"Medicinal chemistry of Tulsi"
(*Ocimum sanctum - holy basil*)

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Abstract:

The plant of "***Ocimum tenuiflorum*** or ***Ocimum sanctum***" belong to family *lamiaceae*.
It is of indian origin . It is generally called "**Tulsi**" - Queen of herbs in Hindu religion.In Ayurveda (traditional Hindu medicine) leaves stem and inflorescence of tulsi plant had been used from ancient time in cough , common cold , headache ,influenza ,chronic fever and recently in diabetic and antifertility. Tulsi plants have such an essential oil , silver or gold nanoparticles ,antiprolifderative components that attracts researcher to study about it and use it to cure cancer like disease. This article is just to emphasize chief chemical compounds present in Tulsi plant and their medicinal importance.

Keywords: Ayurveda , antimicrobial , anticancer , flurbiprofen , eugenol , medicinal.

Introduction

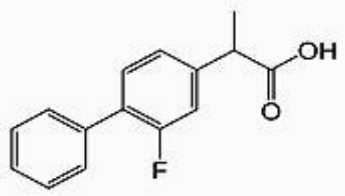
India has a very holistic, majestic and medicinal plant "Tulsi" (ocimum tenuiflorum) It is also called holy basil . It has Indian origin[1]. No doubt , It has been bless for the people of Indian continent either as anti -diabetic [2], antimicrobial [3], anticancer [4] . According to hindu 'Padma Puran' , 'Tulsi' was a woman 'Vrinda' and married to asura king Jalandhar .She was devotee of lord Vishnu .Tulsi is a Sanskrit word which means matchless one [5] . Tulsi is considered a sacred plant by the Hindus and is often planted around Hindu shrines. Therapeutic use of this plant is as old as 4000-5000BC .Tulsi is categorised as Rama -tulsi ,Shyam-tulsi , Vana-tulsi. In Ayurved it is used as adaptogen to counter life's stresses. Medicines are made from their leaves, stems, and seeds. Chemicals in holy basil are thought to fight against many diseases Early research suggests that its essential oil can slow progression and improve survival rate in animals with certain types of cancer. Researchers think this benefit may be explained by the oil's ability to act as an antioxidant [6]. AMPs(antimicrobial peptides) ,HDPs (host defense peptides) ,fulvicacid[6] eucayptol , eugenol etc essential oils are present in it . Fulvic acid is powerful antioxidant Which neutralises free -radicals .It enhances absorption of vitamins and minerals in our body . It is a catalyst with molecular formula C_{135} H_{182} $O_{95}N_5S_2$. Essential oil of tulsi fight against selected microbial pathogens.

CHEMICAL COMPONENTS OF TULSI AND ITS MEDICINAL VALUES

1. Silver nanoparticles [7]

Biosynthesis of stable silver nanoparticles is done using Tulsi (Ocimum sanctum) leaf extract. These biosynthesized nanoparticles[7] is characterized with the help of Atomic Absorption Spectroscopy (AAS), UV-vis spectrophotometer, Dynamic light scattering (DLS), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), and Transmission electron microscopy (TEM). Stability of bio-reduced silver nanoparticles is found to be lethal against both gram-negative and gram-positive microorganisms. It is observed that tulsi leaf extract can reduce silver ions into silver nanoparticles[7] within 8-9 min of reaction time. Meanwhile, this method can be used for rapid and ecofriendly biosynthesis of stable silver nanoparticles of size range 5-30 nm possessing antimicrobial activity Aqueous extract of tulsi leaf is used as reducing agent for the environmentally friendly synthesis of gold and silver nanoparticles[7].

2. Flurbiprofen[8]



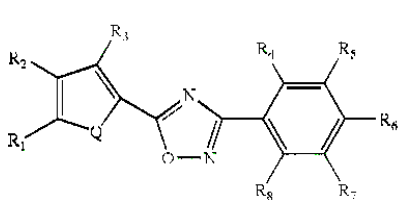
Flurbiprofen

Flurbiprofen[8] has been used to reduce pain, swelling, and joint stiffness from arthritis. This medication is also known as a non-steroidal anti-inflammatory drug (NSAID). The penetration up grating potential of tulsi , turpentine oil on transdermal delivery of flurbiprofen, a potent non-steroidal anti-inflammatory agent has been also investigated these days .

Now the transdermal permeation of flurbiprofen ($C_{15}H_{13}O_2F$) across the rat abdominal skin from binary solvent mixture composition of propylene glycol (PG):isopropyl alcohol (IPA) (28:72%, v/v) has found to be 97.88 micro g/cm(2)/h, significantly higher than other binary solvent mixtures. The corresponding steady state plasma concentration (0.71 micro g/ml) is much lower than required steady state plasma concentration of (3-5 micro g/ml). Hence influence of tulsi and turpentine oil in the optimized binary solvent mixture besides the increased drug load on the flurbiprofen[8] permeation is evaluated. The magnitude of the flux enhancement factor with turpentine oil and essential oil of tulsi are 2.4 and 2.0 respectively at 5% (v/v) concentration beyond which there is no significant increase in the flux. Addition of 2% (w/v) hydroxypropyl methylcellulose (HPMC), as a thickening agent, results in desired field for the fabrication of patch with insignificant effect on permeation rate of flurbiprofen[8]. The reservoir type of transdermal patch formulation, fabricated by encapsulating the flurbiprofen[8] reservoir solution within a shallow compartment moulded from polyester backing film and microporous ethyl vinyl acetate membrane, do not modulate the skin permeation of flurbiprofen[8] through rat skin in case of turpentine formulations whereas flux of formulations with tulsi oil is significantly altered. The effect of penetration enhancer and solvents on the anatomical structure of the rat skin has been studied. Enhancement properties exhibited by turpentine oil and tulsi (holy basil) oil in optimized binary solvent mixture are superior as compared to solvent treated and normal control groups with negligible skin irritation. The fabricated transdermal patches are found to be quite stable. The bioavailability of flurbiprofen with reference to orally are seen in tulsi leaves .

3. Antiproliferative

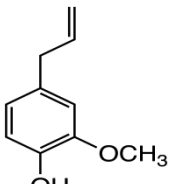
Cancer [9] till today remains the leading cause of death in both developed and developing countries. Plants have been beacon of therapeutic sources for curing diseases from times immemorial. Antiproliferatives [10] are used to inhibit excess cell growth



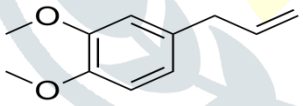
.Antiproliferative[10] effects on tumor cells is in 3-aryl-5-(3′-chlorothiophen-2′-yl)-1,2,4-oxadiazoles [10] that are apoptosis inducers with good activity against several breast and colorectal cancer cell lines. Another interesting scaffold is represented by the 5-arylamino-1,2,4-oxadiazoles, Hence, the present study aimed at evaluating the antiproliferative [10] activity of extract of Ocimum sanctum (tulsi)leaves on oral cancer cell line. To evaluate the antiproliferative [10] effect and to analyze dose dependent cytotoxic activity of aqueous extract of tulsi leaves on KB mouth cell line.

4. Antioxidant component

Ocimum leaves are highly enriched in antioxidant components. Thus, its leaf extracts, if applied in plants, is believed to efficiently scavenge ROS, thereby preventing oxidative damage under drought stress. Tulsi has a powerful anti-oxidant component called eugenol[11] **(4-allyl-2-methoxyphenol)**.



eugenol

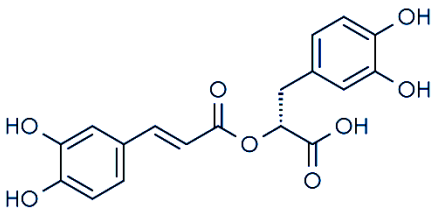


methyl eugenol

Eugenol [11] helps in protecting the heart by keeping one's blood pressure under control and lowering his/her cholesterol levels. Chewing a few leaves of tulsi on an empty stomach early morning everyday can both prevent and protect any heart ailments. Leaves of holy basil are packed with antioxidants and essential oils that produce eugenol [11], methyl eugenol **(4-Allyl-1,2-dimethoxybenzene)** and caryophyllene **(4,11,11-trimethyl-8-methylidenebicyclo[7.2.0]undec-4-ene).** Collectively these two substances help the pancreatic beta cells (cells that store and release insulin) function properly. This in turn helps increase sensitivity to insulin. Lowering one's blood sugar and treating diabetes effectively. An added advantage is that the antioxidants present in the leaves help beat the ill effects of oxidative stress. Thus, tulsi has been shown to protect against the toxic effects of industrial chemicals such as butylparaben, carbon tetrachloride, copper sulfate and ethanol, and common pesticides such as rogor, chlorpyrifos, endosulfan and lindane. Tulsi has also been shown to protect against the toxic effects [11,12] of many pharmaceuticals drugs including acetaminophen, meloxicam, paracetamol, haloperidol and anti-tubercular drugs.

5. Rosmarinic acid;

Rosmarinic acid is the ester of caffeic acid and 3, 4-dihydroxyphenyllactic acid. It is a plant-based compound found in a wide variety of spices, but most well known for being the active ingredient in Rosemary and Perilla Oil.

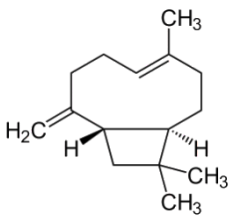


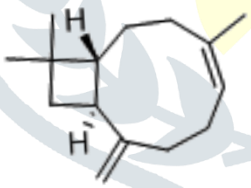
rosmarinic acid

It displays general anti-oxidant and anti-inflammatory effects, and may protect against various forms of cancers. Additionally, it can be absorbed through the skin when in an ethanol base (perillyl alcohol). Leaves of sweet basil contain rosmarinic acid [12] and derivatives. Rosmarinic acid may remove the ciguatoxins[13,14] from their sites of action in food poisoning The use of rosmarinic acid is effective also in a mouse model of Japanese encephalitis[15]

6. β-Caryophyllene (about 8%)

β- Caryophyllene[16] ***trans-(1R,9S)-8-Methylene-4,11,11-trimethylbicyclo[7.2.0]undec-4-ene*** which is also known as caryophyllene or called (−)-β-caryophyllene, is a natural bicyclic sesquiterpene that is a constituent of many essential oils including that of Syzygium aromaticum[17] (cloves), , rosemary, Cannabis sativa and hops. It is generally found as a mixture with isocaryophyllene[18] (the cis double bond isomer) and α-humulene (obsolete name: α-caryophyllene), a ring-opened isomer. β-Caryophyllene is notable for having both acyclobutane [19] ring and a trans-double bond in a nine-membered ringed structure.



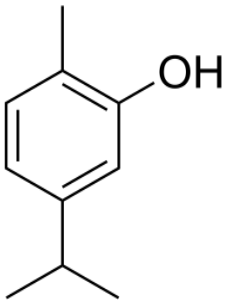


β-Caryophyllene **isocaryophyllene**

β-Caryophyllene is a sweet and dry tasting compound that can be found in a number of food items such as, fig, allspice, pot marjoram, and roman chamomile etc which makes
β-caryophyllene a potential biomarker for the consumption of these food products.
(-) β-caryophyllene is a beta-caryophyllene in which the stereocentre adjacent to the exocyclic double bond has S- configuration while the other remaining stereocentre has R- configuration. It is the most commonly occurring form of β-caryophyllene, occurring in many essential oils, particularly oil of tulsi . It has a role as a non-steroidal anti-inflammatory drug [20], a metabolite and a fragrance. It is an enantiomer of a (+) β -caryophyllene. It also cures anxiety and depression [21].

7. Carvacrol

Carvacrol[22], a monoterpenic phenol, is present in tulsi leaf and has emerged for its wide spectrum activity extended to food spoilage or pathogenic fungi[23], yeast and bacteria as well as human, animal and plant pathogenic microorganisms including drug-resistant and biofilm membrane forming microorganisms.



Carvacrol

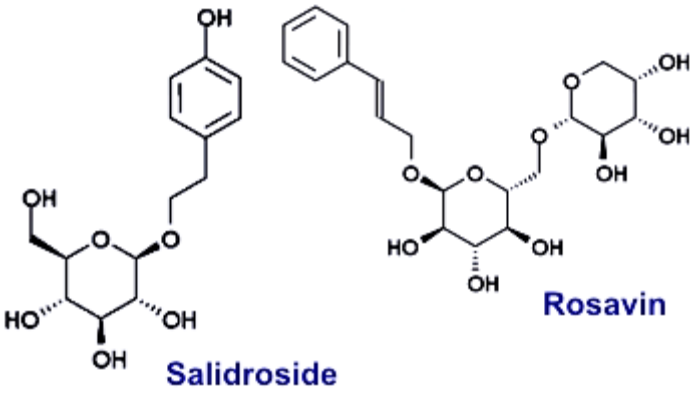
The carvacrol shows antibacterial activity [24] and has been attributed for its considerable effects on the structural and functional properties of cytoplasmatic membrane [25]. of bacteria culture . Many reviews of the published literatures regarding the antimicrobial properties of carvacrol and the recent patents claimed in order to highlight its future applications as a new antimicrobial agent shows its importance It could concern either the natural preservation in the cosmetic and food industries or an alternative which supports the conventional antimicrobial protocols. Interestingly, carvacrol alone or associated with one or more synergistic products could be incorporated in different formulations for biomedical and food packaging applications or food preservative. However, more detailed safe investigations and in vivo studies should be carried out so that this molecule could be used in the future. Tulsi oil, has also been shown to help lower cholesterol in mice that were fed a high-fat diet over 10 weeks. The mice fed with carvacrol alongside the high-fat diet had been observed significantly lowered cholesterol value at the end of the 10 weeks, compared to those that were just given a high-fat diet .Thus cholesterol-lowering effect of tulsi oil is thought to be the result of the phenols carvacrol and thymol present in it .

8. Adaptogen

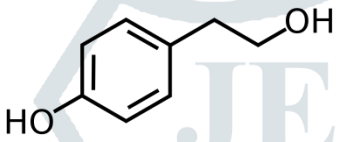
Considered as a potent adaptogen[26], tulsi has a unique combination of pharmacological actions that promote wellbeing and resilience. While the concept of an "adaptogen," or herb that helps with the adaptation to stress and the promotion of homeostasis, is not widely used in Western medicine, Western medical science has revealed that holy basil does indeed possess many pharmacological actions that fulfill this purpose. Some of adaptogens are.

Rosavin [26] is the primary alcohol glycoside responsible [27] for Rhodiola's antidepressant actions .It is also present in tusi plant

Salidroside [26,27] is another primary anti-depressant[27] and anxiolytic compound found in tulsi .
It has been used for centuries; especially within traditional Chinese medicine as a work enhancer. Currently, many body-builders and endurance athletes consume it as a supplement

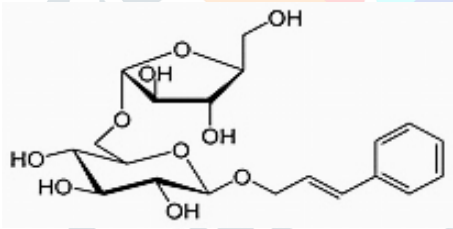


Tyrosol is the main medicinally[28] effective chemical compound found not only in Rhodiola, but also in tulsi oil. In fact, researchers believe that Tyrosol is responsible for most of the reported health benefits within the Asian diet. It's a potent anti-oxidant and cardioprotective [29] ingadient.



tyrosol

Rosarin is a cinnamyl alcohol glycoside; we know very little about how it functions but we do know that it has some adaptogenic [27] inducing properties.



rosarin

Tulsi is an aromatic herb in the basil family Lamiaceae [30] (tribe ocimeae) that is thought to have originated in north central India and now grows native throughout the eastern world tropics. Within Ayurveda, tulsi (holy basil) is known as "The Incomparable One," "Mother Medicine of Nature" and "The Queen of Herbs," and is revered as an "elixir of life" that is without equal for both its medicinal [31] and spiritual properties. Within India, tulsi has been adopted into spiritual lifestyle practices which provide a vast array of health benefits that are just beginning to be confirmed by modern science. Tulsi is perhaps one of the best examples of Ayurveda's holistic lifestyle approaching to health. Tulsi tastes hot and bitter and is said to penetrate the deep tissues, dry tissue secretions[32] and normalize kapha and vata. Daily consumption of tulsi is said to prevent disease, promote general health, wellbeing and longevity and assist in dealing with the stress [31 -34] of daily life. Tulsi is also majestic in giving luster to the complexion, sweetness to the voice and fostering beauty, intelligence, stamina enhancement and a calm emotional disposition. In addition to these health-promoting properties, tulsi is recommended as a treatment for a range of conditions including anxiety [34,] cough, asthma, diarrhea, fever, dysentery, arthritis, eye diseases, indigestion, hiccups, vomiting, gastric, cardiac and genitourinary disorders[35,39], back pain, skin diseases, ringworm, insect, snake [36] and scorpion bites and malaria [37.] Many of the physiological benefits of tulsi can be attributed to its ability to assist with the body's internal housekeeping and protection of the body from toxin-induced[38] damage. These functions are often attributed to tulsi's high content of phenolic compounds and anti-oxidant properties, with Krishna

tulsi (black/purple variety) having a higher phenolic content and anti-oxidant [39] capacity than white Vana tulsi.

CONCLUSION

The medicinal properties of tulsi have been studied in lots of scientific studies including *in vitro,* animal and human experiments. These studies reveal that tulsi has a unique combination of compounds such as eugenol [11] , carvacrol [15,22]**,** etc and their actions include: antimicrobial that includes antibacterial, antiviral, antifungal, antiprotozoal, antimalarial, anthelmintic and also some anti-cholestrol, anti-oxidant , radioprotective, anti-inflammatory[40], anti-diarrheal[40,41] chemopreventive , hepato-protective[42], neuro-protective[43], cardio-protective, anti-diabetic [21,44], anti-hypercholesteroalemia,[45] anti-hypertensive, anti-carcinogenic, analgesic, anti-pyretic, anti-allergic, immunomodulatory[46], central nervous system depressant[47], memory enhancement, anti-asthmatic[44,48], anti-tussive, diaphoretic, anti-thyroid, anti-fertility, anti-ulcer, anti-emetic, anti-spasmodic, anti-arthritic, adaptogenic, anti-stress, anti-cataract, anti-leukodermal[49] and anti-coagulant[41,50] activities. These pharmacological actions of tusli help the body and mind cope with a wide range of chemical, physical, infectious and emotional stresses and restore physiological and psychological function. Modern day of scientific research into tulsi demonstrates the many psychological and physiological benefits of consuming tulsi and provides a testament to the wisdom inherent in Hinduism and Ayurveda, which celebrates tulsi as a plant that can be worshipped, ingested, made into tea and used for medicinal and spiritual values in daily life. In providing a focus for ethical, sustainable and ecological farming practices that provides a livelihood for thousands of farmers, medicine of tulsi goes beyond providing benefits for individuals and households and begins to address broader social, economic and environmental issues Despite the many wonders of science and industry, modern life is fraught with stress and anxiety. However, mobile devices and the web have vastly increased the pace of life and many people feel that they are now drowning in an ever-expanding ocean of data, while industrial agriculture has burdened us with increasing exposure to unhealthy processed and packaged food and a plethora of food packaging materials and other toxic industrial chemicals. Metropolitan -life dwellers are also faced with increasing wealth inequality, social isolation, excessive noise, air, water and soil pollution and disconnection from nature. Thus, while industrial revolution has led to longer lifespans and vast increases in human populations, it is now recognized that the greatest causes of death and disease on the planet are preventable lifestyle-related chronic diseases in this case tulsi plant can fulfill spiritual and health protection for them. No doubt, we are in the midst of a global pandemic of obesity, diabetes, cancer, dementia, depression and other chronic diseases caused by modern lifestyles and their associated lack of physical activity, high intake of alcohol, fat, salt, sugar and tobacco and exposure to a toxic[50] cocktail of industrial chemicals. The solutions to this current health crisis are therefore more likely to be found in the homes, Ayurveda and behaviors of individuals than in western medical clinics, hospital or pharmacies**.** As ancient science and world's oldest medical system, Ayurveda has a holistic approach to health and disease that focuses on preserving and promoting good health and preventing disease through healthy lifestyle practices.These practices include consumption of fresh, minimally processed foods, the use of *Rasayanas* (formulas) that eradicate ageing and disease, sophisticated detoxification practices and regular consumption of adaptogenic herbs that enhance the body's capacity to maintain balance in the midst of a variety of stressors and *bhasmas* which has basic minerals present in it. Ayurveda's regular use of medicinal and culinary herbs draws upon India's incredible biodiversity with a variety that is unsurpassed by any medical system; yet, of all the used herbs, none has a status as comparable to as tulsi or holy basil (*Ocimum sanctum*). Medicines are made from leaves, stems, and seeds of from this "*queen of herbs"*. Chemicals in holy basil are thought to fight against many diseases. At the end we conclude that all essential oils obtained from tulsi plant has many compounds, discussed above, are not only beneficial for stress, anxiety etc, but is ram vana in chronic disease also.

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