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Efficacy of *Ocimum tenuiflorum*: A strong Immunostimulant, Anti-carcinogenic, Antioxidant, Antiviral, Antimicrobial, Insecticidal fungicidal and Antiprotozoal

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Abstract

In Hinduism, the *Ocimum tenuiflorum* plant is revered, and it is extensively used in Ayurvedic and traditional medicine. It's a popular herbal tea that can be used to treat a range of diseases. The molecular structure of *O. tenuiflorum* is complicated, and it contains a number of physiologically active chemicals. *Ocimum tenuiflorum* (tulsi) contains phytochemicals such as oleanolic acid, ursolic acid, rosmarinic acid, eugenol, carvacrol, linalool, and β-caryophyllene. *Ocimum tenuiflorum* essential oil is mostly composed of eugenol (70%), β-element (11.0%),β-caryophyllene (8%), and germacrene (2%), with the remainder consisting of miscellaneous trace chemicals, principally terpenes. They have been found to have antifungal, antibacterial, antiprotozoal, hepatoprotective, anticancer and antiviral properties. Germacrenes are antibacterial and insecticidal compounds generated by a variety of plant species, such as *Ocimum tenuiflorum*, but they also serve as insect pheromones.

Keywords: *Ocimum tenuiflorum*, antifungal, antibacterial, antiprotozoal, hepatoprotective, anticancer and antiviral

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Introduction

Ocimum tenuiflorum (Holy basil), often known as tulsi or tulasi, is a mint family flowering plant (Lamiaceae). *O. tenuiflorum* is native to the Indian subcontinent, including the Himalayas, Malesia, and other tropical and subtropical regions of Asia, but it is now widely cultivated and naturalised around the world, including the Caribbean, Pacific Islands, and portions of Africa. The species was first introduced outside of Asia for medicinal and culinary purposes, and it has been used for these purposes for at least 3000 years. The plant is widely used in Ayurvedic and traditional medicine and is revered in Hinduism. It is commonly used as a herbal tea for a range of diseases. The chromosome number of *O. tenuiflorum* is 2n=36 (Mukherjee and Datta, 2005).The molecular structure of holy basil is quite complicated, and it contains multiple biologically active chemicals (Rastogi *et al.*, 2015). *Ocimum tenuiflorum* (tulsi) contains phytochemicals such as oleanolic acid, ursolic acid, rosmarinic acid, eugenol, carvacrol, linalool, and β -caryophyllene (approximately 8%) (Sundaram *et al.*, 2012).

Tulsi essential oil is mostly composed of eugenol (70%), β -element (11.0%), β -caryophyllene (8%), and germacrene (2%), with the remainder consisting of different trace chemicals, predominantly terpenes (Padalia *et al.*, 2011).Terpenoids are made up of acetate units and have a similar origin to fatty acids. Methanol and camphor (monoterpenes), farnesol, and artemisinin are examples of common terpenoids (sesquiterpenoids). They have been shown to have antifungal, antibacterial, antiprotozoal, and antiviral properties (Cowan, 1999).

Holy basil has substantially more methionine sulfone and tryptophan than regular basil and is a good source of calcium, manganese, and iron. When chia seeds were compared to holy basil seeds, they had higher quantities of asparagine, threonine, serine, glutamic acid, proline, glycine, alanine, valine, isoleucine, leucine, phenylalanine, and lysine.Holy basil leaf extract has been proven to have anti-carcinogenic and antioxidant effects (Devi, 2001). Holy basil also contains vitamins and minerals that can boost the nutritional value of dishes (Anabarasu & Vijayalakshmi, 2007). The seeds ofOcimum tenuiflorum could be utilised to make a variety of medications and food products, and investigation revealed the existence of four pharmacologically significant substances (gallic acid, cinnamic acid, catechol and ascorbic acid).

Oleanolic acid

Oleanolic acidis a non-toxic, hepatoprotective substance that also has anticancer and antiviral activities (Liu, 1995). In vitro, oleanolic acid was discovered to have poor anti-HIV and anti-HCV activity (Mengoni *et al.*, 2002), although more effective synthetic analogs are being studied as possible medicines (Yu *et al*., 2013). In 2005, a significant inhibitor of cellular inflammatory processes was discovered in a synthetic triterpenoid derivative of oleanolic acid. They act by inducing inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 in mice macrophages in response to IFN- γ. They are powerful inducers of the phase 2 response (e.g., increased NADH-quinone oxidoreductase and heme oxygenase 1), which protects cells from oxidative and electrophilic stress (Dinkova *et al.*, 2005).

Oleanolic acid lowered sperm quality and motility, resulting in infertility, according to a 2002 study in Wistar rats. Male rats regained fertility and successfully impregnated female rats after being exposed to them for a short time (Mdhluli *et al*., 2002). In the primary research, oleanolic acid is also employed as a standard to compare the inhibitory effects of other compounds on hyaluronidase, elastase, and matrix-metalloproteinase-1 (similar to diclofenac sodium for comparison of analgesic activity). (Maity *et al*., 2012; Nema *et al.*, 2013)

Ursolic acid

Although Ursolic Acid has been studied for a variety of biochemical effects, no clinical studies have been conducted to show that it provides health advantages in humans. Ursolic acid suppresses cancer cell proliferation in vitro by blocking the STAT3 activation pathway (Pathak *et al.,* 2007). Cancer cells' proliferation may be inhibited, and apoptosis may be induced. (Wang *et al.,* 2011, Wang *et al.*, 2011) Ursolic acid has also been demonstrated to reduce T cell activation and proliferation by inhibiting JNK expression and IL-2 activation in JURKAT leukemic T cells (Kaewthawee *et al.*, 2013), Ursolic acid, a weak aromatase inhibitor (IC50 = 32 M), has been proven to increase muscle and brown fat while decreasing white fat obesity and associated problems in mice when added to their diets. (Kunkel *et al.,* 2012). Ursolic acid also causes eryptosis at physiological doses (the apoptosis-like suicidal cell death in defective red blood cells) (Jilani., *et al* 2011) In mice, it has been proven to prevent muscle atrophy and increase muscular growth, as well as showing possible cardioprotection (Kunkel *et al.,* 2011; Liobikas *et al.,* 2011).

Ursolic acid promotes neuronal regeneration following sciatic nerve damage in mice (Liu *et al.,* 2013). Ursolic acid decreased further damage to neurons and helped rebuild protective sheaths protecting neurons in mice with chronic multiple sclerosis, presumably by decreasing Th17 immune cells and activating precursor cells that grow into myelin-sheath-making cells called oligodendrocytes (Zhang *et al.*,2020). Ursolic acid helps mice with domoic acid-induced cognitive impairments. (Wu *et al.*, 2013). Ursolic acid improves mice's cognitive deficits caused by a high-fat diet by reducing endoplasmic reticulum stress and IB kinase/nuclear factor-B-mediated inflammatory pathways (Lu, *et al.*,2011). Ursolic acid reduces lipopolysaccharide-induced cognitive impairments in mice via inhibiting inflammatory pathways mediated by p38/NF-B. (Wang et al., 2011).

Ursolic acid improves cognition and reduces oxidative damage in senescent mice's brains caused by D-galactose (Lu, *et al.*, 2007). Ursolic acid promotes liver regeneration in mice following partial hepatectomy (Jin *et al.*, 2012). Ursolic acid improves the cellular immune system and pancreatic beta-cell function in diabetic mice on a high-fat diet caused by streptozotocin. UA enhanced skeletal muscle hypertrophy, grip strength, and exercise capacity (Jang, *et al.*, 2009). Improved endurance, lower expression of genes linked to muscle atrophy progression, and lower indications of cumulative tiredness and exercise-induced stress (Jeong *et al.,* 2015). Ursolic acid reduced hepatic steatosis and corrected metabolic abnormalities in rats with non-alcoholic fatty liver disease caused by a high-fat diet (Li *et al.,* 2014).

Rosmarinic acid

Ocimum tenuiflorum contains rosmarinic acid, which is named after rosemary (*Salvia rosmarinus* Linn.). Rosmarinic acid is a caffeic acid ester with another phenolic ring provided by tyrosine via dihydroxy phenyl-lactic acid. (Petersen *et al.,* 2009).

Eugenol

Eugenol and thymol have anaesthetic qualities in general. These 2-alkyl (oxy)phenols, like many other anaesthetics, act as positive allosteric modulators of the GABAA receptor. Despite the fact that eugenol and thymol are too toxic and ineffective for clinical usage, these findings led to the invention of 2-substituted phenol anaesthetics such as propanidid (later discontinued) and propofol. (2017, Tsuchiya). Eugenol and myristicin, which share a structural similarity, both inhibit MAO-A and MAO-B in vitro (Tao *et al.*, 2005).Complete elimination occurs in humans within 24 hours, with the majority of metabolites being eugenol conjugates. (Fischer et al., 1990) Teas, meats, cakes, perfumes, flavourings, and essential oils all include eugenol as a flavour or fragrance component. It's also utilised as an antiseptic and anaesthetic in the immediate area

(Sell *et al.*, 1976). Eugenol can be mixed with zinc oxide to make zinc oxide eugenol, which is used in dentistry for restorative and prosthodontic purposes. Packing a dry socket with eugenol-zinc oxide paste on iodoform gauze is useful for lowering acute discomfort in people who have a dry socket as a consequence of tooth extraction (Tarakji *et al.*, 2015). Root canal sealing is done with eugenol-zinc oxide paste (Ferracane, 2001). Males of a variety of orchid bee species find it attractive.Clove oil is commonly used as an anaesthetic on aquarium and wild fish samples for study and management (Grush *et al.*, 2004). It provides a gentle way to euthanize sick and diseased fish, either by direct overdose or by inducing sleep prior to a eugenol overdose, where it is easily available (Monks *et al.*, 2009). Eugenol can induce liver damage when taken orally in high dosages for a long time. Overdosing can result in a variety of symptoms, including blood in the urine, convulsions, diarrhoea, nausea, unconsciousness, dizziness, fast heart rate, or acute kidney injury. People who have taken too much eugenol or clove oil may be given N-acetyl cysteamine.

Linalool

Linalool is a naturally occurring terpene alcohol that comes in two enantiomers. Linalool is found in 60 percent to 80 percent of fragrant hygiene and cleaning products, including soaps, detergents, shampoos, and lotions. (Eggersdorfer, 2000). Antimicrobial and antifungal properties are found in it (Hussain *et al.*, 2008).Linalool is also used as a pesticide to kill fleas, fruit flies, and cockroaches. It can also be used to eliminate codling moths as a nuisance. Linalool has a synergistic impact with codlemone, a pheromone produced by the codling moth, which promotes male attractiveness (Yang *et al.*, 2004). Linalool is a component of mosquito repellents ["What to look for when you're buying mosquito repellent". South China Morning Post. September 6, 2015. Retrieved December 30, 2015.] however, the U.S. EPA notes that "a preliminary screen of labels for products containing [l]inalool (as the sole active ingredient) indicates that efficacy data on file with the Agency may not support certain claims to repel mosquitos."("EPA Linalool Summary Document Registration Review: Initial Docket" U.S. Environmental Protection Agency. April 2007).

Caryophyllene

Caryophyllene, also known as (-) β-caryophyllene (BCP), is a natural bicyclic sesquiterpene found in the *Ocimum tenuiflorum* plant. In rats, β-caryophyllene is a complete agonist for the cannabinoid receptor type 2 (CB2 receptor) (Ceccarelli *et al.*, 2020). β - Caryophyllene binds to CB2 receptors in mice with a Ki = 155nM affinity (Alberti *et al.*,2017). In a study comparing the pain-killing effects of mice with and without CB2 receptors, the mice without CB2 receptors saw minimal benefit compared to the animals with intact CB2 receptors (Ceccarelli *et al.*, 2020). When compared to the ring-opened isomer - caryophyllene, which may modify CB2 activity, - caryophyllene exhibits the highest cannabinoid activity (Hashiesh*et al.*,2021).

"A focused evaluation of β--caryophyllene, a dietary cannabinoid selective,'s CB2 receptor pharmacological characteristics and therapeutic potential." 140: 111639. Biomedicine and Pharmacotherapy To compare binding, Cannabinol (CBN) binds to CB2 receptors as a partial agonist with a CB2 Ki = 126.4 nM affinity, while Delta-9-Tetrahydrocannabinol binds to CB2 receptors as a partial agonist with a Ki = 36nM affinity (Bow*et al.*, 2016). At low ambient temperatures, caryophyllene aids in improving cold tolerance. To suppress transient receptor potential melastatin 8 (TRPM8), an archetypical cold-activated ion channel in mammals, wild giant pandas frequently roll in horse excrement, which includes beta-caryophyllene/caryophyllene oxide (Zhou, *et al.*, 2020).

Carvacrol

Carvacrol, also known as cymophenol, is a monoterpenoid phenol with the chemical formula $C_6H_3(CH_3)(OH)C_3H_7$. Carvacrol has antibacterial action against e.g. *Cladosporium herbarum*, *Penicillium glabrum*, and fungi such as *Fusarium verticillioides*/*F. moniliforme*, *Rhizoctonia solani*/*R. solani*, *Sclerotinia sclerotiorum*, *Phytophthora capsici*, and *Pseudomonas syringae* (Andersen, 2006).

Germacrenes

Germacrenes are a class of volatile organic hydrocarbons, specifically, sesquiterpenes. Germacrenes are typically produced in a number of plant species e.g., *Ocimum tenuiflorum* for their antimicrobial and insecticidal properties, though they also play a role as insect pheromones. Two prominent molecules are germacrene A and germacrene D (Adio, 2009).

Gallic acid

Gallic acid is a trihydroxybenzoic acid with the formula $C_6H_2(OH)_3CO_2H$ (also known as 3,4,5-trihydroxy benzoic acid). It's phenolic acid. Gallic acid in alkaline solutions is easily oxidized by air. Gallate dioxygenase, a Pseudomonas putida enzyme, catalyzes the oxidation. Gallic acid reacts oxidatively with arsenic acid, permanganate, persulfate, or iodine to produce ellagic acid, as does methyl gallate with iron(III) chloride (Edwin *et al.*, 2007). Intermolecular esters (depsides) of gallic acids, such as digallic and cyclic ether-esters (depsidones), are formed (Edwin *et al.*, 2007). Gallic acid is hydrogenated to produce hexahydrogallic acid, a cyclohexane derivative (Albert *et al.* 1962). Pyrogallol is created by heating gallic acid (1,2,3-trihydroxy benzene). Gallate decarboxylase is the enzyme that catalyzes this reaction. Gallic acid esters, both synthetic and natural, are well-known. Gallate 1-beta-glucosyltransferase catalyzes gallic acid glycosylation (glucose attachment).

Cinnamic acid

Cinnamic acid is a key component in the production of lignols (precursors to lignin and lignocellulose), flavonoids, isoflavonoids, coumarins, aurones, stilbenes, catechin, and phenylpropanoids, among other natural products. The enzyme phenylalanine ammonia-lyase (PAL) acts on the phenylalanine to produce it (Vogt, 2010). Flavorings, synthetic indigo, and certain medications all include cinnamic acid. In the perfume industry, it is used as a precursor to making methyl cinnamate, ethyl cinnamate, and benzyl cinnamate (Budavari *et al.*, 1996). Cinnamic acid is converted to phenylalanine via enzyme-catalyzed amination, which results in the sweetener aspartame (Garbe, 2012). In nonpolar liquids, cinnamic acid can dimerize, resulting in distinct linear free energy correlations (Bradley *et al.* 2015).

Catechol

Catechol is a poisonous chemical molecule with the molecular formula $C_6H_4(OH)_2$. It is also known as pyrocatechol or 1,2-dihydroxybenzene. Of the three isomeric benzenediols, it is the ortho isomer. It was identified through the destructive distillation of the catechin plant extract. Every year, catechol is synthesized as a commodity organic compound, mostly as a precursor to insecticides, flavours, and scents.

The catechol skeleton can be found in a range of natural compounds, including urushiols, which are skin-irritating toxins found in plants like poison ivy, and catecholamines, as well as medications that mimic them (like MDMA), hormones/neurotransmitters, and catechin, which is found in tea. Many pyrocatechin compounds have been proposed as potential therapeutics. Antioxidant and polymerisation inhibitor 4-tert-Butylcatechol is widely used.Chitin is connected to protein by a catechol moiety in the cuticle of arthropods. Cross-linking (tanning and sclerotization), particularly in insects, and, of course, biomineralization, can reinforce the

cuticle (Briggs,1999). Bacteria such as Mycobacterium TB make catechols such as DHSA by metabolising cholesterol (Yam *et al.*, 2009). Dopamine is a catechol produced from tyrosine, an amino acid. The molecular basis for mussel adherence to mineral surfaces is catechol's chelating activity (Saiz *et al.*, 2019).

Ascorbic acid

Vitamin C (also known as ascorbic acid or ascorbate) is a water-soluble vitamin that can be found in *Ocimum tenuiflorum*, citrus fruits, and other fruits and vegetables, as well as being available as a nutritional supplement. Scurvy is a disease that can be prevented and treated with this supplement. Vitamin C is a necessary nutrient for tissue healing, collagen creation, and the enzymatic manufacture of some neurotransmitters. It is vital for immune system function and is required for the operation of numerous enzymes. It also has anti-oxidant properties. The majority of animals can produce vitamin C on their own. Apes (including humans) and monkeys (but not all primates), most bats, some rodents, and a few other creatures, on the other hand, must obtain it through their diet.

There's some evidence that taking vitamins on a regular basis will shorten the duration of a cold, but it doesn't seem to prevent infection. Supplementation hasn't been proven to reduce the risk of cancer, heart disease, or dementia. In mammals, ascorbic acid is a frequent enzymatic cofactor for collagen formation, as well as a potent reducing agent capable of rapidly scavenging a variety of reactive oxygen species (ROS). Given the importance of ascorbate, it's remarkable that the ability to make it hasn't always been conserved. Anthropoid monkeys, Cavia porcellus, teleost fishes, most bats, and some passerine birds have all lost the ability to produce Vitamin C internally in the kidney or liver. Loss-of-function mutations in the gene that codes for L-Gulono—lactone oxidase, the enzyme that catalyzes the last stage of the ascorbic acid pathway, were determined to be the cause of the alteration in every case where genomic analysis was performed on an ascorbic acid auxotroph (Yang, 2013). One explanation for the recurring loss of the ability to synthesise vitamin C is genetic drift; assuming a vitamin C-rich diet, natural selection would not act to preserve it (Zhang*et al.* 2010).

Conclusion

The *Ocimum tenuiflorum* plant is beloved in Hinduism and is frequently utilised in Ayurvedic and traditional medicine. It's a popular herbal tea for a variety of ailments. O.tenuiflorum has a complex molecular structure and contains a number of biologically active compounds. Phytochemicals found in Ocimum tenuiflorum (tulsi) include oleanolic acid, ursolic acid, rosmarinic acid, eugenol, carvacrol, linalool, and -caryophyllene. Tulsi essential oil is largely made up of eugenol (70 percent), -element (11.0 percent), -caryophyllene (8 percent), and germacrene (2 percent), with the rest being made up of other trace compounds, mostly terpenes. Terpenoids are composed up of acetate units and are related to fatty acids in origin. Common terpenoids include methanol and camphor (monoterpenes), farnesol, and artemisinin (sesquiterpenoids).

Antifungal, antibacterial, antiprotozoal, and antiviral effects have been demonstrated in them. Ursolic acid improves cognition and protects senescent mice's brains from D-galactose-induced oxidative damage. Ursolic acid stimulates liver regeneration in mice who have had their livers removed partially. Ursolic acid boosts cellular immunity and pancreatic beta-cell function in diabetic mice fed a high-fat diet-induced by streptozotocin. Skeletal muscle growth, grip strength, and exercise capacity were all improved by the use of UA. Improved endurance, decreased expression of genes linked to muscle atrophy progression, and decreased signs of cumulative weariness and exercise-induced stress. Ursolic acid improved metabolic anomalies and reduced hepatic steatosis in rats with nonalcoholic fatty liver disease produced by a high-fat diet.

Sesquiterpenes are a type of volatile organic hydrocarbons known as germacrenes. Germacrenes are antibacterial and insecticidal compounds generated by a variety of plant species, such as *Ocimum tenuiflorum*, but they also serve as insect pheromones. *Ocimum sanctum* plant extract may operate as a strong immunostimulant in *Clarias batrachus*. crude extract concentrations of *Ocimum sanctum* at 2.5 percent and 5 percent, considerably drops glucose quantity at 5% and substantial increases in RBC, WBC, serum protein, and globulin in the blood of the fish after 15 and 30 days of therapy. It could be attributed to phenolic chemicals such as tannins, saponin, flavonoids, steroids, terpenoids, eugenol, caryophylline, cardiac glycerides, and so on (Gayatri *et al*., 2014).

Ocimum sanctum improved the immunity, development, and survivorship of a common fish, *Clarias batrachus* (Linn.), as evidenced by improved haematological and biochemical markers. As a result, the use of natural materials, such as plant extracts, in the treatment of numerous parasite disorders in fish has a bright future. *Ocimum sanctum* could be used as a home medicine for managing numerous ailments by raising immune levels in the human body (Gayatri *et al*., 2014). Research is needed to determine the extracts' safety and efficacy of *Ocimum tenuiflorum*. More research is needed to determine the extracts' safety and efficacy of *Ocimum tenuiflorum*.

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