

## The Ultimate Herb for Overall Wellness - A Comprehensive Review

Deepak Kumar Yadav<sup>1\*</sup>, Anu Sharma<sup>1</sup>, Vidhi Grover<sup>2</sup> and Garima Mathur<sup>3</sup>

<sup>1</sup>Department of Pharmacy, Metro College of Health Science & Research, (Greater Noida), INDIA.

<sup>2</sup>Department of Applied Sciences, SJPP Damla Yamunanagar, (Haryana), INDIA.

<sup>3</sup>SGVP International School, Ahmedabad (Gujarat), INDIA.

\*Corresponding Author: dy4554335@gmail.com



www.jrasb.com || Vol. 4 No. 2 (2025): April Issue

Received: 03-04-2025

Revised: 10-04-2025

Accepted: 13-04-2025

### ABSTRACT

Holy basil, or Tulsi, is a plant native to the Indian subcontinent that is highly valued in Siddha and Ayurvedic medicine for its therapeutic properties. Tulsi has been shown to shield organs and tissues from physical stressors such as extended physical activity, ischemia, physical restraint, exposure to cold, and loud noises, as well as chemical stressors including industrial pollution and heavy metals. Additionally, Tulsi has been demonstrated to mitigate psychological stress by improving memory and cognitive performance and by lowering blood pressure, cholesterol, and blood glucose levels. It has also been demonstrated to mitigate metabolic stress by having anxiolytic and antidepressant qualities. The predominant cause of global morbidity and mortality is lifestyle-related chronic diseases, many of which can be addressed through Ayurveda with its focus on healthy lifestyle practices and regular consumption of adaptogenic herbs. Scientific studies are increasingly verifying the health benefits of Tulsi (*Ocimum sanctum* Linn), the most important plant in Ayurveda. Tulsi has a special mix of pharmacological activities that have been shown to alleviate physical, physiological, metabolic, and psychological stress. The broad-spectrum antimicrobial activity of Tulsi, which includes activity against a variety of human and animal pathogens, indicates that it can be used as a mouthwash, hand sanitiser, and water purifier in addition to being used in wound healing, animal rearing, food preservation, the preservation of herbal raw materials, and traveller's health issues.

**Keywords-** Ayurveda, Holy basil, lifestyle, *sanctum Ocimum*, stress.

## I. INTRODUCTION

In the Lamiaceae (tribe ocimeae) family of basil, tulsi is a fragrant shrub that is endemic to the eastern tropics and is believed to have originated in north central India [1]. A member of the Lamiaceae family, Tulsi (*O. sanctum* L.) is a highly prized culinary and therapeutic aromatic plant that is native to the Indian subcontinent and has been used in Ayurvedic medicine for more than 3,000 years [2].

Tulsi's many therapeutic benefits have led to its usage in Ayurveda for thousands of years. Every element of the plant, including the seeds and leaves, is functional. Physical endurance is increased by Tulsi, which is regarded as a general vitaliser. Physical and biological activities may be among the many components found in the stem and leaves of holy basil. Conventionally, Tulsi contains a high concentration of eugenol, indicating that

it inhibits COX2, and it is similar to what numerous studies and research have revealed [3]. The therapeutic properties of Holy Basil leaves have led to their widespread use. The herb aids in the bronchial tube's removal of catarrhal and phlegm. The plant aids in avoiding gastrointestinal issues. Respiratory ailments can be cured using this herb. For bronchitis, influenza, and asthma, a decoction of honey, ginger, and Tulsi leaves is beneficial. When illnesses like dengue and malaria strike during the rainy season, Tulsi leaves are quite helpful. In order to reduce fever, the best treatment is to extract the juice from Holy Basil leaves. Tulsi helps decrease blood cholesterol levels and is extremely valuable for heart health [4].

Tulsi has been shown to shield organs and tissues against physical stress caused by ischaemia, prolonged physical activity, physical constraint, exposure to cold, and loud noises, as well as chemical

stress caused by industrial pollutants and heavy metals. It has also been demonstrated that Tulsi can counteract psychological stress by improving memory and cognitive function and by having anxiolytic and antidepressant qualities. Metabolic stress is countered by normalising blood glucose, blood pressure, and cholesterol levels. Because of its many complex restorative benefits, the Tulsi herb is extremely valuable to humanity. Tulsi leaves are often used in Ayurvedic preparation.

Prescription drugs. It is known to lengthen life expectancy. The plant's extracts are widely used to treat a variety of ailments, including the common cold, irritation, intestinal disease, cardiac illness, headaches, stomach problems, kidney stones, heart problems, and

more. [5]. There are two varieties of Tulsi: Green (Ram Tulsi) and Black (Krishna Tulsi). Their chemical and therapeutic qualities are comparable. *Ocimum sanctum* L. (Tulsi), *O. gratissimum* (Ram Tulsi), *O. canum* (Dulal Tulsi), *O. basilicum* (Ban Tulsi), *O. kilimandschicum*, *O. americanum*, *O. camphora*, and *O. micranthum* are among the species that belong to the genus *Ocimum*. They are highly recognised for their therapeutic qualities and are grown all over the world [6]. Vanya (wild) and Gramya (grown in hoes) are other names for tulsi [7]. Colds, coughs, dengue, malaria, bronchitis, asthma, sore throats, influenza, heart problems, eye conditions, mouth infections, insect bites, stress, kidney stones, and more can all be treated with this plant [8].

Table 1: Different Species of Tulsi

S.no	Common name	Botanical name/ Family	Pharmacological activity
1.	Ramatulsi	<i>Ocimum sanctum</i> , Lamiaceae	Used in the treatment of cold. Anti- helminthic activity flue and respiratory tract disorders [9].
2.	Krishna tulsi	<i>Ocimum tenuiflorum</i> , Lamiaceae	Used in skin disease and has antiviral, antifungal, antiseptic, etc activities.
3.	Amrita tulsi	<i>Ocimum tenuiflorum</i> , Lamiaceae	Used in the treatment of antimicrobial activity, and antifungal activity [10].
4.	Vanatulsi	<i>Ocimumgratissimum</i> , Lamiaceae	used to treat flu, headaches, convulsions, fever, diarrhoea, pneumonia, epilepsy, and respiratory tract conditions [11].
5.	Basil	<i>OcimumLamiaceae basilicum</i> ,	Used to treat Diabetes, chronic pain, fever, vomiting, diarrhoea [12].
6.	ThiaBasil	<i>Ocimum hyrsiflora</i> , Lamiaceae	It's has antiseptic, Antifungal etc activities.[13]
7.	Purple tulsi	<i>Ocimumbasil</i> , Lamiaceae	Used in the treatment of cold, headache, and pain kidney malfunction.[14]
8.	Lemon tulsi	<i>Ocimum citriodorum</i> , Lamiaceae	Used in the treatment of the cardiovascular system & has anantiseptic, antifungal activity [12].
9.	Vietnamese tulsi	<i>Ocimum cinnamon</i> Lamiaceae	It has a antiseptic, antifungal and bacterial activities [13].
10.	Kapurtusli	<i>Ocimum kilimondacharicum</i> Lamiaceae	It is used to treat cough, cold, measles, abdominal pain, measles, diarrhea, and diarrhea[15].

## II. PHYTOCONSTITUENTS PRESENT IN DIFFERENT SPECIES OF O. SANCTUM

A considerable quantity of eugenol (>70%), which is known for its antibacterial, cytotoxic, anti-inflammatory, and antioxidant properties, is also present in tulsi essential oil [16]. Based on their specific molecular targets, the introduction of novel bioactive molecules with natural origins, notably from plant sources, may be thought of as a new and effective therapeutic strategy to treat various types of human cancers [17]. Additionally, oxidative stress is a significant factor in the pathogenesis of various cancer forms. Antioxidants have so received a lot of attention as a unique therapeutic approach for cancer. Research has shown that inflammation and oxidative stress are linked processes that contribute to cancer. It has been well

documented that tulsi leaves possess anticancer properties [18].

### Eugenol

According to reports, the total polyphenol and total flavonoid concentrations of *Ocimum* plant extracts made with ultrasound-assisted extraction procedures vary among species [19]. Geranyl acetate ethyl ester levels were much greater in *O. gratissimum* (245.3 mg GAE/g) and *O. basilicum* (246.2 mg GAE/g) than in other *Ocimum* species.

Eugenol, a naturally occurring bioactivechemical, also known as 4-allyl-2-methoxyphenol, is a phenylpropanoid with a substituted guaiacol allyl chain. Holy basil or tulsi leaves (*Lamiaceae*), ginger (*Zingiberofficinale*), oregano (*Origanum vulgare*), clove (*Eugenia caryophyllata*), peppers (*Solanaceae*), thyme (*Lamiaceae*), turmeric (*Curcuma longa*), and the bark and leaves of cinnamon (*Cinnamomumverum*), have all been found to contain

eugenol [20]. The two main natural sources of eugenol are clove and cinnamon, which together account for 45–90% and 20–50%, respectively [21]. However, commercial-level extraction of eugenol is quite expensive and requires lengthy cultivation times; as more affordable alternatives, Ginger, tulsi, and bay can serve as substitutes for cinnamon and clove. The aerial portions of plants, such as the leaves, bark, and flowers, contain the majority of eugenol because these parts also contain a significant amount of essential oils [22,23].

Tulsi leaves also contain a significant amount of eugenol, often between 40 and 71%. However, the amount of eugenol in various plant sections fluctuates according to the season. According to studies, fall harvests of eugenol produce the highest yields when compared to summer types [24]. In the essential oil, the leaves, and the inflorescence, eugenol was found to make up 13.8%, 23.7%, and 7.5% of the total volatile compounds. The most prevalent component in tulsi leaves from all across the world, including those cultivated in Bangladesh, Brazil, India, Cuba, and Germany, was discovered to be eugenol. A chemical analysis of the essential oil taken from the *Ocimum gratissimum* plant revealed that 67 percent of it was eugenol.

#### **Caryophyllene**

Another compound,  $\beta$ -caryophyllene, is a sesquiterpene found in 4.9%, 1.5%, and 1.2% of volatile compounds in the inflorescence, leaves, and oil, respectively, of tulsi grown in Australia. The caryophyllene is a flavour enhancer and fragrance component in many products. The caryophyllene has antibacterial properties as well [25,26].

#### **Ursolic Acid (UrsA)**

One of the most common and extensively researched pentacyclic triterpenes is 3-hydroxy-urs-12-en-28-oic acid, also known as UrsA, having the formula  $C_{30}H_{48}O_3$  and a molecular mass of 456.7 g/mol. UrsA is a terpene that is a secondary metabolite of plants; it is typically soluble in organic solvents but insoluble in water. Tulsi, apples, rosemary, cranberries, bilberries, peppermint, oregano, and prunes are some of the foods that contain significant amounts of the UrsA compound. Urs Acid, which is used to treat ulcers, was extracted from the leaves and stems of *Ocimum forskolei* (Benth) [27]. *Ocimum sanctum* (L.) leaves induced antiproliferative and antistress therapy for rheumatoid arthritis. Additionally, UrsA decreased the level of Bcl-2 to trigger apoptosis in human MCF-7 cells [35,36].

In their study using MDA-MB-231, Yehya et al. [28] found that UrsA suppressed cancer cell invasion, migration, and proliferation, as well as the formation of cell colonies. Moreover, UrsA has been shown to significantly reduce the expression of u-PA and MMP-2 while simultaneously increasing the expression of PAI-1 and TIMP-2. The expression of u-PA, TIMP-2, PAI-1, and MT1-MMP has also been reduced as a result of

UrsA. In addition, Kim et al. [29] investigated whether UrsA has the capability of inducing apoptosis in MDA-MB-231 human BC cells through both extrinsic death receptor pathways and intrinsic mitochondrial death pathways. The results of an investigation using immunoblotting demonstrated that UrsA stimulated the Fas receptor, which was then followed by caspase-8 and PARP activation. In addition to this, UrsA raises the level of expression of Bax, causes the release of cytochrome C, lowers the level of Bcl-2, and activates caspases-9. Additionally, UA decreased the level of Bcl-2 to trigger apoptosis in human MCF-7 cells [30].

#### **Rosmarinic Acid (RA)**

Rosmarinic acid, also known as RA, is a type of flavonoid that is frequently discovered in plants belonging to the Lamiaceae family. Tea, herbs, cooking condiments, spices, and fruits all make use of RA-rich plants such as *Perilla frutescens* (L.), Britton, *Rosmarinus officinalis* L., and *Melissa officinalis* L. These plants are popular all over the world and are used in a variety of applications. Because of its nutritional qualities and the fact that it has been demonstrated to possess powerful antioxidant activity (31). RA is used to make people healthier. RA is an ester of caffeic acid and 3,4-dihydroxyphenyllactic acid and is one of the primary phenolic compounds found in *O. sanctum* [32]. The leaves of *O. sanctum* were extracted with ethanol (EEOS) and analyzed using a trusted LC-MS technique by Shanmugam et al. in 2012. They then identified RA and UrsA as the functional molecules in EEOS. It has been found that rosmarinic acid has powerful antioxidant properties. It protects cells from free radicals, which would otherwise destroy them. Furthermore, cellular damage is brought about by an excess of oxidation in the body. When this acid is present, it inhibits oxidation from happening in excess. In addition to its antioxidant properties, RA has anti-inflammatory properties. Pegenin is another compound in the mixture that can perform the same task. In addition to these two components, eugenol is Tulsi's primary anti-inflammatory catalyst. It is the primary factor that helps keep blood sugar levels stable. It increases insulin secretion by stimulating pancreatic beta cells. It has been found that RA has antimicrobial, immunomodulatory, diabetic, anti-allergic, anti-inflammatory, hepatoprotective, and renal-protective properties [33,34]. In addition, the utilization of RA has a prospective application in the management and prevention of cancer [35]. Research on RA is currently being conducted to investigate its potential uses in the treatment and prevention of cancer [36].

7.86 mg/g of rosmarinic acid is produced by soaking *Ocimum tenuiflorum* L. leaves in 95% ethanol for two weeks, filtering them, and then drying them. This acid prevents squamous cell carcinoma cells from invading the head and neck [37]. After being extracted in 99% methanol, the dried leaves of *Ocimum basilicum* L.

exhibited antiproliferative properties against breast, T-cell, and cervical cancer, with a RA of 3.01 mg/g [38]. An ethanol extract of dried rosemary leaves increased the sensitivity of ovarian cancer cells to cisplatin (DDP) [39]. RA's anti-inflammatory targets for cancer treatment include nuclear factor-kB (NF-kB) and cyclooxygenase-2 (COX-2). RA has been shown to have anti-inflammatory actions in lung, breast, and liver cancer cells by suppressing COX-2 activity and adversely regulating ERK1/2 [40]. Studies revealed that RA decreased cancer cell invasion and regulated the expression of proteins linked to EMT [41].

#### **Apigenin**

Another name for the edible flavonoid apigenin (APG) is 4,5,7-trihydroxyflavone. Because of its low intrinsic cytotoxicity and ability to affect normal cells differently than cancer cells, it has become more and more popular as a medicine that promotes health in recent years. The drug's capacity to target cancer cells more precisely than healthy cells is a result of these two aspects. Particularly when compared to other polyphenols that share structural similarities, this is especially true [42]. Many different types of flavonoids contain the polyphenol apigenin. The strong anti-inflammatory and antioxidant properties of apigenin are an important factor in its potential cancer-preventive effects [43].

Additionally, apigenin prevents cancer cells from proliferating. It is noteworthy that apigenin has a key role in cancer prevention by considerably promoting apoptosis in a variety of cell lines and animal models [44]. This impact of apigenin has been demonstrated in cell lines and animal models. Because of its low toxicity and apparent function in lowering cancer treatment resistance, apigenin is a valuable source for pharmaceuticals. Because of its antioxidant qualities, apigenin is important for controlling the production of free radicals, reducing inflammation and oxidative stress, and controlling cancer. By controlling several cellular signalling pathways, some of which may include angiogenesis, apoptosis, the cell cycle, and other genetic processes, this flavonoid seems to have anticancer properties.

Apigenin strongly suppressed colorectal cancer cell growth, proliferation, migration, invasion, and organoid development by inhibiting the Wnt/catenin signaling pathway [45]. Combination therapy with apigenin and cetuximab also decreases the expression of p-epidermal growth factor receptor, p-Akt, p-signal transducer and activator of transcription 3, and cyclin D1 [46]. Through the signal transducer and activator of the transcription (STAT-3) pathway, apigenin suppressed the expression of MMP-2, MMP-9, and vascular endothelial growth factor (VEGF), all of which play roles in cell migration and invasion. Apigenin effectively blocked STAT3 transcriptional activity, decreased STAT3 nuclear localization, and inhibited STAT3

phosphorylation [47]. Additionally, STAT3 transcriptional activity, STAT3 phosphorylation, and STAT3 nuclear localization were all effectively suppressed by apigenin [48]. Apigenin suppressed ERK1/2 and P90RSK phosphorylation while activating AKT and S6 phosphorylation [49]. Two kinases, AKT and ERK, were both inhibited by apigenin. Moreover, apigenin boosted the antitumour activity of ABT-263 in colon cancer cells by decreasing the expression of pro-survival regulators AKT, Mcl-1, and ERK [50].

#### **Carvacrol**

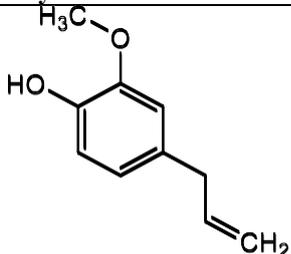
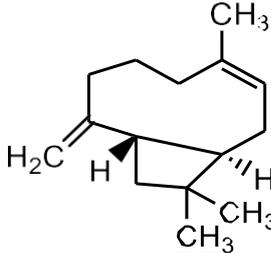
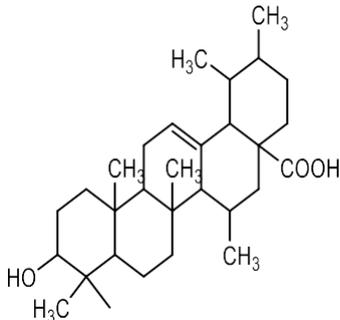
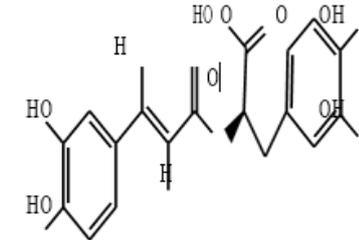
Carvacrol (5-isopropyl-2-methylphenol) and its isomer thymol (2-isopropyl-5-methylphenol) are natural compounds that have been extensively studied. There are several biological effects of these two chemicals. The primary ingredients in the essential oils of a number of plants in the Verbenaceae and Lamiaceae families, such as thyme (*Thymus vulgare* L.), oregano (*Origanum vulgare* L.), and "ale-crim-da-chapada" [51,52,53], are monoterpenoid phenols. There are anti-inflammatory qualities to certain drugs.

Additionally, 1 mM and 0.5 mM carvacrol were able to inhibit the survival and proliferation of lung cancer cells (A549 cell line) and induce early apoptotic features [54,55]. These effects were mainly caused by an increase in malondialdehyde (MDA) and 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels and a suppression of tyrosine kinase receptor (AXL) expression [56]. Carvacrol demonstrated concentration-dependent anticancer effects on hepatic carcinomas (HepG2 cell line), causing cell death and antiproliferative effects [57].

The stimulation of apoptosis and the downregulation of cell proliferation were caused by a mitochondria-mediated mechanism, which also activated caspase-3 and downregulated Bcl-2. The extracellular signal-regulated kinases (ERK) protein and mitogen-activated protein kinases (p38) may potentially cause apoptosis [58]. In a similar vein, Ref. [59] demonstrated that carvacrol at 650 M retarded the cell cycle/mitosis and caused cell death after 24 hours of incubation, resulting in a decrease in S phase cells and an increase in G1 phase cells. Furthermore, in colorectal cancer (Caco-2 cell line) incubation with carvacrol (115 M) reduced cell viability and markedly increased the frequency of early apoptotic cells (71). Additionally, HT-29 and HCT116 cell proliferation was inhibited [60].

Carvacrol also reduced Bcl-2, metalloproteinases 2 and 9 (MMP-2 and MMP-9), phosphorylated extracellular signal-regulated kinases (p-ERK, p-Akt), and cyclin B1, while increasing phosphorylated jun N-terminal kinase (p-JNK) and Bax, resulting in cell cycle arrest in the G2/M phase [61]. It has been demonstrated that carvacrol lowers the viability of the MDA-MB231 and MCF-7 breast cancer cell lines [62,63].

Table 2: Chemistry of Different Phytoconstituents

Phytoconstituent	Structure and of Phytoconstituent	Chemical name	Pharmacological activity
Eugenol		4-Allyl-2-methoxy Phenol	Isoeugenol causes a decrease in the formation of iron-oxygen chelate complex, which is the initiating factor of lipid peroxidation.[64].
Caryophyllene		(1R,4E,9S)-4,11,11-trimethyl-8-methylidenebicyclo[7.2.0]undec-4-ene	activities comprising antimicrobial, anticarcinogenic, anti-inflammatory, antioxidant, antispasmodic, gastric cytoprotection, and anesthetic effects [65,66].
Ursolic acid		(1S,2R,4aS,6aS,6bR,8aR,10S,12aR,12bR,14bS)-10-Hydroxy-1,2,6a,6b,9,9,12a-heptamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydricene-4a(2H)-carboxylic acid.	It exhibits anti-inflammatory [67], anti-oxidant [68], anti-carcinogenic [69], antiobesity [70], anti-diabetic [71], cardioprotective [72], neuroprotective [73].
Rosmarinic acid		(2R)-3-(3,4-Dihydroxyphenyl)-2-[(2E)-3-(3,4-dihydroxyphenyl)prop-2-enyl]oxy}propanoic acid	Antioxidant and anti-allergic agent, oxidation inhibitor of low density lipoprotein, murine cell proliferation inhibitor and cyclooxygenase inhibitor[74].

### III. PHARMACOLOGICAL ACTIVITY OF O. SANCTUM

**1. Anticancer activity:** The anticancer activity of OS has been proved and cited by several investigators[75]. The alcoholic extract (AIE) of leaves of OS has a modulatory influence on carcinogen metabolizing enzymes such as cytochrome P450, cytochrome b5, aryl hydrocarbon hydroxylase and glutathione S-transferase (GST), which are important in detoxification of carcinogens and mutagens [76]. The anticancer activity of OS has been reported against human fibrosarcoma cells culture, wherein AIE of this drug induced cytotoxicity 50g/ml and above. Morphologically, the cells showed shrunken cytoplasm and condensed nuclei. The DNA was found to be fragmented on observation in

agarose gel electrophoresis. OS significantly decreased the incidence of benzo(a)pyrene induced neoplasia of fore-stomach of mice and 3'-methyl-4-dimethylaminoazo-benzene induced hepatomas in rats. The AIE of the leaves of OS was shown to have an inhibitory effect on chemically induced skin papillomas in mice [77]. Topical treatment of Tulsi leaf extract in 7,12-dimethylbenz(a)anthracene (DMBA) induced papillomagenesis significantly reduced the tumour incidence, average number of papillomas/mouse and cumulative number of papillomas in mice. Topical application of the extract significantly elevated reduced GSH content and GST activities [78].

**2. Chemopreventive activity:** The chemopreventive effect of OS leaf extract is probably through the induction of hepatic/extrahepatic GST in mice. Elevated levels of reduced

GSH in liver, lung and stomach tissues in OS extract supplemented mice were also found. Significant antiproliferative and chemopreventive activities were observed in mice with high concentration of OS seed oil. The potential chemopreventive activity of seed oil has been partly attributed to its antioxidant activity [79].

**3. Radioprotective activity:** The radioprotective effect of OS was firstly reported in the year 1995. Two isolated flavonoids, viz., orientin and vicenin from OS leaves showed better radioprotective effect as compared with synthetic radioprotectors. They have shown significant protection to the human lymphocytes against the clastogenic effect of radiation at a low, non-toxic concentrations [80]. 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 [81].

**4. Antioxidant activity:** The antioxidant activity of OS has been reported by many workers [8-11]. The antioxidant properties of flavonoids and their relation to membrane protection have been observed [82]. Antioxidant activity of the flavonoids (orientin and vicenin) in vivo was expressed in a significant reduction in the radiation induced lipid peroxidation in mouse liver [25]. OS extract has significant ability to scavenge highly reactive free radicals [83]. The phenolic compounds, viz., cirsilineol, 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 [84].

**5. Antihypertensive and cardioprotective activity:** The transient cerebral ischemia and long term cerebral hypoperfusion (causing cellular oedema, gliosis and perivascular inflammatory infiltrate) have been prevented by OS [85]. The OS fixed oil administered intravenously produced hypotensive effect in anaesthetized dog, which seem to be due to its peripheral vasodilatory action. Essential fatty acids like linoleic and linolenic acids, contained in the OS oil produce series 1 and 3 (PGE1 and PGE3) prostaglandins and inhibit the formation of series 2 prostaglandins (PGE2). The long term feeding of OS offers significant protection against isoproterenol-induced myocardial necrosis in Wistar rats through enhancement of endogenous antioxidant [86].

## IV. PRECLINICAL TRIALS

### I. Antidiabetic

a) Ethanolic extract of *O. Sanctum L.* significantly decreases the blood glucose, glycosylated hemoglobin and urea with a concomitant increase in glycogen, hemoglobin and protein in streptozotocin-induced diabetic rats [87].

- b) This extract also resulted in an increase in insulin and peptide levels and glucose tolerance. The constituents of *O. Sanctum L.* leaf extracts have stimulatory effects [88] on physiological pathways of insulin secretion, which may underlie its reported antidiabetic action.
- c) In another study the effect of *O. Sanctum L.* on three important enzymes of carbohydrate metabolism [glucokinase (gk), hexokinase (hk) and phosphofructokinase (PFK) along with glycogen content of insulin-dependent (skeletal muscle and liver) and insulin-independent tissues (kidneys and brain) was studied by Vats et al., [89] in streptozotocin (STZ, 65 mg/kg)-induced model of diabetes for 30 days in rats.
- d) Tulsi (*O. Sanctum L.*) leaf powder [90] was fed at the 1% level in normal and diabetic rats for a period of one month and the result indicated a significant reduction in fasting blood sugar, urea, total amino acids level. This observation indicates the hypoglycemic effect of *O. Sanctum L.* in diabetic rats.

### 2. Cardiac activity

- a) Oral feeding of hydroalcoholic extract of *O. Sanctum L.* (100 mg/kg) to male Wistar rats subjected to chronic-resistant stress (6 h/day for 21 days) significantly prevented the chronic-resistant stress-induced rise in plasma cAMP level, myocardial superoxide dismutase and catalase activities [91] as well as the light microscopic changes in the myocardium.
- b) Wistar rats fed with fresh leaf homogenate of *O. Sanctum L.* (50 and 100 mg/kg body weight) daily for 30 days inhibit isoproterenol-induced changes [92] in myocardial superoxide dismutase, glutathione peroxidase and reduced glutathione.
- c) In another study effect of pre- and co-treatment of hydroalcoholic extract of *O. Sanctum L.* at different doses (25, 50, 75, 100, 200 and 400 mg/kg) was investigated against isoproterenol (ISO, 20 mg/kg, Sc) myocardial infarction [107] in rats. *O. Sanctum L.* at the dose of 25, 50, 75 and 100 mg/kg significantly reduced glutathione (GSH), superoxide dismutase and LDH levels. In this study, it was observed that *O. Sanctum L.* at the dose of 50 mg/kg was found to demonstrate maximum cardioprotective effect.
- d) The peroxidation of cardiac lipid [93] membranes resulted from the production of drug-induced oxygen radicals in heart cells. *O. Sanctum L.* ursolic acid (UA) has been found to be protective against lipid peroxidation caused by Adriamycin (ADR). In liver and heart microsomes, UA provided 13 and 17% protection, respectively. It rose to 69% when combined with oleanolic acid (OA), which was extracted from *Eugenia jumbolata*.

**3. Wound healing activity**

- a) Evaluated the wound healing effect of aqueous extract of *O. Sanctum L.* In rats. [109] Wound-breaking strength in incision wound model, epithelization period and percent wound concentration in excision wound model were studied owing to increased per cent wound contraction. *Ocimum sanctum L.* May be useful in the management of abnormal healing such as keloids and hypertropic scars.
- b) Ethanolic extract of leaves of *O. Sanctum L.* Was investigated for normal wound healing and dexamethasone-depressed healing.[94] The extract significantly increased the wound breaking strength, wound epithelializes fast and wound contraction was significantly increased along with increase in wet and dry granulation tissue weight and granulation tissue breaking strength. The extract also significantly decreases the anti- healing activities of dexamethasone in all wound healing models.

**4. Gentotoxicity**

- a) To identify the modifying impact of *O. Sanctum L.*, an in vivo cytogenetic test [95] has been performed on *Allium cepa* root tip cells. Aqueous leaf extract against genotoxicity caused by mercury (Hg) and chromium (Cr). Following treatment with the leaf extract, it was found that the roots' chromosomal abnormalities and mitotic index (MI) significantly improved. The lower dosages of the leaf extract

were shown to be more effective than the higher doses when compared to pre-treated (Cr/Hg) samples.

- b) When administered at 100 mg/kg daily for 7 days and 300 mg/kg daily for 14 days, Immuno-21, a polyherbal formulation that contains *O. Sanctum L.* and other herbal extracts, inhibited both classical and non-classical chromosomal aberration [96] caused by cyclophosphamide (40 mg/kg i.p.) (40–60% of control). This also lessens the rise of micronuclei in the cyclophosphamide-treated mice's bone marrow erythrocytes.

**5. Hypolipidemic**

- a) Administration of *O. Sanctum L.* Seed oil (0.8 gm/kg body weight/day) for four weeks, in cholesterol-fed (100 mg/kg body weight/day) rabbits significantly decreases serum cholesterol, triacylglycerol and LDL + VLDL cholesterol as compared to untreated cholesterol-fed group suggesting the hypo-cholesterolemic [97] activity of *O. Sanctum L.*
- b) Fresh leaves of *O. Sanctum L.* Mixed OS 1 and 2 g in 100 gm of diet given for four weeks brought about significant changes in the lipid [114] of normal albino rabbits. This resulted in significant lowering in serum total cholesterol, triglyceride, phospholipids and LDL-cholesterol levels and significant increase in the HDL-cholesterol and total fecal sterol contents.

**Table 3: Clinical Trails**

Clinical domain	Study design	Participants (age range)	Tulsi extract	Intervention Dosage	Duration	Outcomes measure
Metabolic disorder	Randomized controlled clinical trial	40 male adults T2DM (45–55) years	Tulsi leaves	3 g/day before meal Not	6.5 week	Significant decrease postprandial glucose and fasting blood glucose [98]
	Clinical trials controlled grow parallel		Tulsi powder	2 g/day	2 weeks	Significant decrease postprandial glucose and fasting blood glucose [99]
Immuno modulation	Randomized, placebo-controlled clinical trial	30 healthy Adults (18–30) years	Ethanolic Tulsi leaves extract	1 bar × 2/day (1000 mg tulsi)	2 weeks	performance decreases fatigue and CK levels less increase in lactic acid [100]
	Open clinical trial	20 adults with Asthma	aqueous tulsi leaves, tablet	500 mg × 3/day	1 week	Relief within 3 days, improved vital capacity [101]
Viral infection	Clinical trial	20 cases, viral hepatitis (10–60 years)	Aqueous extract fresh tulsi leaves	10 g daily	2 weeks for mild cases 3 weeks for Severe cases	Symptoms all improved within 2 weeks [102]
	Randomized clinical trial	14 adults, viral encephalitis	Aqueous extract	2.5 g 4 times/day	4 weeks	Increased survival rate compared to steroid

	parallel-controlled		fresh tulsi leaves			[103]
Neurocognition	Randomized, double blind, placebo controlled clinical trial	40 healthy adults (18–30) years	Ethanollic tulsi leaves capsule	300 mg/day before meals	4 weeks	Cognitive flexibility, attention, Improved working memory only after day 15 [104]
	Randomized, double-blind, placebo-controlled	150 adults with stress (18–65) years	OCIBEST † whole plant capsule	400 mg 3 times/day after meals	6 weeks	Reduction in stress related symptoms: fatigue, sleep and sexual problems [105]
	Clinical trials	35 adults with GAD (18–60) years	Ethanollic tulsi leaves capsule	500 mg 2x daily after meals	8 weeks	Self-reported questionnaire ,anxiety, stress, & Depression [106]

## V. CONCLUSION

The numerous psychological and physiological advantages of tulsi consumption are demonstrated by contemporary scientific research on the plant. It also speaks to the wisdom of Ayurveda and Hinduism, which honour tulsi as a plant that can be consumed, worshipped, made into tea, and used for spiritual and medical purposes in day-to-day life.

They are used extensively in ayurvedic medications. It has both corrective and restorative qualities. For sore throats, tulsi leaf-infused water is beneficial. You may also swish it. The flu and cold can be cured by biting tulsi leaves. When consumed early in the day, tulsi leaves filter blood. It aids in protecting the entire respiratory system. It is used as a home-grown cleaner and for body scouring since it has many curative qualities. It aids in dandruff control.

The generally disjointed approach of contemporary allopathic medicine has not been able to handle the increasing number of chronic degenerative environmental, lifestyle, and personal stress-related disorders that afflict contemporary society, despite the many remarkable achievements of western medical science. Traditional herbal remedies and holistic health techniques are beginning to play a significant supplementary role in the prevention and treatment of the passive illnesses that plague modern society. The World Health Organisation has suggested that traditional health and folk medicine systems be combined with contemporary medical therapy in order to better address health issues globally, acknowledging the significance of expanding the western medical perspective.

## REFERENCES

- [1] Bast F, Rani P, Meena D. Chloroplast DNA phylogeography of holy basil (*Ocimum tenuiflorum*) in Indian subcontinent. *Scientific World Journal*. 2014,2014, 847–482.
- [2] Jamshidi N, Cohen MM. The clinical efficacy and safety of tulsi in humans: A systematic review of the literature. *Evid Based Complement Alternat Med*. 2017, 20179217567.
- [3] Dr. Umme Amarah, Dr Laxmikanth Chatra, Dr Prashanth Shenai, Dr Veena K. M., Dr Rachana V. Prabhu and Dr Vagish Kumar., *Miracle Plant -Tulsi.*, *World Journal of Pharmacy and Pharmaceutical Sciences*. 2017, 6(1),2017, 1567-1581.
- [4] KP Sampath Kumar, Debjit Bhowmik, Biswajit, Chiranjib, Pankaj and KK Tripathi Margret Chandira., *Traditional Indian Herbal Plants Tulsi and Its Medicinal Importance Research Journal of Pharmacognosy and Phytochemistry*. 2010, 2(2), 103- 108.
- [5] Chatterjee, Gautam (2001). *Sacred Hindu Symbols*. Abhinav Publications. Pp. 93. ISBN 9788170173977.Simoon.
- [6] Kumar PK. Pharmacological actions of *Ocimum Sanctum*. *Review article Int. J. Advnc. Pharm. Bio. Chem*. 2012, 1(3), 406-414.
- [7] Joseph B. Ethan pharmacological and photochemical Aspects of *Ocimum sanctum* Linn. *The elixir of life. Brit. J Pharma. Res*. 2013, 3(2), 273-29.
- [8] Kress W.J., Wurdack K.J., Zimmer E.A., Weigt L.A., Janzen D.H. Use of DNA barcodes to identify flowering plants. *Proc. Natl. Acad. Sci. USA*. 2005, 102,8369– 8374.
- [9] Joshi K., Chavan P., Warude D., Patwardhan B. Molecular markers in herbal drug technology. *Curr. Sci*. 2004, 87,159–165.
- [10] De Mattia F.D., Bruni I., Galimberti A., Cattaneo F., Casiraghi M., Labra M. A comparative study of the different DNA barcoding markers for the identification of some members of Lamiaceae. *Food Res. Int*. 2011, 44, 693–702.
- [11] Rai P.S., Bellampalli R., Dobriyal R.M., Agarwal A., Satyamoorthy K., Narayana A. DNA barcoding of authentic and substitute samples of herb of the family Asparagaceae

- and Asclepiadaceae based on the ITS2 region. *J. Ayurveda Integr. Med.* 2012, 3,136–140.
- [12] Medicinal Plants. 2004. National Institute of Industrial Research. P. 320
- [13] Gurav, T.P.; Dholakia, B.B.; Giri, A.P. A glance at the chemodiversity of *Ocimum* species: Trends, implications, and strategies for the quality and yield improvement of essential oil. *Phytochem. Rev.* 2022, 21, 879–913
- [14] Rengarajan, T.; Nandakumar, N.; Rajendran, P.; Haribabu, L.; Nishigaki, I.; Balasubramanian, M.P. D-pinitol promotes apoptosis in MCF-7 cells via induction of p53 and Bax and inhibition of Bcl-2 and NF- $\kappa$ B. *Asian Pac. J. Cancer Prev.* 2014, 15, 1757–1762.
- [15] Salehi, B.; Mishra, A.P.; Shukla, I.; Sharifi-Rad, M.; Contreras, M.D.M.; Segura-Carretero, A.; Fathi, H.; Nasrabadi, N.N.; Kobarfard, F.; Sharifi-Rad, J. Thymol, Thyme, and Other Plant Sources: Health and Potential Uses. *Phytother. Res.* 2018, 32, 1688–1706.
- [16] Anusmitha, K.M.; Aruna, M.; Job, J.T.; Narayanankutty, A.; Pb, B.; Rajagopal, R.; Alfarhan, A.; Barcelo, D. Phytochemical analysis, antioxidant, anti-inflammatory, antigenotoxic, and anticancer activities of different *Ocimum* plant extracts prepared by ultrasound-assisted method. *Physiol. Mol. Plant Pathol.* 2021, 117, 101746.
- [17] Khalil, A.A.; ur Rahman, U.; Khan, M.R.; Sahar, A.; Mehmood, T.; Khan, M. Essential oil eugenol: Sources, extraction techniques and nutraceutical perspectives. *RSC Adv.* 2017, 7, 32669–32681.
- [18] Marchese, A.; Barbieri, R.; Coppo, E.; Orhan, I.E.; Daglia, M.; Nabavi, S.F.; Izadi, M.; Abdollahi, M.; Nabavi, S.M.; Ajami, M. Antimicrobial activity of eugenol and essential oils containing eugenol: A mechanistic viewpoint. *Crit. Rev. Microbiol.* 2017, 43, 668–689.
- [19] B Aggarwal, B.; Prasad, S.; Reuter, S.; Kannappan, R.; R Yadav, V.; Park, B.; Hye, K.J.; Gupta, S.; Phromnoi, K.; Sundaram, C.; et al. Identification of novel anti-inflammatory agents from Ayurvedic medicine for prevention of chronic diseases: “reverse pharmacology” and “bedside to bench” approach. *Curr. Drug Targets.* 2011, 12, 1595–1653.
- [20] Kamatou, G.P.; Vermaak, I.; Viljoen, A.M. Eugenol—From the remote Maluku Islands to the international market place: A review of a remarkable and versatile molecule. *Molecules.* 2012, 17, 6953–6981.
- [21] Yadav, M.K.; Chae, S.W.; Im, G.J.; Chung, J.W.; Song, J.J. Eugenol: A phyto-compound effective against methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* clinical strain biofilms. *PLoS ONE.* 2015, 10, e0119564.
- [22] Legault, J.; Pichette, A. Potentiating Effect of  $\beta$ -Caryophyllene on Anticancer Activity of  $\alpha$ -Humulene, Isocaryophyllene and Paclitaxel. *J. Pharm. Pharmacol.* 2010, 59, 1643–1647.
- [23] Alma, M.H.; Mavi, A.; Yildirim, A.; Digrak, M.; Hirata, T. Screening Chemical Composition and in Vitro Antioxidant and Antimicrobial Activities of the Essential Oils from *Origanum Syriacum* L. Growing in Turkey. *Biol. Pharm. Bull.* 2003, 26, 1725–1729.
- [24] Zahran, E.M.; Abdelmohsen, U.R.; Ayoub, A.T.; Salem, M.A.; Khalil, H.E.; Desoukey, S.Y.; Fouad, M.A.; Kamel, M.S. Metabolic Profiling, Histopathological Anti-Ulcer Study, Molecular Docking and Molecular Dynamics of Ursolic Acid Isolated from *Ocimum Forskolei* Benth. (Family Lamiaceae). *South Afr. J. Bot.* 2020, 131, 311–319.
- [25] Carvalho, R.P.R.; Lima, G.D. de A.; Ribeiro, F.C.D.; Ervilha, L.O.G.; Oliveira, E.L.; Viana, A.G.A.; Machado-Neves, M. Eugenol Reduces Serum Testosterone Levels and Sperm Viability in Adult Wistar Rats. *Reprod. Toxicol.* 2022, 113, 110–119.
- [26] Al-Fatlawi, A.A.; Ahmad, A. Cytotoxicity and Pro-Apoptotic Activity of Carvacrol on Human Breast Cancer Cell Line MCF-7. *World J. Pharm. Sci.* 2014, 2, 1134–1415.
- [27] Yehya, A.H.; Asif, M.; Majid, A.M.A.; Oon, C.E. Complementary effects of *Orthosiphon stamineus* standardized ethanolic extract and rosmarinic acid in combination with gemcitabine on pancreatic cancer. *Biomed. J.* 2020, 44, 694–708.
- [28] Kim, S.S.; Oh, O.J.; Min, H.Y.; Park, E.J.; Kim, Y.; Park, H.J.; Han, Y.N.; Lee, S.K. Eugenol suppresses cyclooxygenase-2 expression in lipopolysaccharide-stimulated mouse macrophage RAW264. 7 cells. *Life Sci.* 2003, 73, 337–348.
- [29] Mari, A.; Mani, G.; Nagabhishek, S.N.; Balaraman, G.; Subramanian, N.; Mirza, F.B.; Sundaram, J.; Thiruvengadam, D. Carvacrol Promotes Cell Cycle Arrest and Apoptosis through PI3K/AKT Signaling Pathway in MCF-7 Breast Cancer Cells. *Chin. J. Integr. Med.* 2021, 27, 680–687.
- [30] Nunes, S.R.R.P.; Madureira, A.R.; Campos, D.; Sarmiento, B.; Gomes, A.M.; Pintado, M.M.; Reis, F. Therapeutic and Nutraceutical Potential of Rosmarinic Acid—Cytoprotective Properties and Pharmacokinetic Profile. *Crit. Rev. Food Sci. Nutr.* 2015, 57, 1799–1806.
- [31] Magalhães, D.B.; Castro, I.; Lopes-Rodrigues, V.; Pereira, J.M.; Barros, L.; Ferreira, I.C.F.R.; Xavier, C.P.R.; Vasconcelos, M.H. Melissa

- officinalis L. Ethanol extract inhibits the growth of a lung cancer cell line by interfering with the cell cycle and inducing apoptosis. *Food Funct.* 2018, 9, 3134–3142.
- [32] Petersen, M. Rosmarinic acid. *Phytochemistry* 2003, 62, 121–125.
- [33] Alagawany, M.; El-Hack, M.E.A.; Farag, M.R.; Gopi, M.; Karthik, K.; Malik, Y.S.; Dhama, K. Rosmarinic acid: Modes of action, medicinal values and health benefits. *Anim. Health Res. Rev.* 2017, 18, 167–176.
- [34] Zhao, J.; Xu, L.; Jin, D.; Xin, Y.; Tian, L.; Wang, T.; Zhao, D.; Wang, Z.; Wang, J. Rosmarinic Acid and Related Dietary Supplements: Potential Applications in the Prevention and Treatment of Cancer. *Biomolecules.* 2022, 12, 1410.
- [35] Liu, Y.; Xu, X.; Tang, H.; Pan, Y.; Hu, B.; Huang, G. Rosmarinic acid inhibits cell proliferation, migration, and invasion and induces apoptosis in human glioma cells. *Int. J. Mol. Med.* 2021, 47, 67.
- [36] Utispan, K.; Niyomtham, N.; Yingyongnarongkul, B.; Koontongkaew, S. Ethanol extract of *Ocimum sanctum* leaves reduced invasion and matrix metalloproteinase activity of head and neck cancer cell lines. *Asian Pac. J. Cancer Prev.* 2020, 21, 363.
- [37] Elansary, H.O.; Mahmoud, E.A. In vitro antioxidant and antiproliferative activities of six international basil cultivars. *Nat. Prod. Res.* 2015, 29, 2149–2154.
- [38] Tai, J.; Cheung, S.; Wu, M.; Hasman, D. Antiproliferation effect of Rosemary (*Rosmarinus officinalis*) on human ovarian cancer cells in vitro. *Phytomedicine.* 2012, 19, 436–443.
- [39] Scheckel, K.A.; Degner, S.C.; Romagnolo, D.F. Rosmarinic acid antagonizes activator protein-1-dependent activation of cyclooxygenase-2 expression in human cancer and nonmalignant cell lines. *J. Nutr.* 2008, 138, 2098–2105.
- [40] Han, Y.H.; Kee, J.Y.; Hong, S.H. Rosmarinic acid activates AMPK to inhibit metastasis of colorectal cancer. *Front. Pharmacol.* 2018, 9, 68.
- [41] Jung, C.H.I.Y.; Kim, S.-Y.; Lee, C. Carvacrol Targets AXL to Inhibit Cell Proliferation and Migration in Non-Small Cell Lung Cancer Cells. *Anticancer Res.* 2018, 38, 279.
- [42] Singh, P.; Mishra, S.K.; Noel, S.; Sharma, S.; Rath, S.K. Acute exposure of apigenin induces hepatotoxicity in Swiss mice. *PLoS ONE* 2012, 7, e31964.
- [43] Kaur, P.; Shukla, S.; Gupta, S. Plant flavonoid apigenin inactivates Akt to trigger apoptosis in human prostate cancer: An in vitro and in vivo study. *Carcinogenesis* 2008, 29, 2210–2217.
- [44] Xu, M.; Wang, S.; Song, Y.U.; Yao, J.; Huang, K.; Zhu, X. Apigenin suppresses colorectal cancer cell proliferation, migration and invasion via inhibition of the Wnt/ $\beta$ -catenin signaling pathway. *Oncol. Lett.* 2016, 11, 3075–3080.
- [45] Hu, W.J.; Liu, J.; Zhong, L.K.; Wang, J. Apigenin enhances the antitumor effects of cetuximab in nasopharyngeal carcinoma by inhibiting EGFR signaling. *Biomed. Pharmacother.* 2018, 102, 681–688.
- [46] Cao, H.-H.; Chu, J.-H.; Kwan, H.Y.; Su, T.; Yu, H.; Cheng, B.C.-Y.; Fu, X.-Q.; Guo, H.; Li, T.; Tse, A.K.-W.; et al. Inhibition of the STAT3 signaling pathway contributes to apigenin-mediated anti-metastatic effect in melanoma. *Sci. Rep.* 2016, 6, 21731.
- [47] Granato, M.; GilardiniMontani, M.S.; Santarelli, R.; D’Orazi, G.; Faggioni, A.; Cirone, M. Apigenin, by activating p53 and inhibiting STAT3, modulates the balance between pro-apoptotic and pro-survival pathways to induce PEL cell death. *J. Exp. Clin. Cancer Res.* 2017, 36, 1–9.
- [48] Lim, W.; Park, S.; Bazer, F.W.; Song, G. Apigenin reduces survival of choriocarcinoma cells by inducing apoptosis via the PI3K/AKT and ERK1/2 MAPK pathways. *J. Cell Physiol.* 2016, 231, 2690–2699.
- [49] Shao, H.; Jing, K.; Mahmoud, E.; Huang, H.; Fang, X.; Yu, C. Apigenin Sensitizes Colon Cancer Cells to Antitumor Activity of ABT-263. *Mol. Cancer Ther.* 2013, 12, 2640–2650.
- [50] Salehi, B.; Mishra, A.P.; Shukla, I.; Sharifi-Rad, M.; Contreras, M.D.M.; Segura-Carretero, A.; Fathi, H.; Nasrabadi, N.N.; Kobarfard, F.; Sharifi-Rad, J. *Thymol, Thyme, and Other Plant Sources: Health and Potential Uses.* *Phytother. Res.* 2018, 32, 1688–1706.
- [51] Dos Santos, C.P.; Pinto, J.A.O.; dos Santos, C.A.; Cruz, E.M.O.; de Fátima Arrigoni-Blank, M.; Andrade, T.M.; de Alexandria Santos, D.; Alves, P.B.; Blank, A.F. Harvest Time and Geographical Origin Affect the Essential Oil of *LippiaGracilis* Schauer. *Ind. Crops Prod.* 2016, 79, 205–210.
- [52] Elbe, H.; Yigitturk, G.; Cavusoglu, T.; Baygar, T.; OzgulOnal, M.; Ozturk, F. Comparison of Ultrastructural Changes and the Anticarcinogenic Effects of Thymol and Carvacrol on Ovarian Cancer Cells: Which Is More Effective? *UltrastructPathol* 2020, 44, 193–202.
- [53] Koparal, A.T.; Zeytinoglu, M. Effects of Carvacrol on a Human Non-Small Cell Lung Cancer (NSCLC) Cell Line, A549. In *Animal Cell Technology: Basic & Applied Aspects*; Springer: Dordrecht, The Netherlands, 2003, 207–211.

- [54] Ozkan, A.; Erdogan, A. A Comparative Study of the Antioxidant/Prooxidant Effects of Carvacrol and Thymol at Various Concentrations on Membrane and DNA of Parental and Drug Resistant H1299 Cells. *Nat. Prod. Commun.* 2012, 7, 1934578X1200701.
- [55] Horvathova, E.; Navarova, J.; Galova, E.; Sevcovicova, A.; Chodakova, L.; Snahnicanova, Z.; Melusova, M.; Kozics, K.; Slamenova, D. Assessment of Antioxidative, Chelating, and DNA-Protective Effects of Selected Essential Oil Components (Eugenol, Carvacrol, Thymol, Borneol, Eucalyptol) of Plants and Intact *Rosmarinus Officinalis* Oil. *J Agric Food Chem.* 2014, 62, 6632–6639.
- [56] Özkan, A.; Erdogan, A. A Comparative Evaluation of Antioxidant and Anticancer Activity of Essential Oil from *Origanum Onites* (Lamiaceae) and Its Two Major Phenolic Components. *Turk. J. Biol.* 2011.
- [57] Sanchez, A.; Tripathy, D.; Yin, X.; Luo, J.; Martinez, J.; Grammas, P. Pigment Epithelium-Derived Factor (PEDF) Protects Cortical Neurons in Vitro from Oxidant Injury by Activation of Extracellular Signal-Regulated Kinase (ERK)  $\frac{1}{2}$  and Induction of Bcl-2. *Neurosci. Res.* 2012, 72, 1–8.
- [58] Llana-Ruiz-Cabello, M.; Gutiérrez-Praena, D.; Pichardo, S.; Moreno, F.J.; Bermúdez, J.M.; Aucejo, S.; Cameán, A.M. Cytotoxicity and Morphological Effects Induced by Carvacrol and Thymol on the Human Cell Line Caco-2. *Food Chem. Toxicol.* 2014, 64, 281–290.
- [59] Calibasi Kocal, G.; Pakdemirli, A. Antiproliferative Effects of Carvacrol on Neuroblastoma Cells. *J. Dr. Behcet Child. Hosp.* 2020.
- [60] Fan, K.; Li, X.; Cao, Y.; Qi, H.; Li, L.; Zhang, Q.; Sun, H. Carvacrol Inhibits Proliferation and Induces Apoptosis in Human Colon Cancer Cells. *Anticancer Drugs* 2015, 26, 813–823.
- [61] Jamali, T.; Kavooosi, G.; Safavi, M.; Ardestani, S.K. In-Vitro Evaluation of Apoptotic Effect of OEO and Thymol in 2D and 3D Cell Cultures and the Study of Their Interaction Mode with DNA. *Sci. Rep.* 2018, 8, 15787.
- [62] Li, L.; He, L.; Wu, Y.; Zhang, Y. Carvacrol Affects Breast Cancer Cells through TRPM7 Mediated Cell Cycle Regulation. *Life Sci.* 2021, 266, 118894.
- [63] Ito M, Murakami K, Yoshino M. Antioxidant action of eugenol compounds: role of metal ion in the inhibition of lipid peroxidation. *Food Chem Toxicol.* 2005, 43, 461–466.
- [64] Ojha S.; Al Tae H.; Goyal S.; Mahajan U. B.; Patil C. R.; Arya D. S.; Rajesh M. Cardioprotective potentials of plant-derived small molecules against doxorubicin associated cardiotoxicity. *Oxid. Med. Cell. Longevity* 2016, 2016, 5724973.
- [65] Ojha S.; Javed H.; Azimullah S.; Haque M. E. B-Caryophyllene, a phytocannabinoid attenuates oxidative stress, neuroinflammation, glial activation, and salvages dopaminergic neurons in a rat model of Parkinson disease. *Mol. Cell. Biochemistry* 2016, 418, 59–70.
- [66] Al-Tae H.; Azimullah S.; Meeran M. F. N.; Alaraj Almheiri M. K.; Al Jasmi R. A.; Tariq S.; Ab Khan M.; Adeghate E.; Ojha S. B-caryophyllene, a dietary phytocannabinoid attenuates oxidative stress, inflammation, apoptosis and prevents structural alterations of the myocardium against doxorubicin-induced acute cardiotoxicity in rats: An in vitro and in vivo study. *Eur. J. Pharmacol.* 2019, 858, 172467.
- [67] Patil K. R.; Goyal S. N.; Sharma C.; Patil C. R.; Ojha S. Phytocannabinoids for cancer therapeutics: recent updates and future prospects. *Curr. Med. Chem.* 2015, 22, 3472–3501.
- [68] Parisotto-Peterle J.; Bidone J.; Lucca L. G.; Araújo G. D. M. S.; Falkembach M. C.; da Silva Marques M.; Horn A. P.; dos Santos M. K.; da Veiga V. F. Jr.; Limberger R. P.;
- [69] Teixeira H. F.; Dora C. L.; Koester L. S. Healing activity of hydrogel containing nanoemulsified  $\beta$ -caryophyllene. *Eur. J. Pharm. Sci.* 2020, 148.
- [70] Sharma C.; Kaabi J. M.; Nurulain S. M.; Goyal S. N.; Kamal M. A.; Ojha S. Polypharmacological properties and therapeutic potential of  $\beta$ -caryophyllene: a dietary phytocannabinoid of pharmaceutical promise. *Curr. Pharm. Des.* 2016, 22, 3237–3264.
- [71] Miastkowska M.; Kulawik-Pioro A.; Lason E.; Sliwa K.; Malinowska M.A.; Sikora E.; Kantyka T.; Bielecka E.; Maksylewicz A.; Klimaszewska E., Topical Formulations Based on Ursolic Acid-Loaded Nanoemulgel with Potential Application in Psoriasis Treatment. *Pharmaceutics.* 2023, 15,2559.
- [72] Kashyap D.; Sharma A.; Tuli H.S.; Punia S, Sharma AK. Ursolic acid and oleanolic acid: pentacyclic terpenoids with promising antiinflammatory activities. *Recent Pat Inflamm Allergy Drug Discov.* 2016, 10, 21–33.
- [73] Liobikas J.; Majiene D.; Trumbeckaite S.; Kursvietiene L.; Masteikova R.; Kopustinskiene DM.; Savickas A.; Bernatoniene J. Uncoupling and antioxidant effects of ursolic acid in isolated rat heart mitochondria. *J Nat Prod.* 2011, 74,1640–1644.
- [74] Shishodia S.; Majumdar S.; Banerjee S.; Aggarwal BB. Ursolic acid inhibits nuclear

- factor-kappaB activation induced by carcinogenic agents through suppression of IkappaBalpha kinase and p65 phosphorylation: correlation with down-regulation of cyclooxygenase 2, matrix metalloproteinase 9, and cyclin D1. *Cancer Res.* 2003, 63, 4375–4383.
- [75] Jayaprakasam B.; Olson LK.;Schutzki RE.; Tai MH.; Nair MG. Amelioration of obesity and glucose intolerance in high-fat-fed C57BL/6 mice by anthocyanins and ursolic acid in Cornelian cherry (*Cornus mas*) *J Agric Food Chem.* 2006, 54, 243–248.
- [76] Yu SG.; Zhang CJ.; Xu XE, Sun JH, Zhang L, Yu PF. Ursolic acid derivative ameliorates streptozotocin-induced diabestic bone deleterious effects in mice. *Int J Clin Exp Pathol.* 2015, 8, 3681–3690.
- [77] Senthil S.; Chandramohan G.; Pugalendi KV. Isomers (oleanolic and ursolic acids) differ in their protective effect against isoproterenolinduced myocardial ischemia in rats. *Int J Cardiol.* 2007, 119,131–133.
- [78] Wang Y.; He Z.; Deng S. Ursolic acid reduces the metalloprotease/ anti- metalloprotease imbalance in cerebral ischemia and reperfusion injury. *Drug Des DevelTher.* 2016, 10, 1663–1674.
- [79] Scarpati M.L.; Oriente G. Isolamento e costitudionedell' acidorosmarinico (dal rosmarinus off.) *Ric. Sci.* 1958, 28, 2329–2333.
- [80] ANVISA. Guia de Estabilidade de Produtos Cosméticos. Volume 1. Agência Nacional de Vigilância Sanitária; Brasilia, Brasil. 2004
- [81] Park DH.; Park SJ.; Kim JM.; et al.. Subchronic administration of rosmarinic acid, a natural prolyl oligopeptidase inhibitor, enhances cognitive performances. *Fitoterapia* 2010, 81, 644–8.
- [82] Wang M.; Firrman J.; Liu L.; Yam K. A Review on Flavonoid Apigenin: Dietary Intake, ADME, Antimicrobial Effects, and Interactions with Human Gut Microbiota. *BioMed Res. Int.* 2019, 2019,7010467.
- [83] Mukherjee A.; Waters A.K.; Kalyan P.; Achrol A.S.;Kesari S.; Yenugonda V.M. Lipid-polymer hybrid nanoparticles as a next-generation drug delivery platform: State of the art, emerging technologies, and perspectives. *Int. J. Nanomed.* 2019, 14,1937–1952.
- [84] Patel D.; Shukla S.; Gupta S. Apigenin and cancer chemoprevention: Progress, potential and promise (Review) *International Journal of Oncology.* 2007, 30(1), 233– 245.
- [85] Fenaroli G. Fenaroli's handbook of flavor ingredients. 3<sup>rd</sup> ed. Boca Raton, Fla: CRC Press, Inc.; 1995.
- [86] Sigma Aldrich Merck. [(accessed on 20 July 2021)]. Available online: PubChem. [(accessed on 20 July 2021)]; Available online:
- [87] Kuo P.J.; Hung T.F.; Lin C.Y.; Hsiao H.Y.; Fu M.W.; Hong P.D.; Chiu H.C.; Fu E.
- [88] Carvacrol ameliorates ligation-induced periodontitis in rats. *J. Periodontol.* 2017, 88, e120–e128.
- [89] Vats V.; Yadav SP.; Grover JK. Ethanolic extract of *Ocimum sanctum* leaves partially attenuates streptozotocin-induced alterations in glycogen content and carbohydrate metabolism in rats. *J Ethnopharmacol.* 2004, 90,155–60.
- [90] Madhuri S.; Pandey G. Effect of ProImmu, a herbal drug on estrogen caused uterine and ovarian cytotoxicity. *Biomed.* 2010,5(1), 57-62.
- [91] Pandey G. An overview on certain anticancer natural products. *J Pharm Res* 2009, 2(12), 1799-1803.
- [92] Pandey Govind, Madhuri S. Medicinal plants: Better remedy for neoplasm. *Indian Drug* 2006, 43(11), 869-874.
- [93] Kathiresan K.; Guanasekan P.; Rammurthy N.; Govidswami S. Anticancer activity of *Ocimum sanctum*. *Pharmaceutical Biology.* 1999, 37(4), 285-290.
- [94] Aruna K.; Sivaramakrishnan VM. Anticarcinogenic effects of some Indian plants products. *Food Chem Toxicol.* 1992, 30, 953.
- [95] 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 sulfhydryl level. *Anticancer Drugs.* 1994, 5, 567-572.
- [96] 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.
- [97] Prakash J.; Gupta SK.; Singh N.;Kochupillai V.; Gupta YK. Antiproliferative and chemopreventive activity of *Ocimum sanctum* Linn. *Int JMed Biol Environ.* 1999, 27, 165.
- [98] Prakash J.; Gupta SK. Chemopreventive activity of *Ocimum sanctum* seed oil. *J Ethnopharmacol.*2000,72(1-2),29-34.
- [99] Uma Devi P.; Gonasoundari A. Radioprotective effect of leaf extract of Indian Medicinal Plant *Ocimum sanctum*. *Indian J Exp Biol.* 1995,33, 205.
- [100] Uma Devi P.; Gonasoundari A.; Vrinda B.; Srinivasan KK; Unnikrishanan M.K. Radiation protection by the *Ocimum sanctum* flavonoids orientin and vicenin: Mechanism of action. *Radiat Res.*2000, 154(4), 455-460.

- [101] Gonasoundari A.; Uma Devi P, Rao BSS. Enhancement of bone marrow radioprotection and reduction of WR-2721 toxicity by *Ocimum sanctum*. *Mutat Res* 1998, 397, 303.
- [102] Gholap S.; Kar A. Hypoglycemic effects of some plant extracts are possibly mediated through inhibition in corticosteroid concentration. *Pharmazie*. 2004, 59,876–8.
- [103] Vats V.; Yadav SP.; Grover JK. Ethanolic extract of *Ocimum sanctum* leaves partially attenuates streptozotocin-induced alterations in glycogen content and carbohydrate metabolism in rats. *J Ethnopharmacol*. 2004, 90,155–60.
- [104] Rai V.;Iyer U.; Mani UV. Effect of *Tulasi* (*Ocimum sanctum*) leaf powder supplementation on blood sugar levels, serum lipids and tissue lipids in diabetic rats. *Plant Foods Hum Nutr*. 1997,50,9–16.
- [105] Chattopadhyay RR. Hypoglycemic effect of *Ocimum sanctum* leaf extract in normal and streptozotocin diabetic rats. *Indian J Exp Biol*. 1993,31,891–3.
- [106] Sood S.; Narang D.; Thomas MK.; Gupta YK.; Maulik SK. Effect of *Ocimum sanctum* Linn. on cardiac changes in rats subjected to chronic restraint stress. *J Ethnopharmacol*. 2006, 108,423–7.
- [107] Sood S.; Narang D.; Dinda AK.; Maulik SK. Chronic oral administration of *Ocimum sanctum* Linn. augments cardiac endogenous antioxidants and prevents isoproterenol-induced myocardial necrosis in rats. *J Pharm Pharmacol*. 2005,57,127–33.