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**Review Article** 

## Ocimum Sanctum: Phytochemistry, Therapeutic Uses Pharmacological Activities and Its Anticancer Activities

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### ABSTRACT

The practice of Ayurveda, which is based on the principles of living a healthy lifestyle and eating adaptogenic herbs on a regular basis, has the potential to alleviate a significant number of the chronic diseases that are the main cause of mortality across the globe. Tulasi, also known as Ocimum sanctum Linn, is considered to be the most significant herb in Ayurvedic medicine. Recent scientific research has demonstrated that it imparts a number of positive health effects. An increasing body of research indicates that the unique combination of pharmacological properties that tulsi possesses has the potential to alleviate stress on various levels, including the physical, physiological, metabolic, and psychological levels. Tulsi has been found to protect internal organs and tissues from the damaging effects of heavy metals and industrial pollutants, as well as against the impacts of physical stresses such as cold, excessive loudness, ischemia, and prolonged durations of physical exercise. This has been demonstrated through research. Plants that have medicinal properties are utilized on a daily basis by traditional healers in order to treat a wide variety of ailments. Ocimum sanctum Linn, a small herb that is widely distributed across India and is referred to as Tulsi in Hindi, has a long history of application in traditional medicine for the treatment of a wide range of ailments. These ailments include bronchitis, bronchial asthma, malaria, diarrhea, dysentery, skin diseases, arthritis, painful eye diseases, chronic fever, insect bites, and many others. There is some evidence to suggest that O. sanctum L. may possess qualities that include antibacterial, anticancer, antidiabetic, neuroprotective, and hepatoprotective. It has been demonstrated that O. sanctum L. possesses therapeutic value, as demonstrated by the pharmacological research that was incorporated into this study.

**Keywords:** Phytochemistry, pharmacological activity, anticancer, therapeutic uses

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#### INTRODUCTION

ince the beginning of Ayurvedic medicine, practitioners have relied on the numerous medical properties of Ocimum sanctum L., which is also known

as Tulsi or Ocimum tenuiflorum. This practice dates back thousands of years[1]. Tulsi, also known as the "Incomparable one" of India and the "queen of herbs," is considered to be among the most revered and cherished of the numerous medicinal and health-promoting herbs that are

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native to the Eastern region. As a result of its lengthy history of application in Eastern holistic health systems like as Ayurveda and Unani, the sacred basil that is commonly referred to as Tulsi has received international recognition for the spiritual and religious importance it possesses[2]. In the volume of Ayurvedic literature known as the Charaka Samhita, the character Charaka makes a reference to it. Adaptability to stress is improved by tulsi, which is also considered an adaptogen due to the fact that it improves the balance of a number of different biological systems. According to Ayurveda, it is considered a "elixir of life" because of its powerful aroma and astringent flavor, both of which contribute to an increased longevity[3]. Tulsi extracts are used in the production of Ayurvedic medications for a wide range of conditions, including but not limited to malaria, inflammation, heart disease, headaches, stomach difficulties, and many sorts of poisoning and common colds[4]. Traditional preparations of O. sanctum L. include herbal tea, dried power, and fresh leaf. However, there are also a range of other preparations available. The use of a combination of dried Tulsi leaves and grains has been used for a very long time in order to keep insects at bay[5].

The Charaka Samhita, which is a text from Indian traditional medicine, discusses the religious significance of holy basil (Ocimum sanctum L) as well as its numerous medical applications[6]. These applications include the plant's capacity to reduce blood sugar levels, alleviate anxiety, lower blood pressure, reduce inflammation, and eliminate microorganisms. It is also known as an adaptogen since it assists the body in adjusting to stressful situations, which is why it is called that. When it comes to traditional medicine

(ayurvedic and unani), medicines made from holy basil leaves have been shown to be effective in treating headaches, common colds, and inflammation[7]. There are numerous chemicals that may be discovered in the leaves of Ocimum, including β-caryophyllene, eugenol derivatives, vanillin, rosmarinic acid, ursolic acid, gallic acid, and vanillic acid. However, it is still difficult to extract and identify active flavonoids from these leaves, and there is no obvious association between the antioxidant effects of these substances and the flavonoids themselves. According to Iloki et al., flavones do not dissolve as well in water as they do in alcohols. However, flavones do dissolve better in water[8]. According to the findings of the study, the polarity of the solvent has the greatest impact on the extraction of phytochemicals and the antioxidant capabilities that plants possess. When attempting to determine which fraction includes the highest concentration of polyphenols, flavonoids, and active antioxidant components, it may be beneficial to employ successive fractionation with solvents that have variable degrees of polarity. On the other hand, there is no evidence that the leaves of this herb were extracted in a different manner. Therefore, the purpose of this work was to determine the most effective method for extracting flavonoids and polyphenols from the leaves of O. sanctum by means of a series of fractionations using a variety of solvents, and to investigate any potential relationships that may exist between the components and the antioxidant activity of the preparations that come about as a result of this process. The purpose of this study was to establish which fractions of flavonoids and their derivatives were the most effective in detecting the substances the researchers were looking for.





Figure 1: Ocimum sanctum whole plant

## **Phytochemistry**

The complex phytochemical composition of the revered medicinal herb Ocimum sanctum, which is commonly referred to as Tulsi or Holy Basil, is responsible for the wide variety of positive properties that it possesses[9]. There are numerous essential oils that are found in the plant, including

as eugenol, methyl eugenol,  $\beta$ -caryophyllene, linalool, germacrene D, and camphor. The use of these oils has the potential to eliminate pests, lessen inflammation, alleviate pain, and prevent infections. The volatile compounds contained in the plant are responsible for both the plant's distinctive aroma and its wide range of medicinal applications[10]. There are a number of flavonoids and

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phenolic acids that can be found in abundance in Ocimum sanctum, which also contains essential oils. Some of these flavonoids and acids include rosmarinic acid, apigenin, luteolin, quercetin, and cirsimaritin. Because of their powerful antioxidant characteristics, these polyphenolic compounds have anti-aging, neuroprotective, hepatoprotective effects[11]. Through their ability to scavenge free radicals and reduce oxidative stress, these molecules have these effects. Furthermore, the plant holds a significant quantity of sterols and triterpenoids, such as βsitosterol, ursolic acid, and oleanolic acid, which possess anti-inflammatory, cardioprotective, and anticancer properties[12]. The anti-inflammatory, tumor-inhibiting, and wound-healing capabilities of ursolic and oleanolic acids have been the primary focus of research in recent years. Additionally, the presence of alkaloids and ocimene derivatives, which further boost the plant's pharmacological potential, contributes to the enhancement of the adaptogenic and stress-relieving properties of Ocimum sanctum[13]. It has been demonstrated that the glycosides that are present in

Ocimum sanctum, such as vicenin and orientin, possess potent neuroprotective and radioprotective qualities. This further solidifies the herb's use in both traditional and alternative medicine[14].

The intricate phytochemical makeup of Ocimum sanctum is the reason for its widespread application in Ayurveda and other traditional medical systems for the treatment of a wide variety of ailments[15]. In addition to respiratory illnesses, diabetes, cardiovascular diseases, and immunological dysfunctions, these conditions also include immunological dysfunctions. In addition to the immunomodulatory benefits, the anti-diabetic action helps to regulate blood glucose levels, and the immunomodulatory activity strengthens the body's defense mechanisms[16]. Ocimum sanctum is utilized in the pharmaceutical industry, the nutraceutical industry, and the herbal medicine industry due to the way that its bioactive compounds interact with one another. This is a comprehensive treatment that has a great deal of potential in the medical field[17].

Figure 2: Some phytoconstituents structures of Ocimum sanctum

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#### Therapeutic uses

Plants that have medicinal properties are utilized on a daily basis by traditional healers in order to treat a wide variety of ailments. Ocimum sanctum Linn, a small herb that is widely distributed across India and is referred to as Tulsi in Hindi, has a long history of application in traditional medicine for the treatment of a wide range of ailments[18]. These ailments include bronchitis, bronchial asthma, malaria, diarrhea, dysentery, skin diseases, arthritis, painful eye diseases, chronic fever, insect bites, and many others. It is possible that Ocimum sanctum L. possesses other therapeutic qualities, including those of an adaptogen, diaphoretic, hepatoprotective, cardioprotective, antiemetic, antispasmodic, analgesic, anticancer, antifungal, and antidiabetic. The active component that may be discovered in Ocimum sanctum L. is eugenol (1-hydroxy-2-methoxy-4-allylbenzene), which is primarily responsible for the therapeutic properties of Tulsi[19]. Ocimum sanctum L. has been used for a long time by traditional Indian healers to treat a wide range of maladies due to the plant's widespread occurrence and powerful therapeutic characteristics. However, there is a lack of evidence to justify the incorporation of this practice into contemporary medical thinking[20]. For the past few decades, Indian scientists and researchers have been investigating the pharmacological effects of steam-distilled, petroleum-ether, and benzene extracts of various parts of the Tulsi plant and eugenol on the immune system, reproductive system, central nervous system, cardiovascular system, gastric system, urinary system, and blood biochemistry[21]. These extracts have been used to study the effects of the Tulsi plant on these systems. The purpose of their work is to determine the therapeutic applications of Ocimum sanctum L. in contemporary medical practice. It has been suggested that tulsi possesses therapeutic relevance in the treatment of a variety of illnesses[22].

## Pharmacological activities

#### • Antioxidant activity

Chaudhary et al The leaves of the medicinal plant Ocimum sanctum were first extracted in methanol (OsM), and then they were fractionated in a sequential manner with n-hexane (OsH), ethylacetate (OsE), and butanol (OsB)[23]. This was done in order to identify which solvent was the most effective for obtaining antioxidants from the leaves[24]. Both the total flavonoid contents (TFC) of OsB  $(54.51 \pm 3.5 \text{ mg QE/g})$ extract) and the total polyphenolic content (TPC) of OsB  $(212.26 \pm 6.3 \text{ mg GAE/g extract})$  are found to be quite high[25]. Similarly, OsE displayed a significantly higher total phenolic content (TPC), at 202.71±5.5 mg GAE/g extract. The EC50 values for OsB were determined to be  $3.91 \pm 0.3$  $\mu g/ml$  for DPPH,  $1.6 \pm 0.1$   $\mu g/ml$  for ABTS, and  $2.31 \pm 0.1$ ug/ml for phosphomolybdate[26]. For OsM, the hydroxyl radicals were found to be  $5.3 \pm 0.4 \mu g/ml$ , while for OsE, the phosphomolybdate radicals were found to be  $2.43 \pm 0.1$  $\mu g/ml$ , and ABTS  $(5.3 \pm 0.4 \mu g/ml)$  for phosphomolybdate. These results indicate that OsE may possess potential antioxidant properties[27].

#### Anti inflammatory activity

Anant et al Carrageenan-induced paw edema was utilized to evaluate the anti-inflammatory properties of OS extracts in hexane (STH), chloroform (STC), ethyl acetate (STE),

butanol (STB), and water (STW)[28]. The results of this study were given. The most active extract, STE, was subjected to additional testing in a dose-dependent manner. This was done in addition to verifying its oral toxicological profile and demonstrating its anti-inflammatory, analgesic, and antipyretic activities in small laboratory animals[29]. Establishing a chemical fingerprint through the utilization of high-performance liquid chromatography allowed for the determination of the solid-state terahertz (STE) fraction that was the most active[30]. The ethyl acetate fraction (STE) exhibits the highest level of anti-inflammatory activity, followed by the following fractions: STB, STW, STC, and STH[31]. According to the findings of a dose response study, STE displayed dose-dependent anti-inflammatory, analgesic, and antipyretic potential at a dosage of 2000 mg/kg. Furthermore, the study determined that STE did not cause any side effects[32]. The use of chemical fingerprinting allowed for the identification of flavanoids as being present.

#### Anti microbial activity

Sajjanshetty et al to assess controlled laboratory environment is used to evaluate the effectiveness of Ocimum sanctum, which is an extract derived from Tulsi leaves, as an antibacterial agent[33]. The preparation of the ethanolic extract of Tulsi was accomplished by the use of the cold extraction method. There were five different concentrations that could be obtained by diluting the extract with dimethyl formamide, which is an inert solvent. These concentrations were 0.5, 1, 2, 5, and 10% respective[34]. A positive control was carried out with doxycycline, whereas a negative control was carried out with dimethyl formamide. In order to determine the microbiological characteristics of the extract and the controls, Aggregatibacter actinomycetemcomitans, Prevotella intermedia, and Porphyromonas gingivalis examined the samples[35]. The agar well diffusion method was utilized in order to locate the concentration of Tulsi that resulted in the formation of an inhibitory zone that was comparable to that of doxycycline[36]. The Tukey post hoc test was applied for the purpose of comparing and contrasting the groups, and the one-way analysis of variance was utilized for the objective of analyzing the data. At dosages of 5% and 10%, the antibacterial activity of Tulsi extracts against A. actinomycetemcomitans was equivalent to that of doxycycline, with comparable inhibition zones (P > 0.05). This was the case when comparing the percentages of inhibition[37]. The presence of resistance to Tulsi extract was observed in P. gingivalis and P. intermedia, which exhibited a significant decrease in inhibitory zones (P < 0.05). In light of the fact that it possesses antibacterial properties against A. actinomycetemcomitans, tulsi has demonstrated that it has the potential to serve as an affordable and efficient "adjunct" to traditional periodontal therapy[38].

#### **Antidiabetic activity**

Leila *et al* A methanol extract of Ocimum sanctum L. leaves, which is a fraction that reduces blood sugar, was administered to diabetic rats in order to establish better control over hyperglycemia[39]. This was done in order to achieve the desired results. Additionally, assessments were conducted on the levels of  $\alpha$ -amylase,  $\alpha$ -glucosidase inhibitor, and insulin in the animals. In streptozotocininduced rats, the researchers discovered that the highest dose of methanol extract considerably reduced blood glucose

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levels in comparison to another dose[40]. This demonstrates that the extract has antihyperglycemic properties when it is taken orally. According to the findings of repeated administration of methanol fractions, the ethyl acetatebutanol fraction demonstrated a more effective antihyperglycemic impact than the chloroform and ethanolwater fractions[41]. In addition, the in vitro investigation indicated that the ethyl acetate-butanol fraction had the ability to regulate insulin levels as well as the activities of αglucosidase and α-amylase enzymes, even when the concentration was low[42]. This was in contrast to the other fractions and acarbose, which was used as the positive control. Neither the methanol extract nor the fraction exhibited any change in insulin levels that could be considered statistically significant[43]. It was demonstrated by these findings that the presence of polyphenolics active components made it possible for the active crude extract (methanol) and its active fractions (ethyl acetate/butanol) to dramatically lower glucose levels[44].

#### Hepatoprotective activity

Lahon et al In the field of modern medicine, there is a deficiency in the availability of reliable hepatoprotective pharmaceuticals for the purpose of preventing and treating liver damage caused by drugs[45]. In traditional medicine, the hepatoprotective qualities of the leaves of sacred basil, also known as green tulsi (Ocimum sanctum), a plant belonging to the Lamiaceae family, have been recognized for a long time. It was the goal of this research to establish whether or not Ocimum sanctum possesses hepatoprotective properties on its own or whether or not it possesses synergistic effects when combined with silymarin[46]. The weight of the albino rats in each of the five groups ranged from 150 to 200 grams for each group. Group B had the experimental controls, while Group A contained the normal controls[47]. Normal controls were in Group A. Different quantities of an alcoholic extract of Ocimum Sanctum leaves (OSE) were administered to groups C, D, and E over the course of a period of ten days. The doses applied to groups C, D, and E were as follows: 200 mg/kg BW/day, 100 mg/kg BW/day of silymarin, and 100 mg/kg BW/day of OSE mixed with 50 mg/kg BW/day of silymarin, respectively. For the purpose of inducing hepatotoxicity, Groups B, C, D, and E were given paracetamol at a dosage of 2 grams per kilogram of body weight per day on the seventh day. In order to evaluate the hepatoprotective effect, serum protein tests, albumin globulin ratios, alkaline phosphatases, transaminases, and liver histology were utilized[48]. In order to present the results of the test for each group, the mean and the standard error of the mean (SEM) were utilized. An analysis of variance (ANOVA) using one-way and Bonferoni's test were utilized to compare the research group to the control group. In order for the P-value to be considered significant, it had to be less than 0.01. Furthermore, when compared to groups C, D, and E, which were much closer to normal (P < 0.01), group B had significantly higher levels of liver enzymes and an albumin globulin ratio. Upon histological examination, groups C, D, and E exhibited reduced sinusoidal congestion, hazy edema, fatty changes, and regenerating parts of the liver. Group B, on the other hand, solely had hepatic necrosis.

Fatemah et al Ocimum sanctum L. plant, often known as tulsi and belonging to the libiaceae family, has a long history of usage in traditional medicine as a treatment for a wide variety of medical conditions. These conditions include cancer, diabetes, heart disease, spasms, excessive sweating, and adaptogenic effects[49]. This experiment is being carried out with the purpose of determining the serum metabolites, determining the hepatoprotective efficacy of O. sanctum L. against galactosamine-induced toxicity, and analyzing the bioactive components that are present in each extract. Highperformance thin-layer chromatography (HPTLC) was utilized in order to standardize and analyze the Ayurvedic method of extracting O. sanctum L. for the presence of biochemical markers. Rutin, ellagic acid, kaempferol, caffeic acid, quercetin, and epicatechin are some of the indications that are included in this category. In order to induce hepatotoxicity in adult albino rats, galactosamine was given intraperitoneally at a dose of 400 mg/kg. The quantitative hydroalcoholic and alcoholic extracts of O. sanctum L (100 and 200 mg/kg body weight/day) were compared in order to evaluate the hepatoprotective potential of the extracts. The evaluation included the reduction of histological damage, changes in serum enzymes (AST, ALT, and ALP), and an increase in TBARS. Twenty chemical components of O. sanctum serum metabolites were discovered and described through the process of comparing the mass spectra that were acquired by GC-MS with those that were obtained from the library-Wiley/NIST. We conducted in vitro investigations into the activity at each phase (hexane, chloroform, and ethyl acetate) to evaluate the hepatoprotective efficiency of the various hydroalcoholic extract fractions towards Chang liver cells. Our goal was to determine how the toxicity of CCL4 (40 mM) was affected by the different fractions of the Because hydroalcoholic extract. of its greater hepatoprotective efficiency in comparison to the other fractions, the ethyl acetate fraction of the selected plants was utilized for the purpose of vacuum liquid chromatography (VLC). The ethyl acetate fraction contains high amounts of a number of compounds that are responsible hepatoprotection. These compounds include ruthin (0.34% w/w), ellagic acid (2.32% w/w), kaempferol (0.017 w/w), caffeic acid (0.005% w/w), quercetin (0.038 w/w), and epicatechin (0.057% w/w). Isolated bioactive compounds had a hepatoprotective activity that was significantly more extensive than that of standard silymarin in Chang liver cells that were subjected to CCl4 toxicity. Purified ellagic acid exhibited a range of 70% at 100 µg/ml to 81.33% at 200 μg/ml, while purified rutin exhibited a range of 63.4% at 100 μg/ml to 76.34% at 200 μg/ml. This indicates a significant increase in hepatoprotection when compared to normal silymarin, which exhibited a range of 77.6% at 100 μg/ml to 83.95% at 200 µg/ml. One can observe that the concentration ranges of pure quercetin, epicatechin, and kaempferol are as follows: 54.33% at 100  $\mu g/ml,\,60.64\%$  at 200  $\mu g/ml,\,53.22\%$ at 100 µg/ml, and 65.6% at 200 µg/ml, respectively. On the basis of these findings, it would appear that the bioactive compounds found in O. sanctum L. greatly reduce the amount of liver damage that galactosamine is capable of causing[50].

#### **Neuroprotective activity**

Venuprasad et al Oxidative stress is a factor that contributes to the damage that cells sustain in a variety of diseases, including neurodegenerative disorders. The ocimum sanctum plant is utilized extensively in the treatment of a wide variety of medical ailments in the Indian medical practice known as Ayurveda[51]. The purpose of this study was to investigate whether or not the hydroalcoholic extract of O. sanctum (OSE) might shield SH-SY5Y human brain cells from the oxidative stress that is brought on by hydrogen peroxide (H2O2). It was observed that the extract exhibited significant antioxidant activity against DPPH, 2,2'-azinobis (3ethylbenzothiazoline-6-sulfonic acid) radical, and hydroxyl radicals, as indicated by the IC50 values of 395  $\pm$  16.2, 241  $\pm$ 11.5, and 188.6  $\pm$  12.2  $\mu$ g/ml, respectively[52]. One possible explanation for this is that the extract contains a significant amount of flavonoids and polyphenols. According to the data, the survival rate of cells decreased to 41.5% after being subjected to a challenge of 100 µM H2O2 over a period of 24 hours[53]. On the other hand, the survival rate of cells climbed to 73% after being pre-treated with OSE for a period of two hours. Furthermore, it prevented the cells from losing their form and decreased the amount of lactate dehydrogenase that was released. Lipide peroxidation, DNA damage, the formation of reactive oxygen species (ROS), and the depolarization of the mitochondrial membrane were all avoided by OSE[54]. In addition to restoring levels of catalase and superoxide dismutase enzymes and proteins, the extract resulted in a reduction in the overexpression of HSP-70 activity[55-57].

#### **Anticancer activity**

Mohammad *et al* leaf extract from O. sanctum was tested on the leukemic cell line, and the results were validated using the K562 cell line. In addition to this, we demonstrated that the cytotoxic effect was dose-dependent and that the activity was equivalent across all of the groups that were examined[58]. For as long as anyone can remember, medicinal herbs have been a source of information and inspiration for those working in the pharmaceutical industry[59]. In this study, the specific anti-cancer characteristics of the herb on leukemic cell lines are also explored that are not found in other studies[60]. Although the particular action mechanism was not studied in this study, the anticancer effects of the herb's components have been related to a number of different routes. For example, the herb has been shown to inhibit the growth of cancer cells[61].

Manaharan et al Among the several pharmacological properties that were demonstrated by the essential oil of Ocimum sanctum Linn, antifungal and antibacterial activity were among the most interesting[62]. The purpose of this study was to investigate the anticancer and apoptotic processes that are associated with Ocimum sanctum essential oil (OSEO). To extract OSEO from the leaves, hydrodistillation was utilized as the extraction method[63]. In order to evaluate the proliferation of cells, different dosages of OSEO were used. To investigate the process of apoptosis, tests were conducted using human breast cancer cells that were stained with propidium iodide (PI) and Hoechst. Based on the findings of our research, it was shown that OSEO had a significant impact on the proliferation of MCF-7 cells, with the dosage having a significant impact (IC50 = 170 μg/ml)[64]. The fact that the OSEO caused an increase in the amount of apoptotic nucleic acids that were stained with PI in MCF-7 cells is additional evidence that the OSEO induced cell death. According to the analysis of flow cytometry, it was shown that the apoptotic cell population increased by 16-84% dosage dependently when the cells were treated with OSEO (50-500  $\mu$ g/ml) in comparison to the control group under study. Increasing the ratio of Bax to Bcl-2 and upregulating the apoptotic genes p53 and Bid are both possible outcomes of OSEO[65].

#### **CONCLUSION**

Due to the numerous therapeutic advantages that it offers, Ocimum sanctum has been an indispensable component of traditional medicine for a considerable amount of time. It has been known for a long time for its antibacterial, antiviral, antifungal, antipyretic, antidiuretic, antidiabetic, and antimalarial activities. This is due to the high concentration of metabolites that it contains, which includes flavonoids, phenolics, and terpenoids. Because of the fact that these bioactive compounds have the potential to operate as antioxidants, anticancer agents, antibacterial agents, and antidiabetic agents, it is of the utmost importance to do additional research on them. Over the past several years, there has been a rise in the number of people who are interested in investing in the traditional health-promoting applications of tulsi. Based on the fact that the herb has been used historically in its natural, unprocessed state, it is likely that the nutritional and therapeutic benefits of the herb are the result of the interaction of a large number of phytochemicals that are active. Therefore, the advantages of Tulsi cannot be replicated in their entirety by using the extracts or components that make up the herbal plant. Because of the increasingly diverse range of chronic degenerative diseases that are caused by environmental factors, lifestyle choices, and individual stress, the traditionally fragmented approach of modern allopathic medicine has proven to be insurmountable. This is despite the numerous remarkable achievements that western medical science has accomplished. Traditional herbal therapies and holistic health practices are beginning to play an essential complementary role in the prevention and treatment of the condition known as passive sickness, which is prevalent in today's society. The World Health Organization has recognized the necessity of widening western medical viewpoints and has campaigned for the integration of traditional health and folk medicine systems with modern medical remedies. This is done with the goal of better addressing health problems on a worldwide scale. The body of research that suggests that Tulsi may have both preventative and therapeutic effects against stress-related degenerative diseases that are common in industrialized nations is expanding.

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