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A REVIEW ON THE PROPERTIES OF TULSI - *OCIMUM SANCTUM*:

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INTRODUCTION

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. Of all the herbs used within Ayurveda, tulsi (*Ocimum sanctum* Linn) is preeminent, and scientific research is now confirming its beneficial effects. There is mounting evidence that tulsi can address physical, chemical, metabolic and psychological stress through a unique combination of pharmacological actions. Tulsi has been found to protect organs and tissues against chemical stress from industrial pollutants and heavy metals, and physical stress from prolonged physical exertion, ischemia, physical restraint and exposure to cold and excessive noise. Tulsi has also been shown to counter metabolic stress through normalization of blood glucose, blood pressure and lipid levels, and psychological stress through positive effects on memory and cognitive function and through its anxiolytic and anti-depressant properties. Tulsi's broad-spectrum antimicrobial activity, which includes activity against a range of human and animal pathogens, suggests it can be used as a hand sanitizer, mouthwash and water purifier as well as in animal rearing, wound healing, the preservation of food stuffs and herbal raw materials and traveler's health. Cultivation of tulsi plants has both spiritual and practical significance that connects the grower to the creative powers of nature, and organic cultivation offers solutions for food security, rural poverty, hunger, environmental degradation and climate change. The use of tulsi in daily rituals is a testament to Ayurvedic wisdom and provides an example of ancient knowledge offering solutions to modern problems.

Traditional Uses

Traditionally, Tulsi was consumed as an herbal tea or in the form of dried powder or directfresh leaves or with Honey/Ghee. The dried leaves of Tulsi are used as an insect repellent for stored grains. From ancient times in "Ayurveda" and tribal medicine, Tulsi is being used as a remedy for the treatment of common cold, cough, wound, fatigue, headache, flu, fever, sore throat, and skin diseases or allergies. Leaves crushed in goat's urine and mixed with coconut oil is used against skin allergies. According to "Charaka Samhita" it is used for treatment against snake bites (whole plant used) and scorpion sting (leaf paste) Leaves pounded with onion bulbs are used for cold, cough, and headache. It helps in the maintenance of body glucose level (powdered leave with honey), reduces breathing problems, and increases digestion of foods. Dried leaves with ghee are useful in dysentery, colic, and piles treatment. Leaves paste with black pepper is used to treat diarrhea, and fever. Flower's juice in combination with honey, ginger and onion leaves juice is used for the treatment of bronchitis. In Thailand to treat vomiting, the leaf or entire plant is used. The plant leaves are also used for the purification of drinking water, for memory sharpening, good for nerves, to treat ulcers and mouth infections.

3. Chemical Constituents

The plant shows various therapeutic and medicinal properties, due to the presence of chemical constituents or phyto components. In species, O. tenuiflorum various kinds ofphytoconstituents and their activities were reported. The essential oil extracted from O. tenuiflorumL. consists high amount of Eugenol (near about 70%), other constituents are 11% of Beta- Elemene, 8% of Beta-Caryophyllene, and 2% Germacrene. The leaves of the plant consist of volatile oil (0.7%) made up of eugenol and methyl eugenol in 71% and 20% respectively. It consist carvacrol, sesquiterpene and caryophyllene hydrocarbon also62. Phenolic compounds isolated from the concentrate of fresh leaves and stem of Ocimum sanctum show antioxidants properties. The isolated phenolic compounds are isothymusin, circimaritin, cirsilineol, apigenin, and rosameric acid, and Eugenol (in high quantity) 16. Orientin and Vicenin are the 2 types of flavonoids extracted from aqueous leaf extract. Others like; Ursolic acid, orientin, luteolin, apigenin-7-O-glucuronide, molludistin and luteolin-7-Oglucuronide, are also extracte from the extract of Tulsi leaveas.

This species of *Ocimum* also contains a variety of sesquite rpenes andmonoterpenes; bornyl acetate, β elemene, neral, and pinenes (both α and β), camphene, sitosterol, cholesterol, campesterol, and stigmasterol.

Five types of fatty acids – stearic acid, palmitic acid, oleic acid, linoleic acid, linolenic acid are present in O. sanctum. Tulsi is a excellent source of vitamin C, beta carotene, and Ca2+ions. Tannins, camphor, other flavonoids like; luteolin, orientin, vicenin, and triterpene; urolic acid, with Zn, Mn, and Na ions found in plant extract.

The major chemical constituents of O. tenuiflorum Linn which are possessed in high amounts and leads to several remedial activities are; Eugenol (C10H12O2), Oleanolic Acid (C30H48O3), Linalool (C10H18O), Ursolic Acid (C30H48O3), Beta-Caryophyllene (C15H24), Rosemarinic Acid (C18H16O8), Estragole (C10H12O), Carvacrol (C10H14O), Methyl Cinnamate (C10H10O2) (Fig.1) 11.

Fig. 1: Structure of major chemical constituents of *Ocimum tenuiflorum.*

4. Experimental and Pharmacological Studies

Worldwide various scientific experiments of Ocimum tenuiflorum have been designed to evaluate the pharmacological actions, their after-effects or side effects, and their therapeutic uses against various diseases. Based on various experimental and clinical investigations on Ocimum tenuiflorum, the following pharmacological activities or therapeutic properties were reported.

4.1 Antioxidant Activity

This activity was reported by many researchers. Flavonoids have antioxidant properties and their role in membrane protection was observed. Antioxidant activity of the flavonoids (orientin and vicenin) in vivo resulted in a significant reduction in the radiation-induced lipid peroxidation in mouse liver. Tulsi extract has significantly scavenged high reactive free radicals. The Tulsi extract from leaves and stem have phenolic compounds and showed great antioxidant actions. The rosemarinic acid, isothymusin, cirsilineol, cirsimaritin, eugenol, and apigenin are the name of extracted phenolic commixture.[29]

4.2 Anti-diabetic Activity

When the Tulsi extract is administered orally it results in decrease blood sugar in both, glucose- fed hyperglycemic and streptozotocin-induced diabetic rats. By modulating the intracellular Ca+2 channel the extract of Tulsi stimulates the physiological pathway for the secretion of insulin via stimulating pancreatic β-cell. In clinical studies, placebo-controlled (a randomized and cross-over single-blind trial) –indicates a decrease in blood glucose (fasting-17.6% and postprandial-7.3%) level, quite similarly showed in urine glucose level. Tulsi also have aldose reductase activity, it helps to overcome side effects of diabetes (cataract, retinopathy, etc.)[12,75] Hydro-alcoholic extract of Tulsi found significant against streptozotocin (at dose level- 250 mg/kg body weight) and nicotinamide (at dose level-500mg/kg body weight) in comparison with glibenclamide.[76] Ethanol extract of Tulsi reduces hyperglycemia in alloxan diabetic rats.[74]

4.3 Antimicrobial activity

The leaf extracts and essential oil from Tulsi were reported as having antimicrobial activity. Tulsi is effective against various strains of bacteria and fungi. Alcoholic extract of Tulsi is found effective against Vibrio cholera.

The aq. Extract is effective against Gram-positive and Gram negative bacterial strains. Linalool shows the most prevalent against candidiasis, caused by Candida species. It decreases the growth and metabolism rate of candida by inhibiting proton pumps.

Fixed oil (mainly linolenic acid and ß-caryophyllene) showed growth inhibition against Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, and Bacillus pumilus. It is also resistant to Neisseria gonorrhea strains.

4.4 Chemopreventive Activity

The chemopreventive activity of Tulsi extract was detect ed through the consecration of hepatic/extrahepatic GST in mice.

In Tulsi extract supplemented mice, raised levels of deflated GSH were found in liver, lungs, and stomach tissues. The seed oil of Tulsi in high concentrations showed significant anti-proliferative and chemopreventive exercise in mice. The quiescent chemopreventive activity of seed oil imputed its antioxidant and cancer prevention activity.

4.5 Anticancer Activity

The anticancer property of Tulsi has been experimentally proven and referred by many researchers. The alcoholic extract of Tulsi leaves was highly affected carcinogen metabolizing compounds or enzymes such as cytochrome P450, cytochrome b5, glutathione S-transferase (GST), and aryl hydrocarbon hydroxylase, which are highly important for cancer-causing agents and mutagens. In human fibrosarcoma cell cultures, phytoconstituents are reported to have anticancer activity, here anticancer activity is accounted as morphological changes on culture; shrunken cytoplasm, condensed nuclei, contracted cells, and dense core. Tulsi significantly diminished the incidence of benzo (a) pyrene instigated neoplasia of forestomach of mice and 3'- methyl-4-dimethylaminoazo-benzene persuaded hepatomas in rodents. The beer of Tulsi leaves was significantly reported as an inhibitory effect on artificially induced skin papillomas inmice.

The initiation of papillomagenesis induced by 7, 12-dimethyl benz (a) anthracene (DMBA, a polycyclic aromatic hydrocarbon), when topical treatment of Tulsi e xtract was performed, reduces the tumor occurrence capacity and papilloma formation in mice]. The significantly high reduction of GSH substance and GST exercises are other applications of topicaluse of extracts. The *Ocimum tenuiflorum* fresh leaves, glue, or paste were taken orally can prevent the early occasions of DMBA induced buccal pouch carcinogenesis. The chemical carcinogenesis events were suppressed by inactivating the metabolic process of carcinogen, Tulsi leaf extract activity. The anticancer property of Tulsi was detected in Swiss albino mice bearing Ehrlich ascites carcinoma (EAC) and tumor S 180.

4.6 Radioprotective Activity

The Tulsi phyto-constituents radioprotectivity impact, firstly observed in - 1995. The flavonoids extracted from the leaves of Tulsi; orientin and vicenin indicate betterradioprotective influence as contrasted with synthetic or artificial radioprotectors. They have indicated significant protection towards human lymphocytes against clastogenic action of radiation at mediocre, inoffensive concentrations 88. The combination of Ocimum tenuiflorum extract with WR-2721 (synthetic) shows the high protective activity of bone marrow cell and reduces harmfulness and toxicity of WR-2721 at higher dose.

4.7 Hepatoprotective Activity

The methanol leaf extracts of Tulsi are effective in altering the dimethylnitrosamine implicated hepatotoxicity. The hydro-ethanolic extract of Tulsi leaves orally administrated200mg/kg gave protection against liver injury persuaded by paracetamol, in male Wistar albino rats. Ocimum tenuiflorum cold water extract was adequate against carbon tetrachloride invaded liver injury in albino rats.

4.8 Antifertility Activity

Leaf extracts of Tulsi in benzene and petroleum ether solvent were expressed high antifertility activity in female rats, 80% and 60% respectively.[92] Similarly, the benzene extracts highly responsible for diminishing sperm tally, testis weight, and motility of sperm reported in male rodents . The Ursolic acid; one of the major component of Tulsi, possess antifertility effect. This effect is related to an anti-estrogenic mechanism that is responsible for lacking or arresting male rat spermatogenesis.

4.9 Antipyretic Activity

The fixed oil of Tulsi (*O. tenuiflorum)* showed antipyretic activity.[93] It was assessed by tests on rodents by inducing pyrexia through typhoid-paratyphoid A/B vaccine.

The IP (intraperitoneal) administration of oil significantly reduced the febrile reaction indicating its antipyretic pro perties.

The fixed oil also has an inhibitory effect on prostaglandin. The antipyretic activity of oil at a dose of 3ml/kg was similar to ibuprofen and aspirin.

4.10 Adaptogenic or Antistress Activity

An adaptogenic activity depends upon the immune stimul ant capacity of Tulsi.[11,12] The wholeplant alcoholic extract increased the physical perseverance (survival time) of swimming mice, forestalled stress prompted ulcers and milk actuated leukocytosis respectively in rats and mice, indicating acceptance of vaguely increased.[95]

4.11 Antiulcer Activity

Intra-peritoneal administration of *O. sanctum* fixed oil evoked high antiulcer activity against Indomethacin, Reserpine, Serotonin, alcohol (50% C2H5OH), Histamine, Aspirin, and stress instigated ulcers in rodents.

Lipoxygenase inhibition, antisecretory, and histamine antagonistic effects present in fixed oil significant amount possessed antiulcer activity.

4.12 Anticoagulant Activity

The fixed oil of Tulsi (dose-3ml/kg, intra-peritoneal) demonstrated that prolongation in blood clotting time and the whole reaction was comparable with aspirin (dose-100mg/kg). The impact produced by Tulsi oil on platelets, expected as anti-aggregator.

4.13 Cardioprotective Activity

Ocimum sanctum seed extract in hydro-alcohol showed great efficiency for cardioprotection. Tulsi plants have varieties of bioactive constituents, including quercetin, diosgenin, carotinized, isoflavones, catechin, and sulforaphane have been reported as an enhancer of cardioprotection, hence lacking the risk of cardiac abnormalities.[98] Effect of hydroalcoholic extract of Tulsi investigated against myocardial infarction (MI) rats, MI induced by subcutaneously administered isoproterenol (ISO). The level of glutathione, superoxide dismutase, and LDH reduced significantly in rats. It also inhibits lipid peroxidation. Tulsi at the dose of 50mg/kg shows the maximum rate of cardioprotective.[99]

4.14 Antihypertensive Activity

The *Ocimum tenuiflorum Linn* were prevented transient cerebral ischemia (a brief stroke-like attack) and long-term cerebral hypoperfusion (causing cellular oedema, gliosis and perivascular inflammatory invade).[100] The Tulsi fixed oil contains; linoleic and linolenic acids (essential fatty acids), it produces PGE-1 and PGE-3 (prostaglandins- atrial pressure regulator) and inhibitsP GE-2 (it increases blood pressure and hypertension formation.[20,100]

4.15 Antiviral Activity

The chemical constituents of Tulsi show antiviral activity. Majorly ursolic acid and eugenol demonstrated antiviral activity including influenza.[34]

4.16 Anti HIV

Various studies were suggested that chlorophyll derivatives reported against enveloped viruses including HIV. *Ocimum sanctum* chlorophyll derivative "Pheophytin-a" has a potential anti-HIV agent attacking HIV-1 protease. "Phy-a" was reported as an inhibitor of HIV replication.[101]

4.15.1 Anti dengue virus

Methanolic extract of Tulsi plant exhibit antiviral properties toward dengue virus 1 (DENV 1) through inhibition of viral replication and cytopathic (host cell-structural changes) formation.[102, 103]

4.15.2 Anti covid-19 virus

O. sanctum (Tulsi), phytoconstituents are reported as Anti-covid-19 activity. Out of 46 active phyto-constituents of Tulsi, only three components; Vicenin (flavonoid), Isorientin 4′ -O-glucoside 2″ -O-p-hydroxybenzoate (a flavon), and Ursolic acid (a natural triterpene compound) were showed positive response against covid-19 virus.

In comparison with to built-in ligand N3 for SARS-CoV-2 Mpro, these compounds gave significant binding affinity. Apart from this vicenin reported as highest binding energy (8.97 kcal/mol), it interacts with C and π-donor hydrogen bonding with Glu 166, Thr 190, Gln 189 and Pro 168 residues along with Met 165 (π-sulfur bonding), and Cys 145 (allyl interaction). The isorientin interacts with Arg 40, Arg 105, Arg 188 residues (a positive charged H-bond), and Tyr 54 residue with hydrophobic interaction with binding energy 8.55 kcal/mol. The ursolic acid, binding energy 8.52 kcal/mol binds with Leu 272, Leu 287, and Tyr 239 residues (alkyl and π-alkyl interaction) and with Leu 271 (carbon-hydrogen bonding) residues. They have reduced the capacity of translation of viral proteins.[104]

4.16 Analgesic Activity

Analgesic activity of Tulsi was found in experimental models. It was highly reactive against acetic acid introduced writhing model in rodents (dose-dependent manner). The inhibitory effect of oil was demonstrated due to joint inhibitory effects of histamine, acetylcholine, and prostaglandins.[105]

4.17 Immunomodulatory Activities

The new leaves refined extract of O. sanctum demonstrated alteration in the humoral resistant reaction in pale-skinned rodents. The extract adjusts, cell intervened insusceptible receptiveness and GABergic pathways arbitrate immunomodulatory effects.[106] A randomized double-blind control trial is conducted in healthy volunteers to assess the immunomodulatory action of Tulsi. The results are shown in elevated amounts of interferon-γ and interleukin-4 including T-helper cells and Natural killer cells.[107] A significant enhancement in anti-sheep RBC antibody titer and low % histamine revealed from peritoneal mast cells of stimulated rats (humoral immune response), and the decrease in thickness and % inhibition of leukocyte migration (LMI) of Tulsi seed oil (3 ml/kg, IP) 108. The oral dose of aqueous extract of Tulsi accelerates the production of WBC, RBC hemoglobin and it also enhances the manufacture of antibodies without stirring the biochemical parameters.[109]

4.18 Anticataract activity

The aqueous extract of Tulsi leaves that delayed the cataractogenesis is a preliminary model of cataract (naphthalene cataract in rabbits- 1g/kg and galactosemic cataract in rodents-30%). The higher dose is very much effective.[110]

4.19 Antiarthritic Activity

Wide varieties of chemical constituents were reported as a ntiarthritic activity. In Tulsi essential oil(ursolic acid, apig enin, luteolin) from leaves and flower extract showed anti arthritic activity.[111] It was screened by Singh et al. in 1996 using against formaldehyde-inducted arthritis, Freund's adjuvant arthritis, and turpentine oil-induced joint edema in rats.[112]

4.20 Memory enhancer activity

The whole dried plant or extract of Leaves (aqueous} and entire plant {alcoholic} of Tulsi enhanced the amnesic effect of scopolamine (0.4mg/kg) and maturing initiated memory shortfalls in mice. This greatly abolishes the acetylcholine esterase .and down dormancy (SDL) restraint. Thus, Tulsi is used for the treatment of Alzheimer's, and dementia (psychological disorders).

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