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## Herba Thymi

### Definition

Herba Thymi is the dried leaves and flowering tops of *Thymus vulgaris* L. or of *Thymus zygis* L. (Lamiaceae) (1, 2).

### Synonyms

Lamiaceae are also known as Labiatae.

### Selected vernacular names

Common thyme, farigola, garden thyme, herba timi, herba thymi, mother of thyme, red thyme, rubbed thyme, ten, thick leaf thyme, thym, Thymian, thyme, time, timi, tomillo, za'ater (1, 3–7).

### Description

An aromatic perennial sub-shrub, 20–30 cm in height, with ascending, quadrangular, greyish brown to purplish brown lignified and twisted stems bearing oblong-lanceolate to ovate-lanceolate greyish green leaves that are pubescent on the lower surface. The flowers have a pubescent calyx and a bilobate, pinkish or whitish, corolla and are borne in verticillasters. The fruit consists of 4 brown ovoid nutlets (5, 8, 9).

### Plant material of interest: dried leaves and flowering tops

#### *General appearance*

#### *Thymus vulgaris*

Leaf 4–12 mm long and up to 3 mm wide; it is sessile or has a very short petiole. The lamina is tough, entire, lanceolate to ovate, covered on both surfaces by a grey to greenish grey indumentum; the edges are markedly rolled up towards the abaxial surface. The midrib is depressed on the adaxial surface and is very prominent on the abaxial surface. The calyx is green, often with violet spots, and is tubular; at the end are 2 lips of which the upper is bent back and has 3 lobes on its end; the lower is longer and has 2 hairy teeth. After flowering, the calyx tube is closed by a crown of long, stiff hairs. The corolla, about twice as long as the calyx, is usually brownish in the dry state and is slightly bilabiate (1).

### ***Thymus zygis***

Leaf 1.7–6.5 mm long and 0.4–1.2 mm wide; it is acicular to linear-lanceolate and the edges are markedly rolled toward the abaxial surface. Both surfaces of the lamina are green to greenish grey and the midrib is sometimes violet; the edges, in particular at the base, have long, white hairs. The dried flowers are very similar to those of *Thymus vulgaris* (1).

### **Organoleptic properties**

Odour and taste aromatic (1–3, 5).

### **Microscopic characteristics**

In leaf upper epidermis, cells tangentially elongated in transverse section with a thick cuticle and few stomata, somewhat polygonal in surface section with beaded vertical walls and striated cuticle, the stoma being at a right angle to the 2 parallel neighbouring cells. Numerous unicellular, non-glandular hairs up to 30 µm in length with papillose wall and apical cell, straight, or pointed, curved, or hooked. Numerous glandular hairs of two kinds, one with a short stalk embedded in the epidermal layer and a unicellular head, the other with an 8- to 12-celled head and no stalk. Palisade parenchyma of 2 layers of columnar cells containing many chloroplastids; occasionally an interrupted third layer is present. Spongy parenchyma of about 6 layers of irregular-shaped chlorenchyma cells and intercellular air-spaces (5).

### **Powdered plant material**

Grey-green to greenish brown powder; leaf fragments, epidermal cells prolonged into unicellular pointed, papillose trichomes, 60 µm long; trichomes of the lower surface uniseriate, 2–3 celled, sharp pointed, up to 300 µm in diameter, numerous labiate trichomes with 8–12 secretory cells up to 80 µm in diameter; broadly elliptical caryophyllaceous stomata. Six- to 8-celled uniseriate trichomes from the calyx up to 400 µm long; pollen grains spherical; pericyclic fibres of the stem (1–3).

### **Geographical distribution**

Indigenous to southern Europe. It is a pan-European species that is cultivated in Europe, the United States of America and other parts of the world (2, 3, 5, 10).

### **General identity tests**

Macroscopic and microscopic examinations (1, 5), and chemical and thin-layer chromatography tests for the characteristic volatile oil constituent, thymol [1].

## **Purity tests**

### **Microbiology**

The test for *Salmonella* spp. in Herba Thymi products should be negative. The maximum acceptable limits of other microorganisms are as follows (11–13). For preparation of infusion: aerobic bacteria—not more than  $10^7$ /g; fungi—not more than  $10^5$ /g; *Escherichia coli*—not more than  $10^2$ /g. Preparations for oral use: aerobic bacteria—not more than  $10^5$ /ml; fungi—not more than  $10^4$ /ml; enterobacteria and certain Gram-negative bacteria—not more than  $10^3$ /ml; *Escherichia coli*—0/ml.

### **Foreign organic matter**

Not more than 10% of stem having a diameter up to 1 mm. Leaves with long trichomes at their base and with weakly pubescent other parts not allowed (1). The leaves and flowering tops of *Origanum creticum* or *O. dictamnus* are considered adulterants (3, 5). Other foreign organic matter, not more than 2% (2).

### **Total ash**

Not more than 15% (1).

### **Acid-insoluble ash**

Not more than 2.0% (1).

### **Moisture**

Not more than 10% (1).

### **Pesticide residues**

To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin in Herba Thymi is not more than 0.05 mg/kg (13). For other pesticides, see WHO guidelines on quality control methods for medicinal plants (11) and guidelines for predicting dietary intake of pesticide residues (14).

### **Heavy metals**

Recommended lead and cadmium levels are not more than 10 and 0.3 mg/kg, respectively, in the final dosage form of the plant material (11).

### **Radioactive residues**

For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants (11).

### **Other purity tests**

Chemical, alcohol-soluble extractive, and water-soluble extractive tests to be established in accordance with national requirements.

## Chemical assays

Herba Thymi contains not less than 1.0% volatile oil (2, 3), and not less than 0.5% phenols. Volatile oil is quantitatively determined by water/steam distillation (1), and the percentage content of phenols expressed as thymol is determined by spectrophotometric analysis (1). Thin-layer chromatographic analysis is used for thymol, carvacrol, and linalool (1, 15).

## Major chemical constituents

Herba Thymi contains about 2.5% but not less than 1.0% of volatile oil. The composition of the volatile oil fluctuates depending on the chemotype under consideration. The principal components of Herba Thymi are thymol [1] and carvacrol [2] (up to 64% of oil), along with linalool, *p*-cymol, cymene, thymene,  $\alpha$ -pinene, apigenin, luteolin, and 6-hydroxyluteolin glycosides, as well as di-, tri- and tetramethoxylated flavones, all substituted in the 6-position (for example 5,4'-dihydroxy-6,7-dimethoxyflavone, 5,4'-dihydroxy-6,7,3'-trimethoxyflavone and its 8-methoxylated derivative 5,6,4'-trihydroxy-7,8,3'-trimethoxyflavone) (1, 3–6, 9).



## Dosage forms

Dried herb for infusion, extract, and tincture (1).

## Medicinal uses

### *Uses supported by clinical data*

None.

### *Uses described in pharmacopoeias and in traditional systems of medicine*

Thyme extract has been used orally to treat dyspepsia and other gastrointestinal disturbances; coughs due to colds, bronchitis and pertussis; and laryngitis and tonsillitis (as a gargle). Topical applications of thyme extract have been used in the treatment of minor wounds, the common cold, disorders of the oral cavity, and as an antibacterial agent in oral hygiene (3, 5, 8, 15, 16). Both the essential oil and thymol are ingredients of a number of proprietary drugs including antiseptic and healing ointments, syrups for the treatment of respiratory disorders, and preparations for inhalation. Another species in the genus, *T. serpyllum* L., is used for the same indications (8).

**Uses described in folk medicine, not supported by experimental or clinical data**

As an emmenagogue, sedative, antiseptic, antipyretic, to control menstruation and cramps, and in the treatment of dermatitis (7).

**Pharmacology**

**Experimental pharmacology**

**Spasmolytic and antitussive activities**

The spasmolytic and antitussive activity of thyme has been most often attributed to the phenolic constituents thymol and carvacrol, which make up a large percentage of the volatile oil (17). Although these compounds have been shown to prevent contractions induced in the ileum and the trachea of the guinea-pig, by histamine, acetylcholine and other reagents, the concentration of phenolics in aqueous preparations of the drug is insufficient to account for this activity (18, 19). Experimental evidence suggests that the *in vitro* spasmolytic activity of thyme preparations is due to the presence of polymethoxyflavones (10). *In vitro* studies have shown that flavones and thyme extracts inhibit responses to agonists of specific receptors such as acetylcholine, histamine and L-norepinephrine, as well as agents whose actions do not require specific receptors, such as barium chloride (10). The flavones of thyme were found to act as non-competitive and non-specific antagonists (10); they were also shown to be Ca<sup>2+</sup> antagonists and musculotropic agents that act directly on smooth muscle (10).

**Expectorant and secretomotor activities**

Experimental evidence suggests that thyme oil has secretomotor activity (20). This activity has been associated with a saponin extract from *T. vulgaris* (21). Stimulation of ciliary movements in the pharynx mucosa of frogs treated with diluted solutions of thyme oil, thymol or carvacrol has also been reported (22). Furthermore, an increase in mucus secretion of the bronchi after treatment with thyme extracts has been observed (23).

**Antifungal and antibacterial activities**

*In vitro* studies have shown that both thyme essential oil and thymol have antifungal activity against a number of fungi, including *Cryptococcus neoformans*, *Aspergillus*, *Saprolegnia*, and *Zygorhynchus* species (24–27). Both the essential oil and thymol had antibacterial activity against *Salmonella typhimurium*, *Staphylococcus aureus*, *Escherichia coli*, and a number of other bacterial species (28, 29). As an antibiotic, thymol is 25 times as effective as phenol, but less toxic (30).

**Contraindications**

Pregnancy and lactation (See Precautions, below).

## Warnings

No information available.

## Precautions

### General

Patients with a known sensitivity to plants in the Lamiaceae (Labiatae) should contact their physician before using thyme preparations. Patients sensitive to birch pollen or celery may have a cross-sensitivity to thyme (31).

### *Carcinogenesis, mutagenesis, impairment of fertility*

Thyme essential oil did not have any mutagenic activity in the *Bacillus subtilis* rec-assay or the *Salmonella*/microsome reversion assay (32, 33). Recent investigations suggest that thyme extracts are antimutagenic (34) and that luteolin, a constituent of thyme, is a strong antimutagen against the dietary carcinogen Trp-P-2 (35).

### *Pregnancy: non-teratogenic effects*

The safety of Herba Thymi preparations during pregnancy or lactation has not been established. As a precautionary measure, the drug should not be used during pregnancy or lactation except on medical advice. However, widespread use of Herba Thymi has not resulted in any safety concerns.

### *Nursing mothers*

See Pregnancy: non-teratogenic effects, above.

### *Other precautions*

No information available concerning drug interactions, drug and laboratory test interactions, paediatric use, or teratogenic effects on pregnancy.

## Adverse reactions

Contact dermatitis has been reported. Patients sensitive to birch pollen or celery may have a cross-sensitivity to thyme (31).

## Posology

Adults and children from 1 year: 1–2g of the dried herb or the equivalent amount of fresh herb as an oral infusion several times a day (30, 36); children up to 1 year: 0.5–1 g (36). Fluid extract: dosage calculated according to the dosage of the herb (37). Tincture (1 : 10, 70% ethanol): 40 drops up to 3 times daily (38). Topical use: a 5% infusion as a gargle or mouth-wash (30, 38).

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