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## Thymus serpyllum toxicity, pharmacology, traditional uses, and phytochemical analysis

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### Abstract:

In the upper foothills of India, *Thymus serpyllum* L., an understudied perennial plant in the Lamiaceae family, has long been used to treat respiratory and gastrointestinal conditions. This study aims to fill the gaps in our current knowledge of *T. serpyllum*'s pharmacology, phytochemistry, and traditional uses. Our primary goal is to compile the most recent information on this plant and to encourage more *in vitro* and *in vivo* research to support local claims. The essential oil produced from *T. serpyllum* has attracted a lot of attention as a plant-derived product because of its diverse pharmacological properties, which include antioxidative, antibacterial, anti-inflammatory, and anticancer activity. Ethnomedicinal studies have shown that *T. serpyllum* has great potential for developing new drugs to address a variety of health sector problems. Pharmacological studies by themselves are not enough to justify *T. serpyllum*'s extensive use. Researchers often use either *in vitro* or *in vivo* techniques. More research in the form of well planned pharmacological trials is required to assess these medicinal claims. The evaluation's conclusions will act as a basis for further research. There has been little pharmacological study on *T. serpyllum* despite its broad traditional use; most studies have been carried either *in vitro* or *in vivo*. Additional chemical isolation, in-depth pharmacological research, and possible culinary applications are crucial subjects to investigate.

**Keywords:** Pharmacological properties, phytochemistry, *Thymus serpyllum*, toxicity, traditional applications

### Introduction:

By using medicinal herbs, the modern world is in charge of boosting immune responses and attaining superior health. People have used traditional medicines as an affordable and

convenient way to cure illnesses for millennia, dating back to about 4000 and 5000 B.C. The Chinese were able to get the earliest known herbal medicine composition. The Rig-Veda, which was written between 1600 and 3500 B.C., has the first written account of the usage of herbs as remedies in India. Herbs have long been used in traditional Indian medicine because of their medicinal qualities.[1] Plants may provide novel therapeutic interventions. The Creative Commons Attribution-Non Commercial-Share-alike 4.0 License governs the distribution of the papers published in this open-access journal. As long as appropriate credit is given and the new works are licensed under the same terms, this license allows others to alter, adapt, and produce works based on the original work without receiving payment. either directly or indirectly. According to World Health Organisation (WHO) surveys, most people in developed countries rely on traditional medicine for their health. The need for therapeutic plants is increasing in both developed and developing countries.

Thyme has a significant position as a member of the Lamiaceae family and a large genus within it. There is proof that this versatile plant is used as a spice all throughout the world. According to the World Checklist, there are 220 species of thymus L. among the 7534 species in the thyme genus (<http://apps.kew.org/wcsp/incfamilies.do>). Third, Richard has successfully identified several Thymus species worldwide.[4] Members of the genus Thyme are widely used in the culinary, cosmetic, perfume, and pharmaceutical industries.[5] Among the numerous conditions that thyme may aid with include the common cold, flu, indigestion, nausea, renal disease, ulceration, headache, diabetes, and asthenia.[6] Thyme oil, which includes terpenes, esters, and phenolic compounds, is the primary subject of research. Thyme is one of the most adored herbs in the world because of its aromatic and therapeutic qualities, and thyme oil is no different. It is regarded by many as one among the top ten essential oils (EOs) worldwide.[7] Thus, the goal of this research is to provide current data on the pharmacological traits, phytochemical constituents, traditional applications, and safety profile of *T. serpyllum*. This research gathers phytochemical and pharmacological information that might be used to develop successful intervention plans, close knowledge gaps, and investigate novel therapeutic approaches.

### **Botanical Description and Geographic Distribution**

*T. serpyllum* is a little shrub with a cluster of glossy, blue-green, pointed leaves that become brown over time. It has a nice scent. There are other names for it, such as Breckl and thyme, creeping thyme, and wild thyme. In addition to Asia, Europe, and North America, it may be found in various regions of East Africa. It grows in India, particularly in the Himachal Pradesh, Uttarakhand, and Jammu & Kashmir states.[8] The height of perennial *T. serpyllum* bushes may range from 5 to 7 cm. Its hairy, crawling appearance is adorned with clusters of small, pinkish-purple blossoms.[8] The oval-shaped leaves are smooth on both sides, about 4-6 mm long and 2-4 mm wide, and are covered with long trichomes. The central vein is strong, while the lateral veins at the base of the edge are less noticeable. These leaves are present throughout the year. Because of its distinct aroma, the hermaphrodite *T. serpyllum* plant relies on pollinators including bees, flies, and butterflies. It prefers sandy, rocky, loose, and nutrient-poor soil and thrives in conditions with a medium to dry moisture content and adequate drainage. This species is more prevalent in areas with shade, even though it does well in dry, windy

environments.[9] It develops quickly on regular moist soil and requires more sunshine. Using stem cuttings for propagation is an easy procedure.

### **Thymus serpyllum: A Traditional Herb with Modern Uses**

as well as for therapeutic purposes. They have been used in medicine for a very long time, and they are now an essential part of our cultural and gastronomic heritage. In the past, martyrs and warriors have used it to increase their physical strength and psychic perception since it has the fastest healing and courage capabilities [10]. Greek medical professionals have traditionally used the plant's juice to cure coughs and asthma. They also advise using the paste topically to treat arthritis and clean wounds and scrapes. The plant's juice has long been used in Greek medicine to treat coughs and asthma, and its paste has external applications including curing wounds and scrapes and treating arthritis [13]. Furthermore, the leaves and blooming stems relieve a variety of skin issues, including rashes and itching, as well as period cramps and discomfort.[14] An infusion made from *T. serpyllum* leaves and "jaggery" is well-known for its diuretic properties. The aerial parts of *T. serpyllum* have antiseptic, antiplasmodic, deodorant, and disinfecting qualities in addition to its use in respiratory and gastrointestinal disorders [15]. In the Western Balkans, *T. serpyllum* has improved blood circulation and is an immunostimulant [16]. *T. serpyllum* has long been used by Indian traditional medicine practitioners to treat menstrual cramps [17]. Additionally, it has been used to lessen oedema, eczema, and inflammation [18]. Its antidiarrheal properties have also been recognised by ethnoveterinary medicine. In 2015, the British Pharmacopoeia, Commission Secretariat of the Medicines, and Healthcare Products Regulatory Agency, reported that combining *T. serpyllum* with blackberry leaves effectively cured acute pharyngitis. Additionally, *T. serpyllum* is a prominent element in herbal tea.[20]. Apart from being used in mouthwashes and gargles, *T. serpyllum* essential oil's soothing and disinfecting qualities make it a powerful tool against a range of ailments.[21]

### **Plant biology**

Over the last 20 years, a plethora of studies have investigated the phytoconstituents profile of *T. serpyllum* EO [Table 1].[22] is a The genus *Thymus* is classified by a number of chemical substances, including germacrene, thymol, carvacrol,  $\beta$ -terpinyl acetate, linalool, geraniol, citral, and (E)-caryophyllene.[23] Thymol levels in essential oils extracted from thyme cultivated in India ranged from 60% to 64.6%, in contrast to those in essential oils extracted from thyme cultivated in Estonia, which ranged from 0% to 0.4%. Thymol (16.5%–18.8%), 4,8-cineole (14.0–18.0%), and thymoquinone (2.6%) were all reported by Aziz et al. [24]. The essential oils of *T. serpyllum* cultivated in Muzaffarabad, Jammu include 1,8-cineole (14.0%–18.0%) and spathulenol (1.3%–2.1%).

**Table1: Various classes of phyto compounds present in *Thymusserpyllum***

Category of phyto compounds	Phytoconstituents
Phenolic acids and flavonoids	Gallic acid, rosmarinic acid, caffeic acid, ferulic acid, rosmarinic acid-glucoside, protocatechic acid, protocatechic acid-hexoside, chlorogenic acid, naringin, luteolin-o-diglucuronide, kaempferol-o-glucuronide, rutin, luteolin-o-glucuronide, apigenin-o-glucuronide, methylkaempferol-o-rutinoside, luteolin, luteolin-7-o-rutinoside, luteolin-7-o-glucoside, apigenin-7-o-glucoside, apigenin, quercetin, eriodictyol-7-o-glucuronide, 8-prenylnaringenin, taxifolin, catechin, apigenin 6,8-di-c-glucoside [28,29]
Triterpenic acid	Oleanolic acid, betulinic acid, ursolic acid, corosolic acid [29]
Monoterpene hydrocarbon	Tricyclene, $\alpha$ -Pinene, <i>o</i> -cymene, camphene, sabinene, $\beta$ -pinene, $\beta$ -cymene, $\alpha$ -phellandrene, myrcene, thymol, $\alpha$ -terpinene, <i>p</i> -cymene, limonene, $\alpha$ -thujene, terpinene, thymol acetate [30,31]
Monoterpene oxidized	1,8-Cineole, linalool, $\delta^3$ -carene, terpenolene, $\alpha$ -thujone, cis-sabinene hydrate, camphor, $\alpha$ -campholene, sabinene hydrate, trans-sabinene hydrate, borneol, isoborneol, <i>p</i> -mentha-3,8-diene, terpinen-4-ol, cis-sabinol, <i>p</i> -cymen-8-ol, cis-chrysanthenol, carvacrol acetate, geranial, methyl carvacrol, methylthymol, thymol methyl ether, menthol, nerol, carvone, fenchyl alcohol, carvacrol methyl ether, thymoquinone, geraniol, bornyl acetate, $\beta$ -citronellol, carvacrol, geranyl acetate, linalyl acetate, terpinyl acetate [30,31]
Sesquiterpene hydrocarbons	Copaene, $\beta$ -bourbonene, $\alpha$ -elinene, $\gamma$ -cadinene, calamenene, $\delta$ -cadinene, $\alpha$ -cadinene, germacrene D, -abolene, epi-sesquiphellandrene, bicyclogermacrene, valencene, $\alpha$ -bisabolol, cis-bisabolene, $\alpha$ -cymene, -cymene, $\beta$ -ocinene, $\alpha$ -ylangene, $\beta$ -longipinene, longifolene, cubebene, $\beta$ -elemene, muurolene, amorphene, aromadendrene, $\alpha$ -humulene, allo-aromadendrene, (E)- $\beta$ -farnesene, $\beta$ -caryophyllene, isodene, iso-caryophyllene, trans-caryophyllene, spathulenol, elemol, trans-nerolidol,

caryophyllene oxide, cadrol,  $\alpha$ -campholene aldehyde, linalylpropanoate, isopulegone, tetradecanal, trans-carbyl propionate, ethyl cinamate, geranyl butyrate, bicyclgerma, piperitol, cadrol, crene, p-mentha-1-(7),8-diene, isoborneol, cubebene, longyclene, longifolene, isovaleric acid,

cis-dihydrocarvone, p-cymene-2,5-diol,  $\beta$ -bisabolene, heptanoic acid, hexadecanoic acid, 2-nonanone, caffeic acid ethylester [30]

Others

1-octen-3-ol, 3-octanol, 3-octanone, 3-penten-2-ol, 4-methyl-2-pentanol, 6-methyl-5-hepten-2-one [31]

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Jammu and Kashmir is a state in India. Aziz et al. [24] reported that the essential oil of *T. serpyllum* contained safrole, cyclohexane, and spathulenol. Additionally, higher levels of thymol (58.25%), transgeraniol (55.93%), lavandulyl acetate (28.51%), nerol (2.76%), and E-citral (2.58%) were discovered by the Northern Kazakhstani researchers. Trans-geraniol, lavandulyl acetate, nerol, and e-citral were identified as the main constituents of *T. serpyllum* essential oil from different regions of Southern Italy. [25] Due to their high concentrations and safety, as confirmed by the World Health Organization's food additive guidelines, thymol and carvacrol are well-known food additives that draw a lot of business. [26] Thymol and *T. serpyllum* plants may be used as spices, under the FDA standard

([www.fda.gov/downloads/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/UCM142644.pdf](http://www.fda.gov/downloads/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/UCM142644.pdf); accessed July 5, 2019). However, nonvolatile secondary metabolites of *T. serpyllum*, including rosmarinic acid, ursolic acid, and oleanolic acid, have attracted a lot of attention. [27] While Table 1 lists the many phytoconstituents present in *T. serpyllum* essential, Figures 1-4 illustrate the two-dimensional structures of phytochemicals.

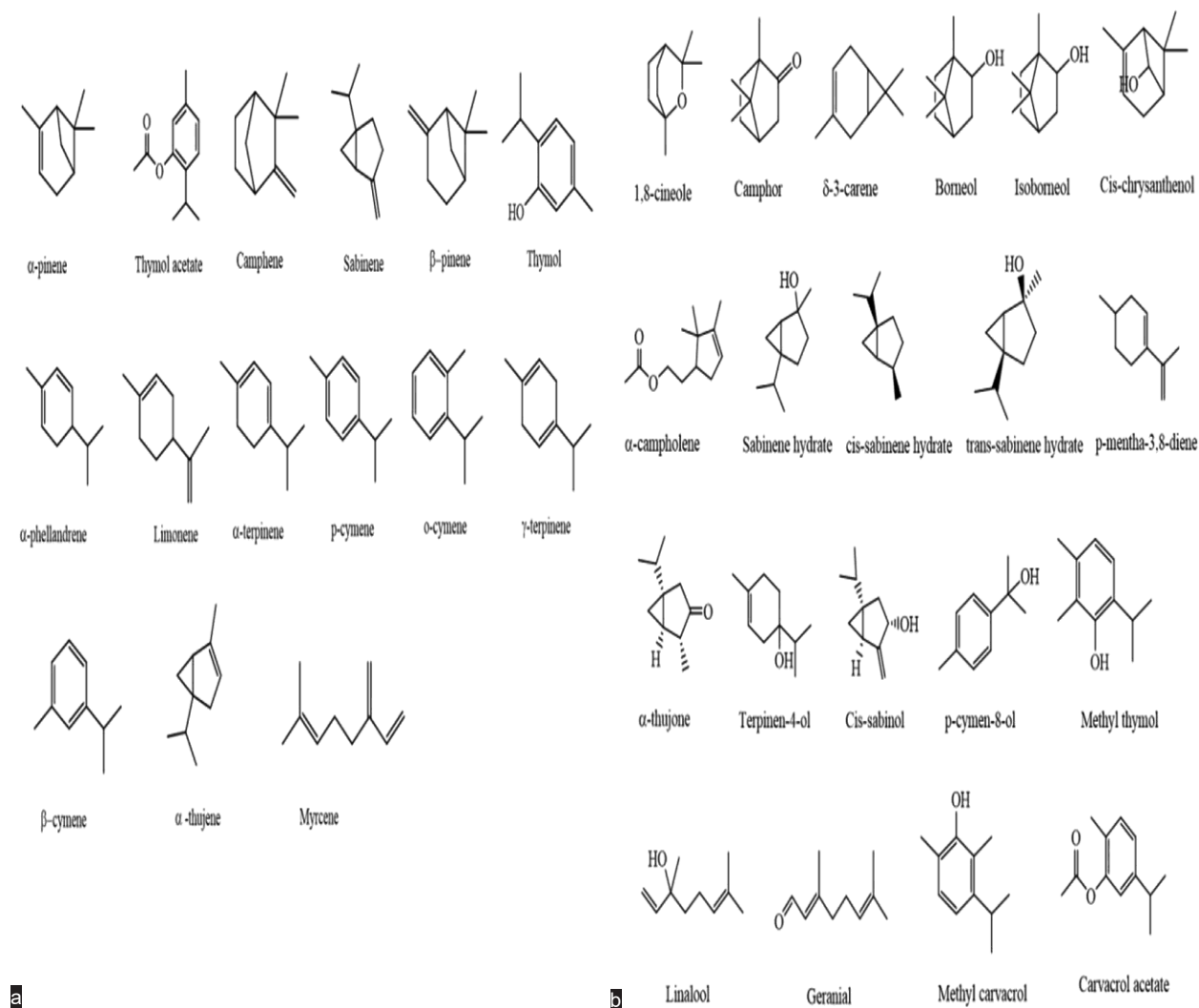
### **Thymus serpyllum: A Pharmacological Tool**

Numerous studies have shown the diverse biological activity of *T. serpyllum* extracts and compounds, which include anti-inflammatory, anti-bacterial, anti-oxidative, and anti-cancer effects. Furthermore, recent studies have investigated the interactions between carvacrol and thymol and the COVID-19 nucleocapsid phosphoprotein. [32] Twenty-five phytochemicals of *T. serpyllum* essential oil showed inadequate binding to SARS coronavirus 2 (PDB ID: 6VYO), according to another study. [32] However, these in silico researches may be further validated by appropriate in vitro and in vivo studies. a some of *T. serpyllum*'s important biological applications.

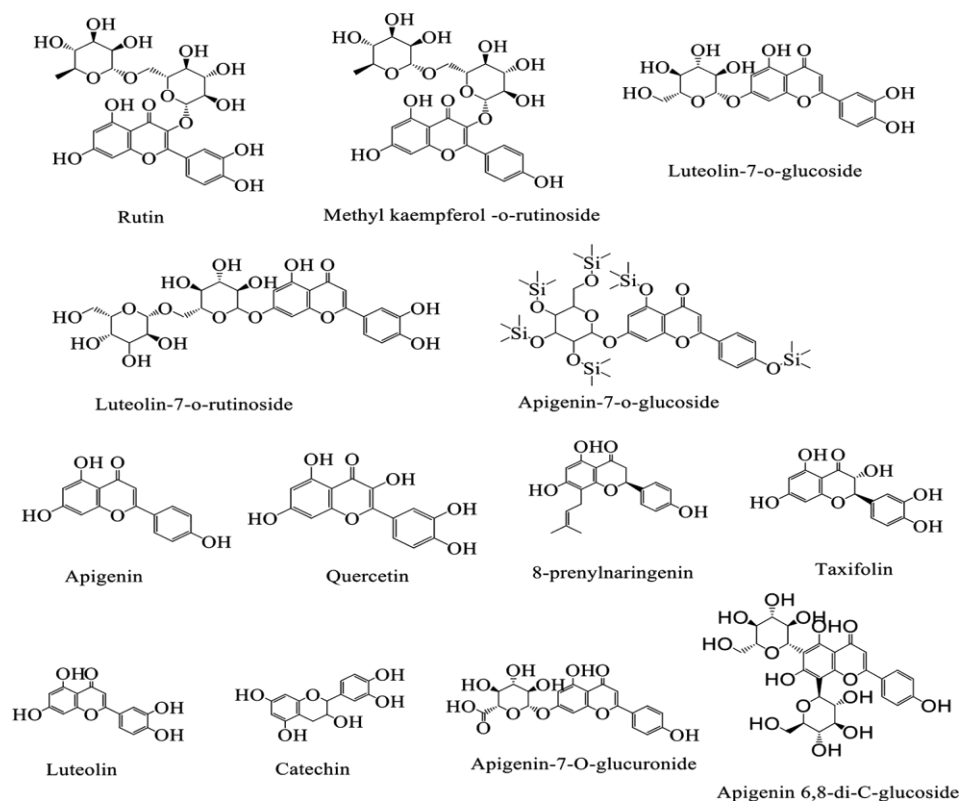
### **Features of an antioxidant**

The antioxidant potential of *T. serpyllum* extracts was examined in many studies. Using the 2,2-diphenylpicrylhydrazyl (DPPH) approach, Kulisic et al. [33] demonstrated the antioxidant activity of the essential oil of *T. serpyllum* flower heads and stalks, with an IC50

of around  $0.40 \pm 0.05$  g/L. The ethanolic and aqueous extracts of *T. serpyllum* also demonstrated its antioxidant properties; the DPPH test findings showed IC50 values of  $13.2 \pm 0.3$  g/ml and  $31.6 \pm 0.8$  g/ml, respectively. Page 34 Furthermore, Mihailovic-Stanojevic used the ABTS assay ( $IC_{50} = 8.60 \pm 0.05$  mM Trolox) and the Ferric ion reducing antioxidant power (FRAP) test ( $IC_{50} = 16.59 \pm 1.06$  mM Fe (II) equivalents) to describe the antioxidant activity of a water extract of *T. serpyllum*.

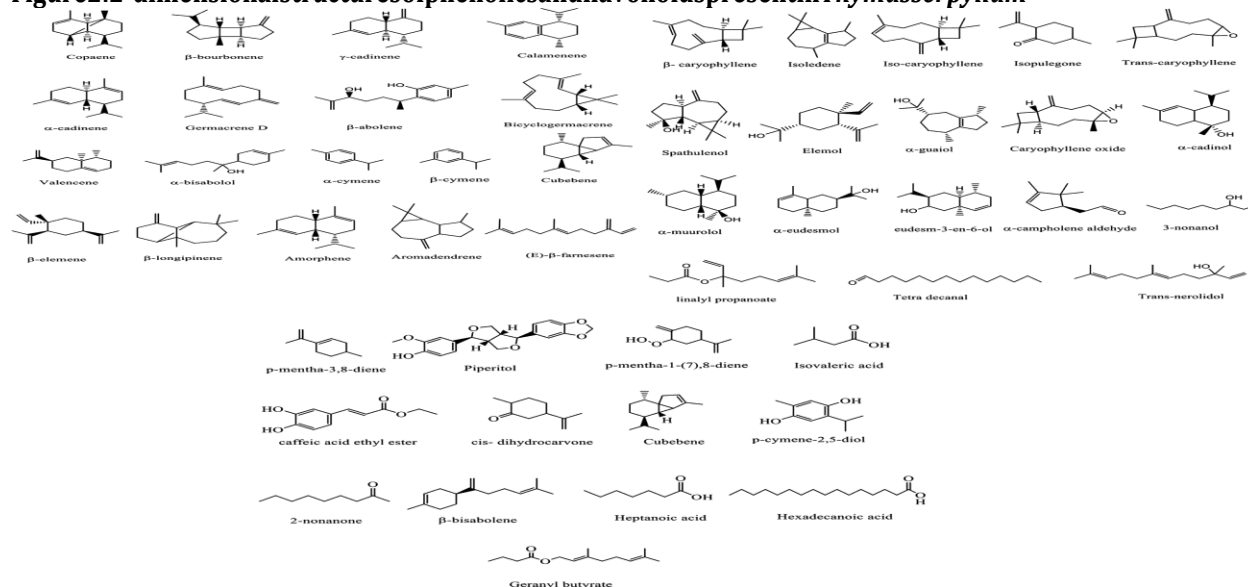


**Figure1:**2-dimensionalstructures*Thymusserpyllum*phytocompounds:(a)Monoterpenehydrocarbonspresentin*Thym*



*usserpyllum*and(b)Oxidized

**Figure2:**2-dimensionalstructuresofphenolicsandflavonoidspresentin*Thymusserpyllum*



**Figure3:**2-dimensionalstructuresofsesquiterpenehydrocarbonspresentin*Thymusserpyllum*

with others.The free radical scavenging activity was shown with an IC50 of 3.00-3.17 mg/mL in *T. serpyllum* extracts that were aided by ultrasound (22). Antioxidant activity of

T. serpyllum EO isolated from entire plants was also shown by Nikolic et al. [15] using the DPPH technique (IC50 0.96 g/mL). The phenolic concentration, together with the rosmarinic and caffeic acids [22], gave this plant its antioxidant efficacy [36]

### Impact on microbes

Numerous studies have shown the antibacterial capabilities of essential oils and extracts from various *T. serpyllum* species. [15, 28, 30, 37–40] The antibacterial and antifungal activity is presented in Table 1. The study found that *T. serpyllum*'s antibacterial qualities are due to its thymol and carvacrol. [15] Curcumin and *T. serpyllum* methanolic and ethyl acetate extracts were discovered to possess antifungal and antibacterial qualities (Farrukh et al.). *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli*, *Aspergillus fumigatus*, *Candida albicans*, *Candida parapsilosis*, and *Aspergillus niger* were among the bacteria and yeasts that were tested against these characteristics. The MIC, or minimal inhibitory concentration, varied between 2000 and 4000 g/ml. [42] After 30 minutes of exposure, *T. serpyllum* EO's bactericidal effectiveness against every strain tested was 100%. According to Varga et al. [28], *T. serpyllum*'s essential oil contains 25.8% carvacrol and 32.2% thymol. Both diluted and concentrated (100%) versions of the EO have been tried.

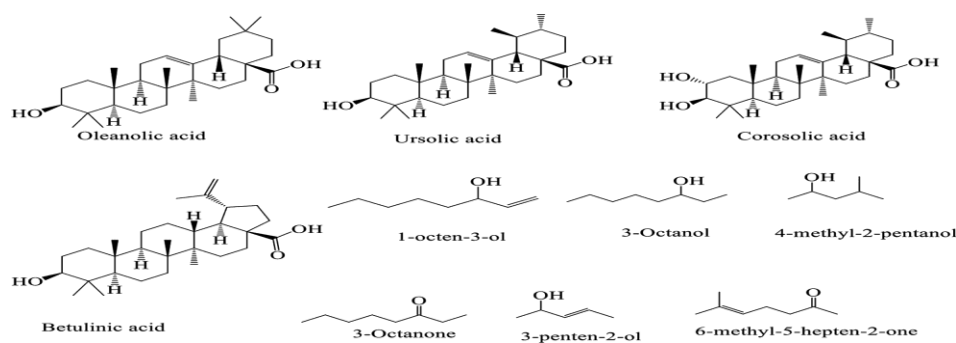


Figure 4: 2-dimensional structure of triterpenic acids and other phytochemicals in *Thymus serpyllum*

Half of the samples examined for *Saccharomyces cerevisiae*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, *Listeria innocua*, *Candida albicans*, and *Cronobacter akazakii* showed 100% cell death in an agar well diffusion experiment. Verma et al. evaluated the chemical and bactericidal properties of *T. serpyllum* L.'s primary and secondary essential oils [30]. The secondary EOs of *T. serpyllum* included 92.5% phenolic phytochemicals, compared to 42.1% in the primary EO. Interestingly, the secondary EO demonstrated antibacterial solid activity against every strain of bacteria and fungus tested, with ferric ion reducing antioxidant capabilities (ZOI) ranging from 20 to >35 mm and MIC values ranging from 1/3200 to 1/6400. Ouedrhiri et al. [38] examined the combined effects of essential oils of wild thyme (*T. serpyllum*), oregano (*Origanum compactum*), and marjoram (*O. majorana*). They discovered that the combination had a good synergistic effect against *S.*

aureus bacteria ( $P < 0.001$ ). However, combining wild thyme essential oil with oregano had a synergistic impact against *S. aureus* and *E. coli*. Salaria et al. recently reported the synergistic potential of *T. serpyllum* essential oil (EO) with antifungal medications to treat candida infections [40]. The effectiveness of silver nitrate nanoparticles (AgNPs) made from water-based *T. serpyllum* extracts against bacteria was discovered by Erci and Torlak [39]. In the presence of AgNPs, *B. cereus* was unable to traverse a  $12.23 \pm 0.54$  mm region. In contrast, the inhibition zone measured  $13.86 \pm 0.58$  mm when treated against *S. aureus*. Using AgNPs, the diameters of the inhibitory zones for *S. typhimurium* and *E. coli* were  $10.60 \pm 0.53$  mm and  $9.98 \pm 1.02$  mm, respectively. These studies clearly showed the therapeutic benefits of wild thyme extracts and essential oils in the fight against microbial infections.

### Impact on inflammation reduction

By inhibiting the synthesis of interleukin-6 and Src tyrosine kinase in the splenocytes of Balb/c mice, Kindl et al. investigated *T. serpyllum*'s anti-inflammatory response in vitro.[44] Unlike polyphenols such as luteolin ( $IC_{50} = 8 \mu\text{M}$ ), luteolin-7-O-glucoside ( $IC_{50} = 40 \mu\text{M}$ ), and rosmarinic acid, *T. serpyllum* methanolic extract showed a modest dose-dependent inhibition of Src kinase ( $IC_{50} = 115-167 \mu\text{g/ml}$ ). Both acid ( $IC_{50} = 61 \mu\text{M}$  at  $0.01 \mu\text{M}$ ) and staurosporine (a Src tyrosine kinase inhibitor) have  $IC_{50} = 0.005 \mu\text{g/ml}$ . The MTS assay was also used to evaluate the cytotoxic properties of polyphenols and *T. serpyllum* extract. The addition of *T. serpyllum* extract and polyphenols ( $200-0.8 \mu\text{g/ml}$ ) reduced the production of IL-6. At a high concentration of *T. serpyllum* ( $200 \mu\text{g/ml}$ ), the cytokine production in the treated cells was reduced by more than 95%, and the  $IC_{50}$  value for IL-6 production was found to be  $49.5 \pm 9.6 \mu\text{g/ml}$ . Using *T. serpyllum* extract ( $200-0.8 \mu\text{g/ml}$ ) showed no signs of cytotoxicity.

### Activity against cancer and cytotoxicity

The cytotoxic and anticancer properties of *Thymus sp.* solvent extracts, essential oils, and phytochemicals have been shown in several studies. The cytotoxic and Hep-2 activity against a mouse leukemia model was shown by Jaafari et al. [45]. In a study conducted by Nikolic et al., [15] it was shown that *T. serpyllum* essential exhibited anticancer properties against MCF-7, NCI-H460, HCT-15, HeLa, and others. The essential *T. serpyllum* showed a 50% inhibition of growth ( $GI_{50} = 52.69 \pm 3.28 \mu\text{g/ml}$ ),  $GI_{50} = 37.17 \pm 3.18 \mu\text{g/ml}$ ,  $GI_{50} = 7.02 \pm 0.07 \pm 0.07 \pm 0.07 \mu\text{g/ml}$ , and  $GI_{50} = 17.71 \pm 3.23 \mu\text{g/ml}$ .

**Table 2: Antimicrobial activity of extracts and *Thymus serpyllum* essential oil against different bacterial and fungal species**

Part used	Extracts/EO	Method	Tested strains	Key results
Aerial parts	EO	Agar well diffusion	<i>K.pneumoniae</i> <i>P.aeruginosa</i> <i>E. coli</i> <i>S.aureus</i> <i>B. subtilis</i>	15–40mm, 100% bactericidal after 30min exposure. Ineffective against <i>P.aeruginosa</i> [43]
Aerial part	Ethanol, butanol, methanol, hexane, ethyl-acetate, and aqueous extracts	Microdilution method	<i>E.coli</i> , <i>P.aeruginosa</i> , <i>S.aureus</i> , <i>S.epidermidis</i> , <i>C.albicans</i> , <i>C.parapsilosis</i> <i>A. fumigatus</i> <i>A.niger</i>	Only ethyl-acetate and methanolic extract exhibited significant activity against all tested bacteria and fungi, displaying MIC values ranging from 2000–4000 µg/mL [42]
Whole plant	EO	Microdilution method	<i>Ochratoxin</i> producing strains: <i>A.ochraceus</i> , <i>A.ochraceus</i> , <i>A.carbonarius</i> , and <i>A.niger</i>	MIC ranged between 0.625 and 2.5 µL/mL [37]
Aerial parts	EO	Agar diffusion method	<i>P.aeruginosa</i> , <i>C.sakazakii</i> , <i>L.innocua</i> and <i>S.pyogenes</i> , <i>C.albicans</i> , <i>S.cerevisiae</i>	Complete inhibition of the growth of all these strains by 50% and 100% EO [40]
Aerial parts	Primary EO and secondary EO	Disk diffusion method and microdilution method	<i>S.aureus</i> , <i>S.epidermidis</i> , <i>E.faecalis</i> , <i>S.mutans</i> , <i>E.aerogenes</i> , <i>K.pneumoniae</i> and pathogenic fungi: <i>C.neoformans</i> and <i>C.albicans</i>	Φ-20–>35mm MIC ranged between 1/3200 and 1/6400 [30]
Aerial parts	EO of <i>T.serpyllum</i> in combination with EO of <i>O.compactum</i> (oregano), and <i>O.majorana</i> (marjoram)	of <i>T.serpyllum</i> Microdilution method and checkerboard assay	<i>B.subtilis</i> , <i>S.aureus</i> and <i>E.coli</i>	Antibacterial synergistic effect was observed with combination of EO of <i>T.serpyllum</i> with EO of marjoram against <i>S.aureus</i> , while combination of EO of oregano and EO of <i>T.serpyllum</i> showed significant synergistic activity against <i>S.aureus</i> and <i>E.coli</i> [38]
Aerial parts	EO of <i>T.serpyllum</i> in combination with EO of <i>O.majorana</i> (marjoram)	of <i>T.serpyllum</i> Microdilution method and checkerboard assay	<i>E.coli</i> and <i>S.aureus</i>	Synergistic antibacterial effect of EO of <i>O.majorana</i> and <i>T.serpyllum</i> with FIC index of 0.725 [38]
Leaves	AgNPs of aqueous extracts	Agar well diffusion	<i>B. cereus</i> <i>S.aureus</i>	Φ-12.23±0.54mm Φ-13.86±0.58mm

<i>E. coli</i>	$\Phi$ -9.98±1.02mm
<i>S. typhimurium</i>	$\Phi$ -10.60±0.53mm

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*K. pneumoniae*=*Klebsiella pneumoniae*, *P. aeruginosa*=*Pseudomonas aeruginosa*, *E. coli*=*Escherichia coli*, *S. aureus*=*Staphylococcus aureus*, *B. subtilis*=*Bacillus subtilis*, *S. epidermidis*=*Staphylococcus epidermidis*, *C. albicans*=*Candida albicans*, *C. parapsilosis*=*Candida parapsilosis*, *A. fumigatus*=*Aspergillus fumigatus*,

*A. niger*=*Aspergillus niger*, *A. ochraceus*=*Aspergillus ochraceus*, *A. carbonarius*=*Aspergillus carbonarius*, *C. sakazakii*=*Cronobacter sakazakii*, *L. innocua*=*Listeria innocua*, *S. pyogenes*=*Streptococcus pyogenes*, *S. cerevisiae*=*Saccharomyces cerevisiae*, *E. faecalis*=*Enterococcus faecalis*, *S. mutans*=*Streptococcus mutans*,

*E. aerogenes*=*Enterobacter aerogenes*, *C. neoformans*=*Cryptococcus neoformans*, *B. cereus*=*Bacillus cereus*, *S. typhimurium*=*Salmonella typhimurium*,

*T. serpyllum*=*Thymus serpyllum*, *O. majorana*=*Origanum majorana*, *O. compactum*=*Origanum compactum*,  $\Phi$ =Zone of inhibition in mm, MIC=Minimum inhibitory concentration, FIC=Fractional inhibitory concentration, EO=Essential oil, AgNPs=Silver nitrate nanoparticles

The half-life of the HepG2 gene is about  $34.96 \pm 2.90 \mu\text{g/ml}$ . It was shown that *T. serpyllum* EO was cytotoxic to the MCF-7, LNCaP, and NIH3T3 fibroblast cell lines. According to research, compounds such as the sesquiterpene caryophyllene are partly responsible for the EO's antiproliferative effects.[46] Lazarevic et al. [47] demonstrated that the antiproliferative activity of *T. serpyllum* EO was limited when applied to oral squamous cell carcinoma cultures and the SCC-25 cell line. Against MCF-7, LNCaP, and NIH-3T3 cell lines, the oil showed similar effects with IC50 values of 95.8, 105.0, and 105.0 mg/ml, respectively.[46] According to Berdowska et al. [48], the aqueous extract from *T. serpyllum* was evaluated for cytotoxicity against both wild-type MCF-7 (wt) cells and cancer cells (MCF-7/Adr). Thymol, a major constituent of *T. serpyllum* essential oil, has been shown to have antiproliferative action in acute promyelotic leukaemia (HL-60) cells.[49] Thymol and carvacrol demonstrated dose-dependent cytotoxicity against colorectal cancer, breast cancer, and the P815 mastocytoma cell proliferation model. Similarly, Jaafari et al. found a correlation between the carvacrol concentration and the cytotoxic activity of *T. serpyllum* EO.[45] Therefore, research into the potential therapeutic benefits of thyme essential oils and phytochemicals in the treatment of cancer in humans is feasible.

### Activity against malaria

Researchers Hussain et al.[31] used an antihembiocrystallization test to look at the antimalarial effects of *T. serpyllum* essential oil. The antimalarial activity of *T. serpyllum* oil was found to be 46.1% at a concentration of 10 mg/ml. The antimalarial potential of *T. serpyllum* EO and its components has to be further investigated in in-depth investigations using different doses and model systems.

### Safety Investigations

The US Food and Drug Administration has declared thyme "food safe" when consumed in the authorised therapeutic dosages. For six months, mice were able to breathe in thymol hydrofluoroalkane at concentrations ranging from 0.1% to 0.5% without suffering any adverse effects on their lungs or respiratory systems, according to research by Xie et al. [50]. However, there is little information on the negative effects of administering T. serpyllum EO. It is crucial to do thorough research that focus on the toxicity features using various doses and model systems in order to better understand the safety profile of T. serpyllum EO.

### **Alternative Uses of Biotechnology**

#### **Activity of food preservatives**

By preventing the growth of food microbes, the phytochemicals found in T. serpyllum EO, such as thymol, carvacrol, terpenoids, and others, have been shown to be beneficial in enhancing food safety and quality. These phytochemicals either prevent bacteria from destroying food products or serve as antimicrobials to fight food-borne illnesses.[51] Wild thyme is an essential medicinal plant due to its antibacterial and antioxidant properties.[15] Cakes fermented with T. serpyllum EO were reported to help prevent fungal infections by Hagan et al. [52].

#### **Pest control ability**

Thymol, the main active component of T. serpyllum's essential oil, has been shown to be resistant against common housefly (*Musca domestica*) larvae and pupae. According to recent data, T. serpyllum thymol may result in contact and fumigant toxic responses. Both thymol and T. serpyllum EO are toxic to housefly larvae and pupae, according to these findings, which may make them effective strategies for controlling housefly populations. Szczepanik et al. have previously documented the insecticidal properties of T. vulgare's carvacrol and thymol [53]. Regrettably, no research has yet been done on T. serpyllum EO's insecticidal properties. However, no prior research has been done on T. serpyllum EO's insecticidal effects.

#### **Environmental protection**

T. serpyllum has a variety of pharmacological actions. In an effort to develop novel herbal treatments, T. serpyllum has aroused the interest of both scientists and the general population.

T. serpyllum is primarily found in North American, East African, Nepalese, Pakistanese, Indian, and Chinese cuisines.[8] Due of its limited availability and high medicinal importance, researchers are trying to cultivate T. serpyllum in vitro utilising tissue culture techniques. In order to meet the industrial need for this herb, Dear Sir/Madam Rajan Rolta, Advisor at Tridev Aushadhi Utpadhan Society, Rohal, Chirgaon, District Shimla, Himachal Pradesh, India, is also attempting to produce T. serpyllum in its natural environment. In Rohal, Chirgaon, District Shimla, Himachal Pradesh, India, an adviser at the TridevAushadhiUtpadhan Society is another person working to address the industrial need for T. serpyllum.

### **Considerations for the Future and Final Thoughts**

*T. serpyllum* aerial portions have been utilised to treat urinary tract, stomach, and esophageal infections. Due to its pharmacological relevance, essential oils from this species have gained popularity in modern medicine. Growth stage, location, and harvesting season are among of the factors that determine the phytochemical composition and production of *T. serpyllum* EO, which is important for industrial, cosmetic, and medical purposes. According to recent research, *T. serpyllum* essential oil exhibits potent antioxidant and antibacterial properties. However, further study is needed to determine if thymol, carvacrol, and other ingredients may be used to combat cytotoxicity, inflammation, malaria, and hypertension. The food sector finds the plant appealing due to its potential use as a nutritional supplement and antioxidant, while the pharmaceutical industry finds it beneficial due to its diverse pharmacological properties.

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