Gupta 2005; Kousik and Baldev 2012; Harun-Al-Rashid et al. 2013), etc. In addition *Ocimum sanctum* also exhibits anticancer, anti-diabetic, antimicrobial, antifungal, adaptogenic, and diaphoretic properties (Kousik and Baldev 2012; Harun-Al-Rashid et al. 2013). This book chapter aimed to collect and compile detail data regarding traditional uses, major chemical constituents, pharmacological potentials, clinical study, and marketed formulation of tulsi.

4.1.1 Morphology

Ocimum sanctum is an erect, perennial herb with characteristic aroma and growing up to height of 30–60 cm (Fig. 4.1). It is commonly propagated through seeds (Pandey et al. 2014). The leaves of tulsi are up to 5 cm long and simple, branched, opposite, obtuse, elliptical, oblong with dentate margin. The small hairy structures are found from the root to stem (Pattanayak et al. 2010). The flowers are small and reddish purple in color presented in compact clusters on cylindrical spikes. Fruits are

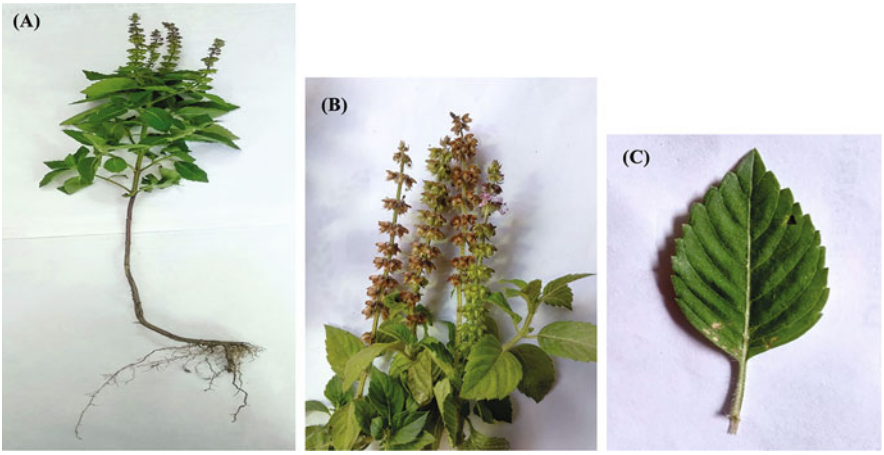

Fig. 4.1 (**a**) Tulsi plant, (**b**) flowers of tulsi, (**c**) tulsi leaf

small and when ripe seeds appear reddish yellow in color. Leaves are light green to dark purple greenish in color (Singh et al. 1996).

4.1.2 Taxonomic Classification

Kingdom: Plantae
Sub-kingdom: Tracheobionta
Super-division: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Sub-class: Asteridae
Order: Lamiales
Family: Lamiaceae
Genus: *Ocimum*
Species: *sanctum*
Binomial name: *Ocimum sanctum* L

4.1.3 Cultivation

Ocimum sanctum is a vital aromatic and medicinal plant which yields several aroma chemicals. Tulsi have wide uses in pharmaceutical industry, perfumery, cosmetics industry, and indigenous systems of medicine. Cultivation of the tulsi pant needs a favorable environment and necessary soil condition to rise into aroma-rich plant (Varghese et al. 2014). The cultivation of *Ocimum sanctum* can be well explained through below mentioned sub-heading (Vidhani et al. 2016; Saran et al. 2017):

(a) **Soil Condition**
Though *Ocimum sanctum* thrives well on a wide range of soils, it is well cultivated in saline and alkaline to moderate acidic soils with rich loam and poor laterite. For better vegetative growth of plant, well-drained soils are preferred (Böhme and Pinker 2014).

(b) **Climate**
The better plant growth with high oil content has been found in high temperature and long days. Tulsi flourishes well under light rainfall and slightly humid conditions. *Ocimum sanctum* is moderately tolerant to frost and drought (Cohen 2014).

(c) **Propagation**
Tulsi is propagated through fresh seeds. There is chance of deterioration due to high cross-pollination, and over generations of seeds, fresh seeds from pedigree stock are selected for plantings (Pattnaik and Chand 1996; Mandal et al. 2000).

(d) **Land Preparation**
The land proposed for cultivation of tulsi is well plowed and brought to fine tilth plot of convenient sizes. The recommended fertilizers of 15 t/ha as basal dose and enough farm yard manure are mixed well in soil (Selvam et al. 2013; Smitha and Tripathy 2016).

(e) **Nursery**
After the well preparation of land for cultivation, elevated seed beds (15 × 4 × 9 ft. size) are thoroughly prepared. 10 kg/bed farm yard manure and 200–300 g seeds/hectare are sown for healthy seedlings (Adhikari et al. 2014; Mridha and Rahman 2015). After sowing of seeds, the seed beds are irrigated using sprinkler hose. The seeds develop buds in 8–12 days, but the seedlings are ready to transfer in another place after 6 weeks at 4–5 leaf stage. After 15–16 days, 2% urea is sprayed before transplantation which promotes the healthy seedling growth (Anbarasan et al. 2016).

(f) **Transplanting**
Transplantation of seedling is done at 4–5 leaf stage with enough spacing for proper respiration of plants (Anbarasan et al. 2016). To get batter and high herbage with quality yield, the seedlings are transplanted at a spacing of 40 × 40 cm or 50 × 30 cm or 40 × 50 cm. Irrigation is done immediately after transplantation (Smitha et al. 2019). The gap filling and replacement of poor basils are done before the second irrigation to get uniform basil stand (Chandelia and Sharma 2011).

(g) **Manure and Fertilizer Application**
It is necessary to frequently restore the soil level to previous condition to get high oil yield. It is necessary to apply farm yard manure at 10 t/ha before planting. Freshly prepared manure and compost prepared from human excreta and city waste are avoided (Singhal et al. 2011). The best fertilizer dose recommended for tulsi cultivation is 120 kg nitrogen (N) and 60 kg P_2O_5 and K_2O per hectare, whereas 120 kg of nitrogen (N) and 105 kg each of P_2O_5 and K_2O per hectare are required for saline and alkaline soils. 50 and 100 ppm

concentration of cobalt and manganese is used as micronutrients (Vetal et al. 2013; Khan et al. 2014).

(h) **Irrigation**
The season and moisture content of soil determine the requirements of irrigation of tulsi (Tomar and Minhas 2004). One irrigation is done immediately after transplantation, and three irrigations per month are done during summer season, whereas irrigation is done as per necessity (Suthar and Saran 2020).

(i) **Weeding**
For proper growth of the plant, weeding is much more necessary. Weeds have to be removed to inhibit the competition with transplanted herb for nutrients. The first and second weeding is done after 1 month and 2 months after planting the herb. Hoeing and earthing up operation is done after the second weeding, and mulch should be used to inhibit the growth of weeds and to maintain soil moisture (Cohen 2014).

(j) **Pest Control**
Few pests and diseases affect tulsi. Thus insecticides and pesticides are used to get rid of such pests. 10,000 ppm concentration of Azadirachtin spray is used to control *Cochlochila bullita* and leaf rollers (Kamaraj et al. 2008; Shetty et al. 2008). Spraying wettable sulfur (4 g/L of water) and drenching Bavistin 1% prevent crops from *Oidium* spp.-, *Rhizoctonia solani*-, and *Rhizoctonia bataticola*-like diseases (Kamaraj et al. 2008).

(k) **Harvesting**
Harvesting of tulsi plant is done after 90–95 days of planting. The crop harvesting is recommended on bright sunny days at full bloom phase to achieve higher amount of essential oil. Tulsi is not supposed to be harvested while there was rain in the previous day (Zheljazkov et al. 2008b). To avoid contamination the herb should be cut at 15–20 cm above ground level, and the surfaces that touch with plant during and after harvest should be cleaned well. The next harvest is done at every 65–75-day interval (Zheljazkov et al. 2008a).

(l) **Expected Yield**
The expected yield of tulsi plant is found to be 5 tons per hectare after harvesting 2–3 times in a year. The whole plant contains about 0.1–0.23% of essential oil with yield of 10–23 kg per hectare (Zheljazkov et al. 2008a).

4.2 Phytochemistry of Tulsi

4.2.1 Chemical Constituents

Several medicinal uses of *Ocimum sanctum* have been discussed along a long year of human civilization. The wide variety of treatments using *Ocimum sanctum* was possible due to its complex chemical constituents. The leaves, stem, roots, inflorescence, and seeds of *Ocimum sanctum* were analyzed. Most components were found in all the plant parts but were in different concentrations. Several phytochemicals like tannins, saponins, phlobatannins, flavonoids, phenolics, terpenoids, glycosides,

Table 4.1 Summary of different phytochemicals present in *Ocimum sanctum*

S. no.	Chemical class	Phytochemical	References
1	Phenolic compound	Caffeic acid (1), chlorogenic acid (2), vanillic acid (3), ocimumnaphthanoic acid (4), methylsalicylic glucoside (5), gallic acid methyl ester (6), gallic acid ethyl ester (7), protocatechuic acid (8), 4-hydroxybenzoic acid (9), vanillin (10), 4-hydroxybenzaldehyde (11), rosmarinic acid (12), caffeic acid ester (13)	Kelm et al. (2000), Aqil et al. (2006), Prasannabalaji et al. (2012), Kaur (2014) and Narendra Babu et al. (2018)
2	Flavanoids	Isothymunin (14), isothymusin (15), cirsimaritin (16), orientin (17), isoorientin (18), isovitexin (19), vicenin (20), apigenin (21), salvigenin (22), crisilineol (23), eupatorin (24), gardenin (25)	Ali and Dixit (2012) and Baliga et al. (2013)
3	Phenyl propanoids	Eugenol (26), eugenyl-β-D-glucoside (27), citrusin C (28), ferulaldehyde (29), bieugenol (30), dehydrodieugenol (31)	Suanarunsawat et al. (2010) and Sonar et al. (2017)
4	Neolignans	Tulsinol A (32), tulsinol B (33), tulsinol C (34), tulsinol D (35), tulsinol E (36), tulsinol F (37), tulsinol G (38)	Varshney et al. (2020)
5	Coumarins	Ocimarin (39), aesculetin (40), aesculin (41)	Pandey and Madhuri (2010)
6	Steroids	B-β, β-sitosterol-3-o-β-D-glucopyranoside (42), stigmasterol (43), campesterol (44)	Kumar et al. (2010) and Pandey and Madhuri (2010)
7	Terpenes	Bornyl acetate (45), β-elemene (46), neral (47), α-pinene (48), β-pinene (49), camphene (50), ocimene (51), β-caryophyllene (52), bergamotene (53), germacrene (54), α-bisabolene (55), β-bisabolene (56)	Muthuraman et al. (2008) and Ahmad et al. (2010)

and steroids with other mineral and micronutrients were confirmed by different chemical tests of various solvent extracts (Singh and Chaudhuri 2018). The phytochemicals present in *O. sanctum* are enlisted in Table 4.1 and Fig. 4.2. Phenolic compounds are important secondary plant metabolites and show notable health benefits. These compounds play different physiological roles in plants; they are used as growth regulators and as important precursor molecules for the biosynthesis of other molecules such as lignin and suberin, which are produced as a defense

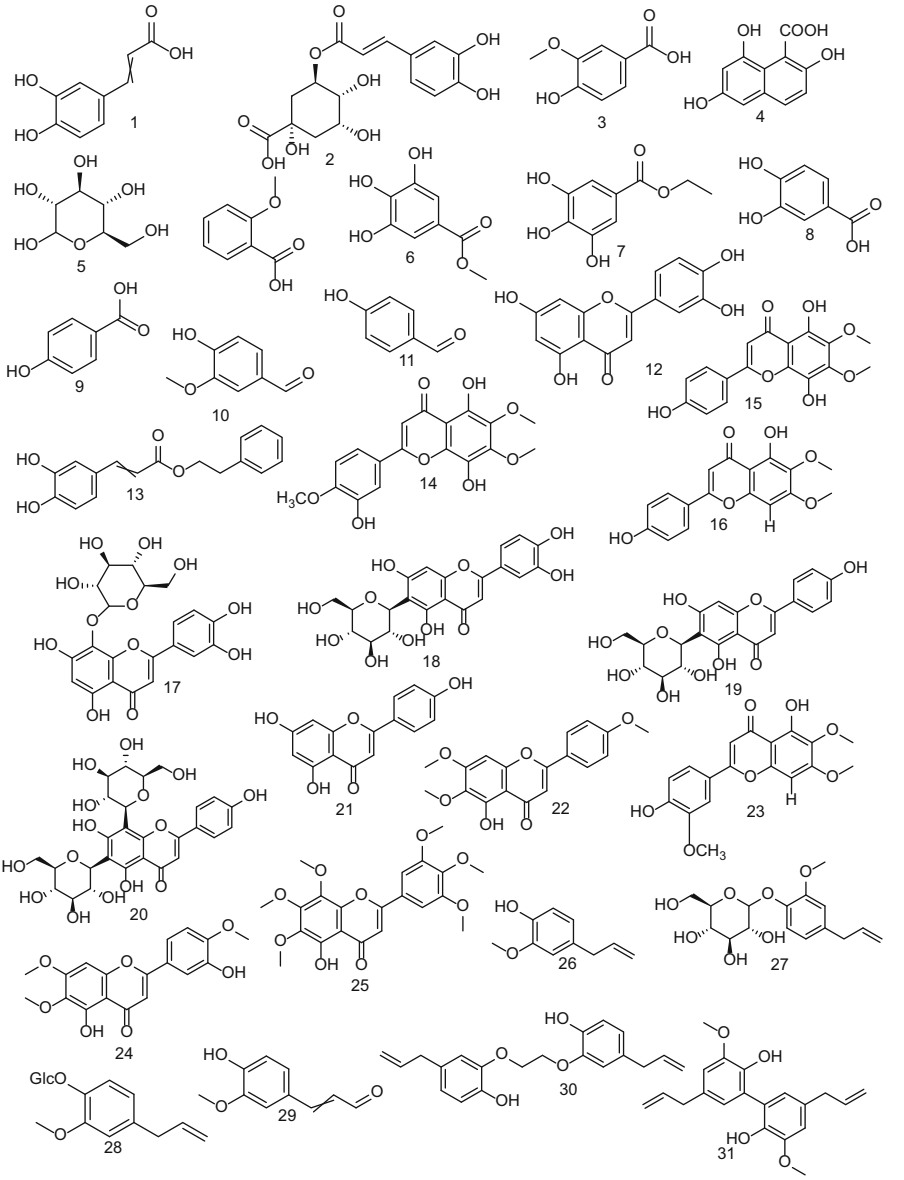

Fig. 4.2 The phytochemicals present in *O. sanctum*

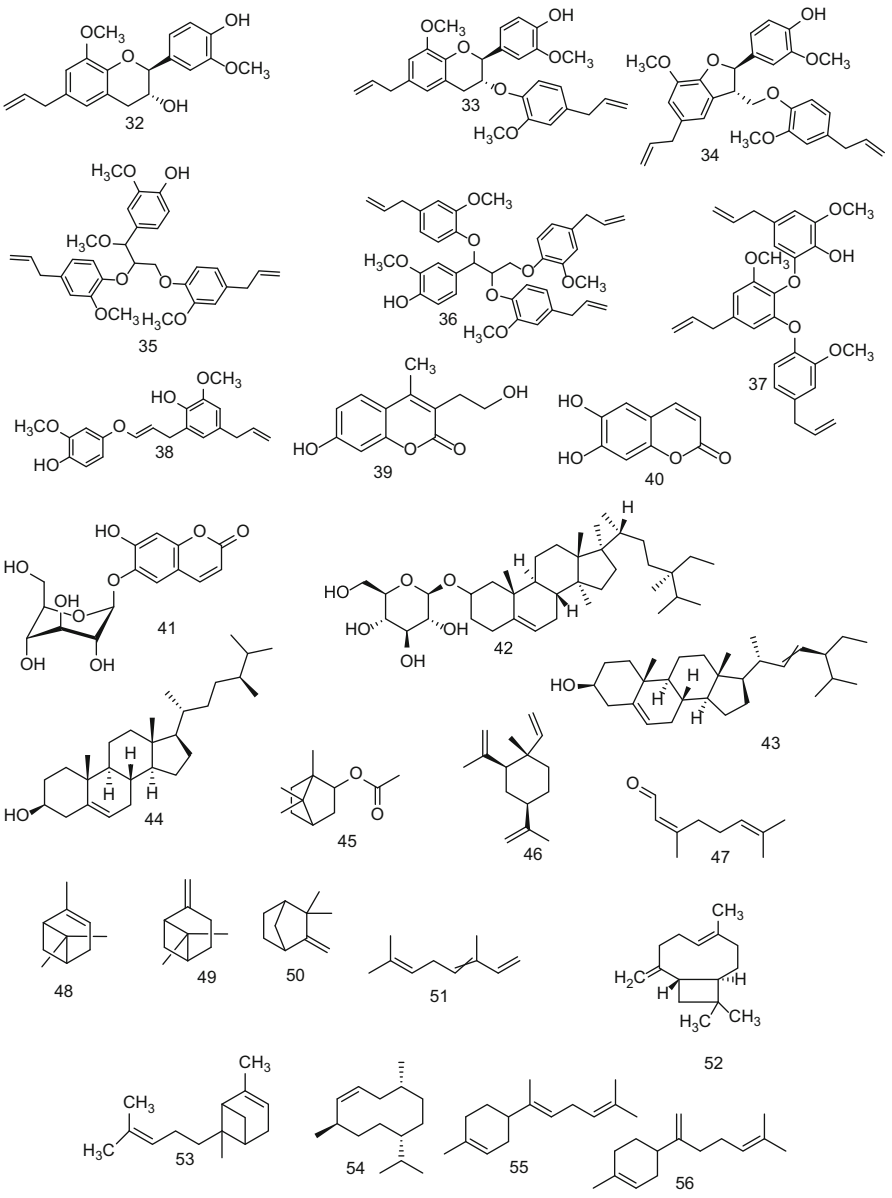

Fig. 4.2 (continued)

against different biotic and abiotic stresses. Terpenes are major constituents of essential oil (Gupta et al. 2007; Mahajan et al. 2013). They are well known for organoleptic properties in various plants. They show many ecological roles, which

include antimicrobial and allelopathic properties along with herbivorous preventive and pollinator attractant.

4.2.2 Essential Oil

Essential oils are secondary metabolites from plants and composed of mainly volatile terpenes and hydrocarbons. They have characteristic strong odor. The quality, quantity, and composition of essential oil in individual plant may vary due to the weather, soil contents, plant organ, age, and vegetative cycle stage (Pandey et al. 2014). *O. sanctum* produces a higher amount of essential oil. The volatile oil from leaves consists of eugenol ($C_{10}H_{12}O_2$) and methyl eugenol ($C_{11}H_{14}O_2$) as major contents and other constituents, namely, carvacrol ($C_{10}H_{14}O$), ursolic acid ($C_{30}H_{48}O_3$), linalool ($C_{10}H_{18}O$), and limatrol (Table 4.2). The volatile oil from seed contains sitosterol ($C_{29}H_{50}O$) and fatty acids (Garg 2005; Salles Trevisan et al. 2006; Nerio et al. 2010).

Besides the secondary metabolites, the study revealed the presence of vitamin C, calcium, and phosphorous along with other micronutrients.

4.3 Ethnobotanical/Traditional Uses

Ocimum sanctum known as tulsi belongs to the Laminaceae family, the and plant is very important because of their healing potentials. OS is medicinally important herb, and it was well known for its medicinal activity from ancient periods of time. OS has been well described for its therapeutics and medicinal activity in Ayurveda and explained as Dashemani Shwasaharni (anti-asthmatic) and anti-kaphic drug (Kaphaghna). In Hindu culture *Ocimum sanctum L.* is sacred, and our ancestors used medicinal plants in daily life in south Asia to treat various illnesses (Gupta et al. 2014). Tulsi is well known as "The incomparable One," "Mother Medicine of the nature," and "The Queen of the Herbs" and is respected as "elixir of life." As tulsi is found to be rich in aromatic nervine essential oils, it is a great choice to sooth the nervous system and support our body's ability to respond the stress. Different parts

Table 4.2 List of bio-active essential oil present in *O. sanctum*

S. no.	Compounds	References
1	Eugenol ($C_{10}H_{12}O_2$)	Pandey et al. (2014) and Salles Trevisan et al. (2006)
2	Methyl eugenol ($C_{11}H_{14}O_2$)	Pandey et al. (2014) and Salles Trevisan et al. (2006)
3	Carvacrol ($C_{10}H_{14}O$)	Pandey et al. (2014) and Garg (2005)
4	Ursolic acid ($C_{30}H_{48}O_3$)	Pandey et al. (2014) and Nerio et al. (2010)
5	Linalool ($C_{10}H_{18}O$)	Pandey et al. (2014) and Nerio et al. (2010)
6	Limatrol	Pandey et al. (2014) and Salles Trevisan et al. (2006)
7	Sitosterol ($C_{29}H_{50}O$)	Pandey et al. (2014), Garg (2005) and Nerio et al. (2010)

Table 4.3 Illustrating ethnobotanical use of tulsi

S. no.	Preparations/parts used	Traditional use
1	Aqueous decoction of tulsi leaves	Treatment of gastric and hepatic disorder
2	Herbal preparation with tulsi whole plant	Symptomatic treatment of viral hepatitis
3	Mixed juice of tulsi with triphala	Use as eye drop for glaucoma, cataract, chronic conjunctivitis
4	Juice of leaves of tulsi	Treatment of chronic fever, dysentery, hemorrhage, and dyspepsia
5	Decoction of tulsi leaves	Remedy for cold
6	Tulsi leaves (crude)	To treat vomiting and used as anthelmintic and antidote for dog bite, scorpion bite, and insect bite
7	Fresh tulsi leaves with pepper	Use as a prophylactic against malaria in the morning time
8	Ayuverdic preparation containing *Ocimum sanctum* L., *Allium sativum*, *Piper nigrum*, and *Curcuma longa*	Antimalarial against *Plasmodium falciparum* and *Plasmodium vivax*
9	Decoction of root of tulsi	Use as a diaphoretic in malarial fever
10	Aqueous decoction of whole plant	Use as anti-diabetic to lower the blood sugar level
11	Paste of tulsi leaves	Treatment of ring worm and other skin diseases
12	Fresh leaves and flower tops of *Ocimum sanctum*	Used as smooth muscle relaxant
13	Seed of tulsi (crude)	Treatment of disorder of genitourinary system

like leaves, flowers, stem, root, seeds, etc. of tulsi plant have been used by traditional experts as expectorants, pain reliever, antiasthmatic, antiemetic, diaphoretic, anti-diabetic, hypotensive, antistress, anticold, stomachic etc. (Pandey and Madhuri 2010). The contemporary preparations of this sacred plant are herbal tea, decoction of leaves, powder in dry form, and preparation of fresh leaves with honey or ghee. The traditional or ethnobotanical use of tulsi (Table 4.3) can be well summarized in points (Mallikarjuna et al. 2011; Bhattacharyya and Bishayee 2013; Kumar et al. 2013; Gupta et al. 2014):

- It is applied on affected surface to reduce swelling and pain.
- Tulsi is effective in various skin disorders. Traditionally people use its paste to treat rashes, insects' bites, and itching. Tree or whole plant is used in ring worm infections and also leukoderma (Gupta et al. 2014).
- Freshly prepared juice of *OS* is applied in nasya karma to get relief from headache and disease of the head and neck.
- Leaf extract is used for cosmetic purpose to reduce scars, acne, and pimples.
- It is used to treat indigestion, constipation, and intestinal parasite.
- Dry and crush leaves of tulsi are very efficient to cure fever and lower respiratory tract problems.

- Traditionally it is efficiently employed as cardiac tonic and blood purifier.
- It has been used as mild aphrodisiac to treat impulsive ejaculation.
- People use it as anti-diabetic, hepatoprotective, and hypolipidemic agent from very ancient time.
- Fresh juice obtained after crushing the leaves of tulsi is widely used for myringitis (inflammation in internal ear).
- The leaves of *Ocimum sanctum* have been widely used to stop bleeding, cure eye diseases, and heal wounds in ruminants.

4.4 Pharmacological Potential

Several scientific studies have discovered plethora of pharmacological potential of tulsi extract (steam distilled, pet. Ether extract, benzene extract) on the various systems like cardiovascular system, immune system, CNS, gastric system, and urinary system (Joshi et al. 2013). Exploring the literatures and scientific researches, it is found that tulsi shows a unique pharmacological activity that promotes health and resilience. Tulsi was used as potent adaptogens from ancient time in India which helps to relieve from the stress and the promotion of homeostasis (Cohen 2014). After much more study, it is shown that tulsi undeniably possess many pharmacological potentials. Various study shows that OS has a unique combination of actions that include antimicrobial, mosquito repellent, anti-diarrhea, antioxidant, anti-cataract, chemoprevention, radioprotection, hepatoprotection, neuroprotection, cardioprotection, anti-diabetic, anti-hypercholesterolemia, anti-hypertensive, anti-carcinogenic, analgesic, anti-pyretic, anti-inflammatory, anti-allergic, immunomodulatory, central nervous system stress, memory enhancement, anti-asthmatic, anti-tussive, diaphoretic, anti-thyroid, antifertility, antiulcer, anti-emetic, anti-spasmodic, antiarthritic, anti-stress, anti-leukodermal, and anti-coagulant activities (Buddhadev et al. 2014; Chandra and Abad Farooq 2014; Hussain et al. 2017).

4.4.1 Stress Resilience

Ocimum sanctum has been documented for extensive stress resilience in modern medicinal and pharmacognostic researches and studies. It has been found that tulsi possesses a potent adaptogenic properties (Mahdi et al. 2003). Preclinical studies have shown that *Ocimum sanctum* avoids stress-induced ulcer in rats in comparison to antidepressant drugs. It was found that tulsi plant extract exhibits anti-stress activity in albino rats by improving SDH level (Singh et al. 2012c). The abovementioned pharmacological potentials help the mind to cope up with several variety of chemical, physical, infectious, and emotional stress to reestablish psychological as well as physiological functions. Chewing 12 leaves of tulsi twice a day helps a person to get efficient relief from stress (Jothie Richard et al. 2016).

4.4.2 Anti-diabetic Potential

Diabetes is a metabolic disorder where level of sugar is increased in blood either because pancreatic β-cells are unable to produce sufficient insulin or because the body system is unable to respond to the insulin produced by the body. Tulsi is reported as anti-diabetic in many researches and studies. It is found to be much more effective in diabetes mellitus. Consumption of aqueous decoction of whole plant lowers the blood sugar level (Patil et al. 2011a). The ethanolic extract of the *OS* is subjected to the perfused pancreases for insulin secretion. It is observed that ethanolic extract stimulates the physiological pathway of insulin secretions by assessing the three important enzymes, i.e., glucokinase (GK), hexokinase (HK), and phosphofructokinase (PFK), along with insulin-dependent and insulin-independent tissues from the brain and kidney (Rani and Khullar 2004). Similar study has been conducted and was found reports eliciting a significant drop in mean FBS level from 174.35 mg/dL to 114.50 mg/dL, PP2 BS from 247.31 mg/dL to 152.02 mg/dL, and HBA1C. Furthermore preclinical studies have reported that use of both aqueous and alcoholic extracts of *OS* showed significant decrease in the level of blood sugar and glycosylated hemoglobin. The anti-diabetic properties of tulsi reported by various studies concluded that treatment of AQOS (aqueous extracts of *Ocimum sanctum* L.) significantly lowered blood glucose level in DM rats; this concludes the fall in fasting blood sugar and HbA1C (Patil et al. 2011b; Grover et al. 2002).

4.4.3 Antifungal Activities

Mycosis is the common fungal infection caused by the inhalation of spores of fungi or contact of fungal colony with skin. Keeping the body clean and staying in the dry environmental condition will minimize the infection though there is need of fungicides (Pandey and Madhuri 2010). The spectroscopic analysis of *Ocimum sanctum* revealed the presence of higher composition of methyl chavicol and linalool which have good antifungal activity against *Candida* and can be applied in treatment of various fungal infections (Singh and Chaudhuri 2018). The synergetic effect of essential oil of tulsi extract with azole (ketoconazole and fluconazole) is reported for candiodosis. The combination of ethanolic extract of leaves of tulsi with *Cassia alata* has shown anti-Cryptococcus activity even at higher temperature and lower pH. The investigation of antifungal activity of tulsi against dermatopathic fungi by 38A NCCLS method showed 200 μg/mL as MIC (minimum inhibitory concentration) and MFC (minimum fungicidal concentration) (Garg 2005). Extract of *Ocimum sanctum* disturbs ergosterol biosynthesis and membrane integrity and acts as antifungal medicine (Balakumar et al. 2011).

4.4.4 Antihypertensive and Cardioprotective Activities

Cardioprotective activities of *Ocimum sanctum* are found greatly effective in myocardial necrosis induced by isoproterenol in Wistar rat through upgrade of endogenous antioxidants (Singh et al. 2012b). Protection against the adriamycin (ADR)-induced lipid peroxidation in heart and liver microsomes is achieved by the ursolic acid derived from *Ocimum sanctum* (Zehra et al. 2019). The OS has been noted for the significant forestallation of transient cerebral ischemia and long haul cerebral hypoperfusion. Basic unsaturated fat contents like linoleic and linoleic acids promote the production of PGE 1 and PGE 3 which restrain the arrangement of PGE 2. Thus *Ocimum sanctum* offers huge assurance against the treatment of hypertension and cardiac problems (Krishna et al. 2014).

4.4.5 Hepatoprotective Activity

Ocimum sanctum shows response to the hepatoprotective activity. The studies have revealed that OS progresses the metabolic breakdown, purging dangerous/toxic chemicals from blood promoting healthy liver work (Singh et al. 2012a). Aqueous extract of tulsi shows the synergistic effect with gentamycin to control the rise in serum creatinine and urea in blood (Pandey and Madhuri 2010). The hepatoprotective potential of tulsi is also noted for the hepatotoxicity by paracetamol in rat. Hydro-alcoholic extract of tulsi leaves on oral administration (200 mg/kg) shows remarkable protection against liver injury induced by paracetamol. It was achieved by significant drop of serum enzyme aspartate aminotransferase (AST), alkaline phosphatase (ALP), and alanine aminotransferase (ALT) (Cohen 2014). Marked reduction in fatty acid degeneration of liver was also seen in histopathological examination. Leaves and seeds of tulsi have been detailed for diuretic activity and diminishment of urinary uric acid in albino rabbits. The continuous administration of water extract (3 g/100 g) of tulsi leaves for 6 days orally was beneficial against CCL4-induced liver dysfunction in albino rats (Lahon and Das 2011).

4.4.6 Antioxidant Activity

The physiological process like generation of energy in mitochondria, cell development regulation, and detoxification of xenobiotic in the human body leads to the formation of reactive free radicals (Kelm et al. 2000). The stressful lifestyle and various environmental factors like pesticides, chemical pollutants, and UV radiations contribute to ROS overproduction which causes tissue damage leading to deterioration of health condition. The phytoconstituents and secondary metabolites have significant role in scavenging the free radicals. Antioxidants from the tulsi, especially polyphenolic compounds, effectively impede hydrolytic and oxidative enzyme, decrease blood glucose and lipid level, and enhance immunity; therefore

flavonoids have attracted attention to different issues mainly oxidative stress (Aqil et al. 2006). Existence of hydroxyl groups and keto group in phytochemicals of OS imparts free radical scavenging property and produce antioxidant activity (Shetty et al. 2008). Various in vitro study and research have been done to access the antioxidant potential of tulsi extract. Remarkable results were obtained in scavenging DPPH radical, superoxide radicals, ABTS radical, hydroxyl radicals, and reduction of phosphomolybdate ion (Veeru et al. 2009).

4.4.7 Antifertility Activity

Ocimum sanctum has significant antifertility activity in animals. It has been noticed from phytoconstituents from leaves, ursolic acid. The impact has been attributed to its antiestrogenic impact in male and inhibitory impact on ovum implantation in females. The OS leaves extract on benzene and petroleum ether showed 60–80% of antifertility activity in female rat. The extract of *Ocimum sanctum* in male rats exhibited increase sperm count, motility, and also weight of testis (Pandey and Madhuri 2010; Pattanayak et al. 2010).

4.4.8 Antiarthritic Activity

The antiarthritic potential was assessed against various chemicals produced from joint inflammations in rodents. Due to mimicking human rheumatoid diseases, Freund's complete adjuvant-induced arthritis in the rat is an extensively used model to perform preclinical studies. For evaluation of antiarthritic potential, rat was injected with adjuvants, and inflammation in paws and joint nodules within the ear and tail (delayed systemic response) was induced. For the management of induced arthritic disease, fixed oil of OS was given at dose of 3 mL/kg (ip), and notable edema inhibition was achieved comparable to aspirin (100 mg/kg, ip). A notable inhibition of inflammation and arthritic nodules was noticed (Awuchi 2019). Antiarthritic potential of OS was also studied on formaldehyde-induced arthritis in rats, and marked improvement in the arthritic condition was achieved as result on daily application of OS fixed oil for 10 days ip. The fixed oil diminished the aroused paws up to a great extent (Singh et al. 2012a). The sequential release of mediators in turpentine oil-induced arthritis and carrageenan-induced paw edema, i.e., serotonin and histamine in earlier, kin in middle, and prostaglandins in later phase, is well inhibited by the fixed oil constituents of OS. These abovementioned mediators are inhibited by OS, so it is natural that fixed oil could inhibit inflammatory reaction involving different inflammatory mediators. The conclusion from the above study suggests potentially useful antiarthritic activity of fixed oil from OS (Pattanayak et al. 2010).

4.4.9 Antiulcer Activity

Antiulcer potential of *OS* was appraised on animals with induced gastro-intestinal ulcer. Fixed oil of *O. sanctum* possesses significant antiulcer and anti-inflammatory activity through antagonistic effect on the several chemicals and mediators responsible for gastric ulceration (Kousik and Baldev 2012). The management of gastric ulceration induced by NSAIDs, ethanol, histamine, reserpine, serotonin, and stress is accomplished due to lipoxygenase inhibitory, histamine antagonist, and antisecretory effects of the fixed oil extracted from OS (Kelm et al. 2000; Pattanayak et al. 2010). Drug possessing anti-inflammatory and antiulcer activity having null ulcerogenic effect has great importance in this modern era of allopathic medicine. A well-illustrated flowchart signifying the cause and management of gastric ulcer explains the marked antiulcer activity of OS shown in Fig. 4.3 (Singh and Majumdar 1999).

4.4.10 Anthelmintic Activity

The essential oil from *Ocimum sanctum* has extensive anthelmintic property. In the *Caenorhabditis elegans* model when tested in vitro, eugenol showed an ED50 of 62.1 μg/mL. Several studies have revealed essential oil of OS as the putative anthelmintic principle (Kousik and Baldev 2012). Ursolic acid found in tulsi has more efficient anthelmintic potential as compared to albendazole. It was found that ursolic acid paralyzes and kills worms at great extent (Inbaneson et al. 2012).

4.4.11 Anti-inflammatory Activity

Anti-inflammatory potential of OS is appraised in rats via carrageenan-induced paw edema, and it was found that 3 mL/kg fixed oil of OS when administered intraperitoneally inhibits edema due to true anti-inflammatory action not due to counter-irritant property (Singh et al. 1996). The anti-inflammatory effect of oil is found independent on pituitary adrenal axis when evaluated in adrenalactomized and nonadrenalactomized rats (Mondal et al. 2009). A significant inhibitory action on various mediators of inflammation like histamine, serotonin, bradykinin, and prostaglandins was ascertained when tested on inflammatory mediator-induced edema. *Ocimum sanctum* exhibits anti-inflammatory potential via inhibition of both COX and LOX pathways of arachidonic acid metabolism (Singh et al. 2007). The relative contribution of OS fixed oil toward COX inhibition and LOX inhibition and inhibitory effect of antihistamine in arachidonic acid-induced paw edema were evaluated (Singh et al. 2007). The fixed oil of OS shows an excellent edema inhibitory potency than indomethacin or caffeic acid, a potent COX and lipooxygenase inhibitor. Thus the above results highlight the potent anti-inflammatory activity of *Ocimum sanctum* (Singh and Chaudhuri 2018).

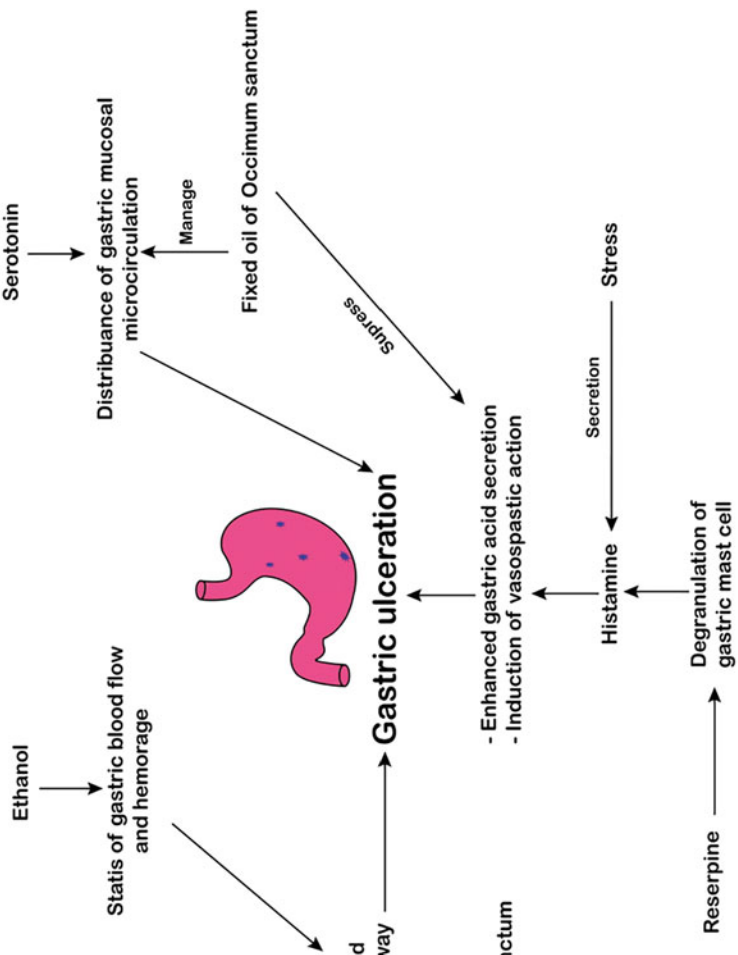

Fig. 4.3 Flowchart showing the antiulcer potential of tulsi

4.4.12 Analgesic Activity

Pain is a distressing feeling often marked as cardinal signs of inflammation. The analgesic potential of OS fixed oil was estimated by means of chemical and thermal induced pain model. These include acetic acid writhing test and formalin-induced paw licking test, the formalin-induced model as a chemical pain model while tail flick, tail clip, and tail immersion method as a thermal-induced pain model (Kaur 2014). For the thermal induced pain model, response time of rat to pull back its tail from hot water or a hot wire is noted in tail immersion or tail flick model, while in tail clip method, response time to extricate the clip was noted. The insufficient elevation of pain threshold of rat toward heat emphasizes the non-central action of OS fixed oil. Thus, to differentiate the central and peripheral analgesia potency of OS fixed oil, acetic acid-generated writhing response in rat was used. Ethyl acetate extract of OS exhibited extensive inhibition of writhing persuaded by acetic acid and formalin-induced paw licking in dose-dependent manner. Therefore analgesia activity of OS oil appears to be superficially facilitated and achieved by additive inhibitory effects of histamine, acetylcholine, and prostaglandin (Prakash and Gupta 2005; Pandey et al. 2014).

4.4.13 Antipyretic Activity

Prostaglandins (PGE) mediate pyrogenic fever; hence inhibition of prostaglandin synthesis results in the antipyretic action of drugs. Various anti-inflammatory drugs including NSAIDs are supposed to inhibit prostaglandin synthesis. The antipyretic power of the OS has been tested with typhoid, a paratyphoid vaccine A/B that used pyrexia in mice (Kelm et al. 2000). Intra-peritoneal administration of fixed oil of OS (3 mL/kg) reduced the pyretic response in rats as compared to aspirin. The fixed oil from *Ocimum sanctum* is moreover found to impede the synthesis of prostaglandin emphasizing its antipyretic potential (Balakumar et al. 2011; Kaur 2014).

4.4.14 Anticancer Activity

Extensive studies, experiments, and clinical studies prove that OS holds a prodigious potential not only as prevention but moreover within the treatment of a wide range of cancers and tumors in human. The chemoprotective and antitumor therapeutic efficacy can be elucidated by potential of enzyme to elucidate activity and signal transduction pathways modulating strength as well as antioxidant, antiproliferative, anti-invasive, immunomodulatory, antiangiogenic, and anti-metastatic properties of OS. It plays a pivotal role in treatment and prevention of cancer by altering the several carcinogen metabolizing enzymes like CYP450, CYB5, aryl hydrocarbon hydroxylase (Karthikeyan et al. 1999a), etc., antioxidant enzymes such as CAT and SOD, and GSH and GSH-related enzymes like GST and GSH-Px (Tables 4.4 and 4.5). Studies have revealed that extract of OS mediates a notable decrease in volume

Table 4.4 In vitro studies for anticancer potential of *O. sanctum*

Phytoconstituents tested	Cancer cell lines	Anticancer effects	Mechanism of action	Concentration of phytoconstituents	References
Ethanolic extract of leaves	A549 human non-small-cell lung carcinoma	Cytotoxicity	↑SUB-G1 ↑Apoptosis ↑Cyt.c ↑Caspase-9 ↑Bax ↓pAKT ↓pERK	25–200 μg/mL	Karthikeyan et al. (1999a)
Ethanolic extract of leaves	Mouse Lewis lung carcinoma	Decrease cell viability and inhibition of cell adhesion and invasion	↓MMP-9	25–100 μg/mL	Niture et al. (2006)
Ethanolic extract of leaves	HFS-1080 human fibrosarcoma	Cytotoxicity	↑Lipid peroxidase ↓GSH	50–400 μg/mL	Magesh et al. (2009)
Ethanolic and aqueous extracts of leaves	HT29 human colon cancer	Attenuation of alkylation-induced carcinogenesis	↑MGMT ↑GSTP1 proteins and mRNAs	10–20 μg/mL	Kim et al. (2010)
Vicenin; vicenin + docetaxel	PC-3, DU-145, and LNCaP human prostate carcinoma	Induction of antiproliferative, antimigration, and antiangiogenic effects	↑Apoptosis ↑E-cadherin ↓CDK4 ↓hTERT ↓c-Myc ↓Cyclin D1 ↓VEGF ↓Cyclin B1 ↓PCNA ↓Bax ↓Bcl-2 ↓G2/M	50 μmol/L	Nagaprashantha et al. (2011)

Table 4.5 In vivo studies for anticancer potential of *O. sanctum*

Phytoconstituents tested	Animal model (chemically induced cancer models)	Anticancer effect	Mechanism of action	Dose	Route of administration	Duration	References
Leaf paste	B[a]P-induced gastric carcinogenesis in male mice and 3′-MeDAB-induced hepatocarcinogenesis in male Wistar rats	Prevented the occurrence of tumor in the stomach and liver		600 mg/g	Diet, ad libitum	10–14 weeks	Aruna and Sivaramakrishnan (1992)
Ethanolic extract of leaves	DMBA-induced skin papillomagenesis in male Swiss albino rat	Reduction of incidence, multiplicity, and cumulative number of papilloma	↑GSH ↑GST	5 mg/kg	Topical	2–15 weeks	Prashar et al. (1994)
Ethanolic extract of leaves	MNNG-induced gastric carcinogenesis in male Wistar rat	Suppression of incidence of gastric carcinoma	↑Cyt. C ↑Bax ↑Caspase-3 ↓PCNA ↓GST-P1 ↓CK ↓VEGF ↓Bcl-2	300 mg/kg	Orally	2 times per week for 24 weeks	Manikandan et al. (2007)
Isolated seed oil	MCA-induced fibrosarcoma in Swiss albino mice	Enhanced survival rate; suppression of tumor volume and its incidence	↑GSH ↑SOD ↑GST ↑CAT ↓MDA	100 mg/kg	Orally	15 weeks	Prakash et al. (1999)

(continued)

Table 4.5 (continued)

Phytoconstituents tested	Animal model (chemically induced cancer models)	Anticancer effect	Mechanism of action	Dose	Route of administration	Duration	References
Ethanolic extract of leaves + extract of leaves of neem	MNNG-induced gastric carcinogenesis in male Wistar rat	Suppression of incidence of gastric carcinoma	↑TBARS ↑LOOH ↑CD ↑PC ↑Cyt. C ↑Bax ↑Caspase-3 ↓PCNA ↓GST-P1 ↓Bcl-2 ↓VEGF ↓CK	150 mg/kg	Orally	3 times per week for 26 weeks	Manikandan et al. (2008)
Fresh leaf juice	DMBA-initiated and croton oil-promoted multiorgan carcinogenesis in Swiss Webster mice	Exhibit complete protection against liver and skin tumor	N/A	Not specified	Topical	3 times a week for 20 weeks	Serrame (1995)
Fresh leaves paste; aqueous and ethanolic extract of leaves	DMBA-induced buccal pouch carcinogenesis in male Syrian golden hamsters	Attenuated the incidence of papilloma and carcinoma with increased survival rate	N/A	1 g/kg (paste) 30 mg/kg 300–800 mg/kg (extract)	Topical Topical Orally	16 weeks	Karthikeyan et al. (1999b)

Ethanolic extract of leaves	MCA-initiated; DMBA-initiated; AFB_1-initiated; TPA-promoted skin tumorigenesis in female Swiss albino mice	Decreased skin tumors with improvement of histological appearance	↑GST; ↑QR; ↑IL-1β;↑TNF-α; ↓GGT; ↓GST-P; ↓LPO;↓GSH; ↓AHH; ↓ERD; ↓ODC	100 μL/mouse	Topical	2 times per week for 24 weeks	Rastogi et al. (2007)
Eeugenol	DMBA-initiated and croton oil-promoted skin carcinogenesis in female Swiss albino mice	Inhibited the number of papilloma	↓Lipid peroxidation; ↓SOD	2 mg/mouse	Topical	6 weeks	Bhattacharyya and Bishayee (2013)
Xenograft cancer models							
Ethanolic extract of leaves	C57BL/6 mice inoculated with Lewis lung carcinoma cells	Decreased tumor volume and weight		50 and 100 mg/kg	Intraperitoneally	Every other day for 18 days	Magesh et al. (2009)
Aqueous and ethanolic extracts of leaves	Male Swiss albino mice xenografted with sarcoma—180 cells	Reduced tumor volume with increase in survival		800–1200 mg/kg	Orally	3 times per week for 4 weeks	Karthikeyan et al. (1999a)
Alcoholic aqueous leaf extract	Male C57BL and Swiss albino mice injected with $B_{16}F_{10}$ murine melanoma cells and/or irradiated	Attenuated tumor volume and improved survival	↓Chromosomal aberration; ↑GSH; ↑GST	200 mg/kg	Orally	Once	Monga et al. (2011)

(continued)

Table 4.5 (continued)

Phytoconstituents tested	Animal model (chemically induced cancer models)	Anticancer effect	Mechanism of action	Dose	Route of administration	Duration	References
Ethanolic extract of leaves	Female C57BL/6 mice injected with Lewis lung carcinoma cells	Inhibited the formation of metastatic lung nodules and lung weight	↑SOD; ↑CAT; ↑GSH-P_x	50 and 100 mg/kg	Intraperitoneally	Every other day for 18 days	Kim et al. (2010)
Vicenin-2; vicenin-2 + docetaxel	Athymic nude nu/nu mice transplanted with PC-3 prostate cancer cells	Reduced tumor weight, tumor cross-sectional area, and angiogenesis	↓Ki-67; ↓CD31; ↑E-cadherin; ↑PARP; ↓pAKT; ↓pRB; ↓PCNA; ↓cyclin D1; $VIGF_1R$; ↓fibronectin	1 mg/kg (vicenin-2), 0.01 mg/kg (docetaxel)	Orally	Every other day for 8 weeks	Nagaprashantha et al. (2011)
Methanolic extract of leaves	Swiss albino mice inoculated with Ehrlich ascites carcinoma cells	Reduced tumor volume and tumor weight and prolonged survival	Hematological alterations	50 mg/kg	Intraperitoneally	Once daily for 9 days	Saiful Islam et al. (2011)

of tumor, tumor cell size, rise in body weight, and survival rate of mice having sarcoma-180 solid tumor when administered 200 mg/kg, po (Singh et al. 1996; Kelm et al. 2000).

4.4.15 Antiviral Activity

Viral infections are the major causes of devastations for human and animal health worldwide. Being an obligate intracellular parasite, any intervention will affect the cellular metabolism of the host; thus, developing an antiviral drug is a great challenge for mankind (Tang et al. 2012). This has diverted attention of the researchers and scientists to develop antiviral drug from the native traditional plant (Cohen 2014; Kaur 2014). Several studies have revealed the antiviral property of *Ocimum sanctum*. Evaluation of antiviral potential against orthomyxovirus and paramyxovirus has shown the significant viral infection inhibitory potential of tulsi (Mohan et al. 2011). The ethanolic extraction of the air part of tulsi contains details of the content of flavonoids and polyphenolic compounds; these are further described before having the same antimicrobial properties. In silico experiments of phytochemicals such as SARS-CoV-2 primary protease inhibitors suggest that flavonoids and polyphenolic chemicals of tulsi, especially luteolin-7-*O*-glucuronide and chlorogenic acid, can bind by combining the active residual Cys145 of the COVID-19 main protease and inhibiting the immune system (Mohapatra et al. 2020). OS extract has shown a preventive degree against coronavirus due to its potential to restrain replication of coronavirus bolstered with its immunomodulatory feature and angiotensin-converting enzyme (ACE) II inhibiting potency (Varshney et al. 2020).

Studies show chemicals from OS like methyl eugenol, oleanolic acid, and ursolic acid which have a strong binding effect on both spike glycoprotein and RNA polymerase of novel coronavirus. These compounds showed better binding energy than the positive control (STGYC and remdesivir) (Kumar 2020).

4.4.16 Antimicrobial Activity

Ocimum sanctum has been described for its antimicrobial potency against Gram-positive and Gram-negative bacteria. The results have shown that the essential oil and extract of leaves (aqueous, alcoholic, and chloroform) are equally effective against both strains of bacteria (Cohen 2014; Kaur 2014). Tulsi's antibacterial activity was evaluated against bacteria responsible for tooth decay, i.e., *Streptococcus mutans*, and it was confirmed that mouthwash with tulsi is equally effective as 0.2% chlorhexidine and listerine (Prakash and Gupta 2005; Singhal et al. 2011). Flavonoid content of OS showed significant efficacy against UTI-causing bacterial strains, e.g., *Escherichia coli*, *Proteus*, *Klebsiella pneumoniae* (gram –ve), *Staphylococcus aureus*, and *Staphylococcus cohnii* (gram +ve) using disk diffusion method. Orientin and vicenin synergistically show significant inhibition on bacterial

growth compared to individual inhibitory potential of flavonoids (Prasannabalaji et al. 2012).

4.5 Clinical Efficacy of Tulsi [Clinical Study]

Tulsi has been reported beneficial for several disorders and diseases. Despite of abundant availability and extensive antiquity of traditional use of *Ocimum sanctum*, comparatively limited human interventions study has been done on clinical efficacy (Grover et al. 2002; Ghorbani 2013). Plethora of bioactive secondary metabolite constituents of tulsi act alone or synergistically to inhibit the inflammatory ailments, and regular consumption of tulsi assists in normalizing numerous metabolic disorders. A summary and critically evaluated human clinical trials enhance and potentiate the tulsi's efficacy against various metabolic disorders, viral infections, neurocognition, and immunomodulation (Gupta et al. 2014; Ahirwar et al. 2018) which are well illustrated via Tables 4.6 and 4.7.

4.6 Nutritional Value

In addition to secondary metabolites, *O. sanctum* also contains several components which are of great nutritional values (Pattanayak et al. 2010; Kaur 2014). The herb is very low in calories. Fresh basil leaf is prodigious source of vitamin A; it is found that 175% of daily required dose is fulfilled by intake of 100 g fresh basil leaf. Basil herb contains a weighty amount of minerals like potassium (K), manganese (Mn), copper (Cu), and magnesium (Mg). Basil leaves are extremely rich in iron. 100 g of fresh leaves contains 3.17 mg of iron. Various researches have revealed the following components which are of great nutritional values and represented in Table 4.8 (Kumar et al. 2010; Prasannabalaji et al. 2012).

4.7 Conclusion

OS is widely cultivated from the beginning of human civilization for its medicinal importance and as an herbal tea. Ayurveda, Siddha, and Unani described medicinal properties of this plant in the traditional system of medicine. The herbal drug remains devoid of side effects, so researches on the herbal plant were increasing and scientific research showed OS has huge biological potential. Research showed OS has various secondary metabolite, vitamins, and minerals. These phytoconstituents elucidate various pharmacological effects. Tulsi has significant pharmacological potential and has been clinically proved for both its beneficial application and effectiveness. The various clinical trials are completed, and some are still going on to establish its efficacy for chronic disease. However, some marketed product is also available as nutraceutical products.

Table 4.6 A summary and critically appraise human clinical trials of *Ocimum sanctum*

Clinical domain	Year of study	Study design	Tulsi extract (phytoconstituents)	Participants (age group)	Dosage	Duration	Outcomes	References
Metabolic disorders	1964	Clinical trail	Whole plant decoction, powder	10 adults T2DM	14 g/day	12 weeks	Reduced blood glucose level in 9 participants	Kochhar et al. (2009)
	1986	Randomized placebo controlled cross-over	Fresh juice (75% Tulsi)	20 adults (45–64 years) Hypertension	3 mL/day	10 days (+5 days wash-out)	Significant decrease in BP	Matsukawa et al. (1987)
	1986	Randomized placebo controlled cross-over	Fresh juice (75% Tulsi)	16 adults (45–65 years) Hypertension	30 mL 2 times/day before meal	12 days	Significant lower in BP by 25%	Matsukawa et al. (1987)
	1996	Randomized, single-blind, placebo-controlled cross-over	Tulsi powder leaves	40 adults (41–65 years) T2DM	2.5 g/day in morning before meal	5 weeks (+5 days wash out)	Significant decrease in fasting glucose, PP glucose and urine glucose	Agrawal et al. (1996)
	1997	Clinical trial controlled group	Tulsi powder leaves	27 adults (45–65 years) T2DM/MeS)	1 g/day in morning before meal	4 weeks	Improvement in lipid profile, glycated proteins (HbAlc), blood sugar, and UA	Rai et al. (1997)

(continued)

Table 4.6 (continued)

Clinical domain	Year of study	Study design	Tulsi extract (phytoconstituents)	Participants (age group)	Dosage	Duration	Outcomes	References
	2009	Randomized, clinical trials	Tulsi leaves powder	90 male adults (40–60 years) T2DM/MetS	2 g/day	12 weeks	Improved T2DM symptoms, decrease in polydipsia, polyphagia, and BP	Kochhar et al. (2009)
	2010	Placebo controlled clinical trial	Aqueous extract of tulsi leaves	40 adults (45–55 years) T2DM	500 g/day	8 weeks	Significant improvement in lipid profile	Dineshkumar et al. (2010)
	2012	Randomized placebo-controlled clinical trials	Tulsi leaves + glibenclamide drug	60 adults (30–65 years) T2DM	300 mg/day tulsi + 5 mg glibenclamide	13 weeks	Significant decrease in fasting blood and PP glucose, reduce HBA1c	Somasundaram and Manimekalai (2012)
	2012	Randomized, clinical trial	Aqueous tulsi leaves	100 adults (≥40 years) MetS	5 mL/2 days before meal	12 weeks	Improvement in lipid profile, BP, and fasting blood glucose	Jamshidi and Cohen (2017)
	2012	Randomized, double-blind, placebo-controlled cross-over	Ethanolic extract of tulsi	22 healthy adults (22–37 years)	300 mg/day before food	4 weeks (+3 week wash-out)	Reduction in lipid profile in 6 participants	Jamshidi and Cohen (2017)

	2012	Clinical trial	Whole tulsi plant	5 adults (60–80 years) Psychosomatic	3 g/2 days	12 weeks	Significant improvement in lipid profile	Jamshidi and Cohen (2017)
	2013	Randomized, single-blind parallel group	Tincture from tulsi	200 adults Gouty Arthritis	10 drops 3 times/day	12 weeks	Significant reduction in serum uric acid	Ahmad et al. (2013)
	2014	Clinical study case report	Fresh tulsi leaves	3 adults T2DM	Fresh leaves 3 times daily	5 weeks	Significant decrease in blood glucose reaching near normal level	Jamshidi and Cohen (2017)
	2015	Clinical trial controlled parallel group	Tulsi leaves powder	30 adults T2DM	2 g/day	2 weeks	Significant decrease in fasting and PP blood glucose level	Ahangarpour et al. (2017)
	2016	Randomized controlled clinical trial	Tulsi leaves capsule	40 male adults (45–55 years) T2DM	3 g/day before meal	6.5 weeks	Significant decrease in PP glucose and fasting blood glucose	Chauhan (2017)
	2016	Randomized parallel group clinical trial	Tulsi leaves capsules	30 adults (17–30 years) Obesity	250 mg/day 2 times daily before meal	8 weeks	Improvement in lipid profile except TC, BMI, TG, and IR	Satapathy et al. (2017)

(continued)

Table 4.6 (continued)

Clinical domain	Year of study	Study design	Tulsi extract (phytoconstituents)	Participants (age group)	Dosage	Duration	Outcomes	References
Immunomodulation	1983	Open clinical trial	Aqueous tulsi leaves tablet	20 adults Asthma	500 mg 3 times/day	1 week	Relief within 3 days, improvement in vital capacity	Mayank and Vikas (2014)
	2011	Randomized, double blind, placebo-controlled cross-over	Ethanolic extract of tulsi leaves	22 healthy adults (22–37 years)	300 mg/day	4 weeks (+3 weeks wash-out)	Increase in interferon-γ, cytokine level, and interleukin-4 level	Jamshidi and Cohen (2017)
	2014	Randomized, placebo-controlled clinical trial	Ethanolic extract of tulsi leaves in Bar	30 healthy adults (18–30 years)	1 bar 2 times/day (1000 mg tulsi)	2 weeks	Loss of fatigue and increase in physical performance, less increase in lactic acid	Martins et al. (2018)
Neurocognition	2008	Clinical trials	Ethanolic tulsi leaves capsules	35 adults with GAD (18–60 years)	200 mg 2 times daily after meals	8 weeks	Reduction in stress, anxiety, and depression	Bhattacharyya et al. (2008)
	2012	Clinical trials	Powder of whole tulsi plant	24 adults (60–80 years) Psychosomatic	3 g two times per day	12 weeks	Stress reduction, significantly lowered biological age score	Verma et al. (2012) and Jamshidi and Cohen (2017)

	2012	Randomized, double-blind, placebo controlled clinical trial	OCIBEST Whole plant capsule	150 adults (18–65 years) Stress	400 mg 3 times/day after meal	6 weeks	Reduction in stress related symptoms: fatigue, sleep, and sexual problems	Jamshidi and Cohen (2017)
	2015	Randomized, double-blind, placebo controlled clinical trial	Ethanolic tulsi leaves capsules	40 healthy adults (18–30 years)	300 mg/day before meal	4 weeks	Improved memory power only after 15 days, cognitive flexibility	Jamshidi and Cohen (2017)
Viral infections	1983	Randomized clinical trial parallel controlled	Aqueous extract of fresh tulsi leaves	14 adults Viral encephalitis	2.5 g 4 times/day	4 weeks	Increased survival rate as compared to steroid	Joshi (2014)
	1986	Clinical trial	Aqueous extract of fresh tulsi leaves	20 case, (10–60 years) Viral hepatitis	10 g daily	2 weeks for mild cases, 3 weeks for severe cases	Improvement in symptoms within 2 weeks	Jamshidi and Cohen (2017)

Table 4.7 Completed and ongoing clinical trials

S. no.	Title	Condition	Intervention	Status	Result	Location	Reference
1.	Comparative evaluation of antiplaque and antigingivitisEfficacy of *Ocimum sanctum* (Tulsi) extract	Periodontal diseases, gingivitis, periodontitis	*Ocimum sanctum*, chlorhexidine gluconate, propylene glycol	Completed	N/A	GCD Indore, Indore, Madhya Pradesh, India	NCT03474146 (2018)
2.	Effect of Tulsi (*Ocimum sanctum*) on biochemical parameters in young overweight and obese subjects	Obesity	Drug: Tulsi (*Ocimum sanctum* Linn.) capsules	Completed	N/A	All India Institute of Medical Sciences, Bhubaneswar, Odisha, India	Satapathy et al. (2017)
3.	Trial of an herb and mineral combination product on fasting glucose in adults at risk for developing diabetes	Prediabetes	Dietary supplement: herb and mineral combination product, dietary supplement: placebo	Completed	N/A	• Radiant Research, Chicago, Illinois, United States • Central Kentucky Research Associates, Lexington, Kentucky, United States • Quest Research Institute, Bingham Farms, Michigan, United States • Radiant Research, Cincinnati, Ohio, United States • Providence Health Partners Center for Clinical Research, Dayton, Ohio, United States • Mountain View Clinical Research, Greer, South Carolina, United States	Zhang et al. (2015)

4.	Tulsi consumption and its effects on cognition, stress and anxiety	Cognitive change	Drug, *Ocimum sanctum*; drug, placebo	Completed	N/A	Narayana Hrudayalaya Limited, Mazumdar Shaw Multispecialty Hospital, Bangalore, Karnataka, India	Chong et al. (2019)

Table 4.8 Nutritive value per 100 g (source: USDA National Nutrient data base)

Principle	Nutrient value	Percentage of RDA
Protein	3.15 g	6%
Dietary fiber	1.60 g	4%
Total fat	0.64 g	2%
Carbohydrates	2.65 g	2%
Energy	23 Kcal	1%
Phytonutrients		
Lutein-zeaxanthin	5650 μg	–
Beta-carotene	3142 μg	–
Beta-cryptoxanthin	46 μg	–
Vitamins		
Vitamin K	414.8 μg	345%
Vitamin A	5275 IU	175%
Vitamin C	18 mg	30%
Vitamin E	0.80 mg	5%
Folates	68 μg	17%
Pyridoxine	0.155 mg	12%
Niacin	0.902 mg	6%
Riboflavin	0.076 mg	6%
Pantothenic acid	0.209 mg	4%
Thiamin	0.034 mg	2.5%
Minerals		
Manganese	1.15 mg	57%
Copper	385 mg	43%
Iron	3.17 mg	40%
Calcium	177 mg	18%
Magnesium	64 mg	16%
Zinc	0.81 mg	7%

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