Volatile oils Containing Monocyclic Monoterpenes as Active Constituents

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PEPPERMINT (nane) MENTHAE FOLIUM

Mentha x piperita

Lamiaceae

The taxonomy of the *Mentha* genus is greatly complicated by the common occurence of hybrid species, polyploid species, and the abundance of morphological variations ; there are numerous forms, and from one to the next, the plants display gradual changes.
The species listed in European pharmacopoieas for its dried leaves is a hybrid of *Mentha aquatica* and *M. spicata*.

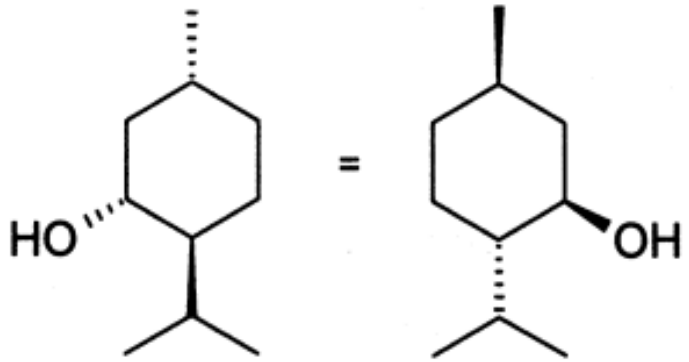
Mentha aquatica

Mentha spicata

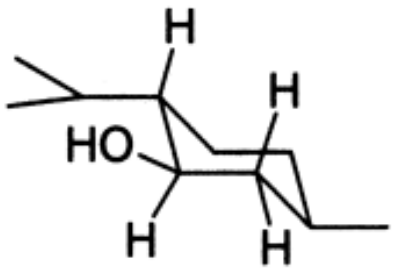
Both species grow wildly in Cyprus

Chemical Composition : The peppermint leaf contains many compounds; triterpenes, carotinoids, phenolic acids (up to 7%), and flavonoids, eriocitrin (eriodictyol 7-O-rutinoside) as the major compound. The essential oil represents from 10 to 30 ml/kg of the weight of the dried drug. Its composition varies as a function of multiple factors, intrinsic and extrinsic, including the cultivation conditions, climatic variations, and harvest time.

The chief constituent is always (-)-menthol (30-40%, sometimes more than 50%). It occurs alongside (-)-menthone (15-25%), (-)-menthyl acetate, (-)-menthofuran (sometimes absent), (+)-isomenthone, (+)-pulegone, (+)-neomenthol, (-)-piperitone and other compounds. (+)-pulegone is found in the young leaves, but disappears rapidly later on.

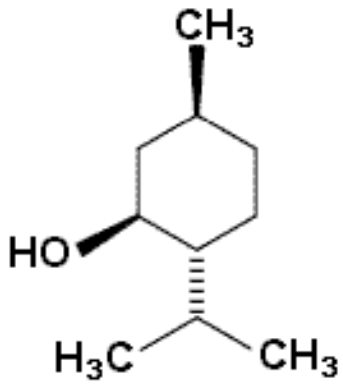


(-)-Menthol

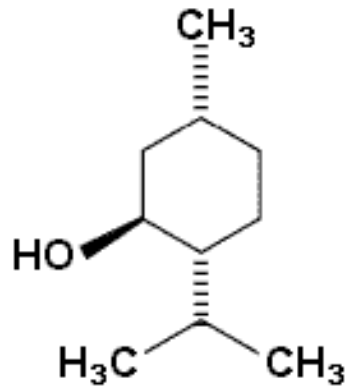


Chair form of
(-)-Menthol

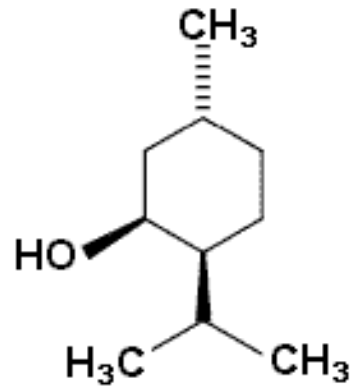
(+)-Menthol



(+)-Isomenthol



(+)-Neomenthol



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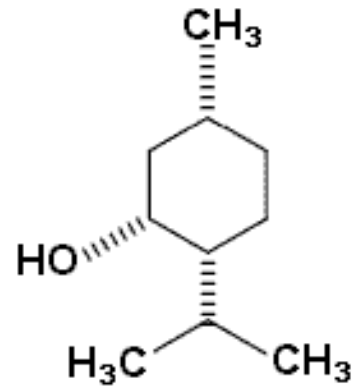
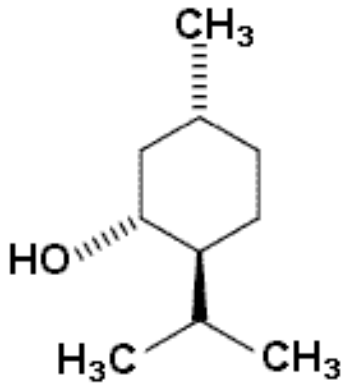
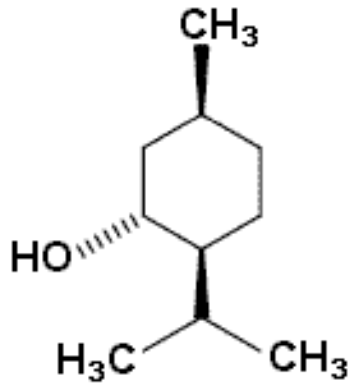
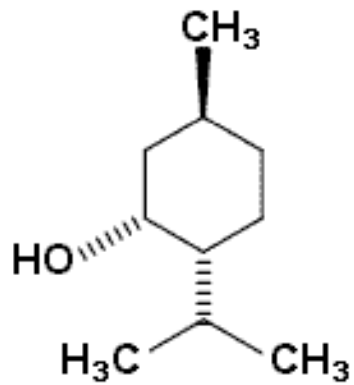




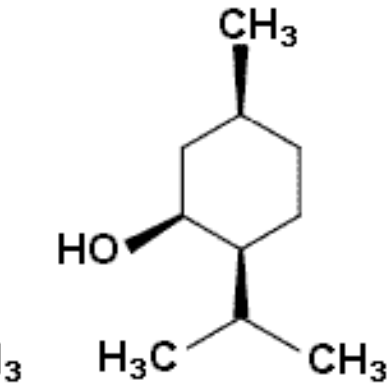
(-)-Menthol



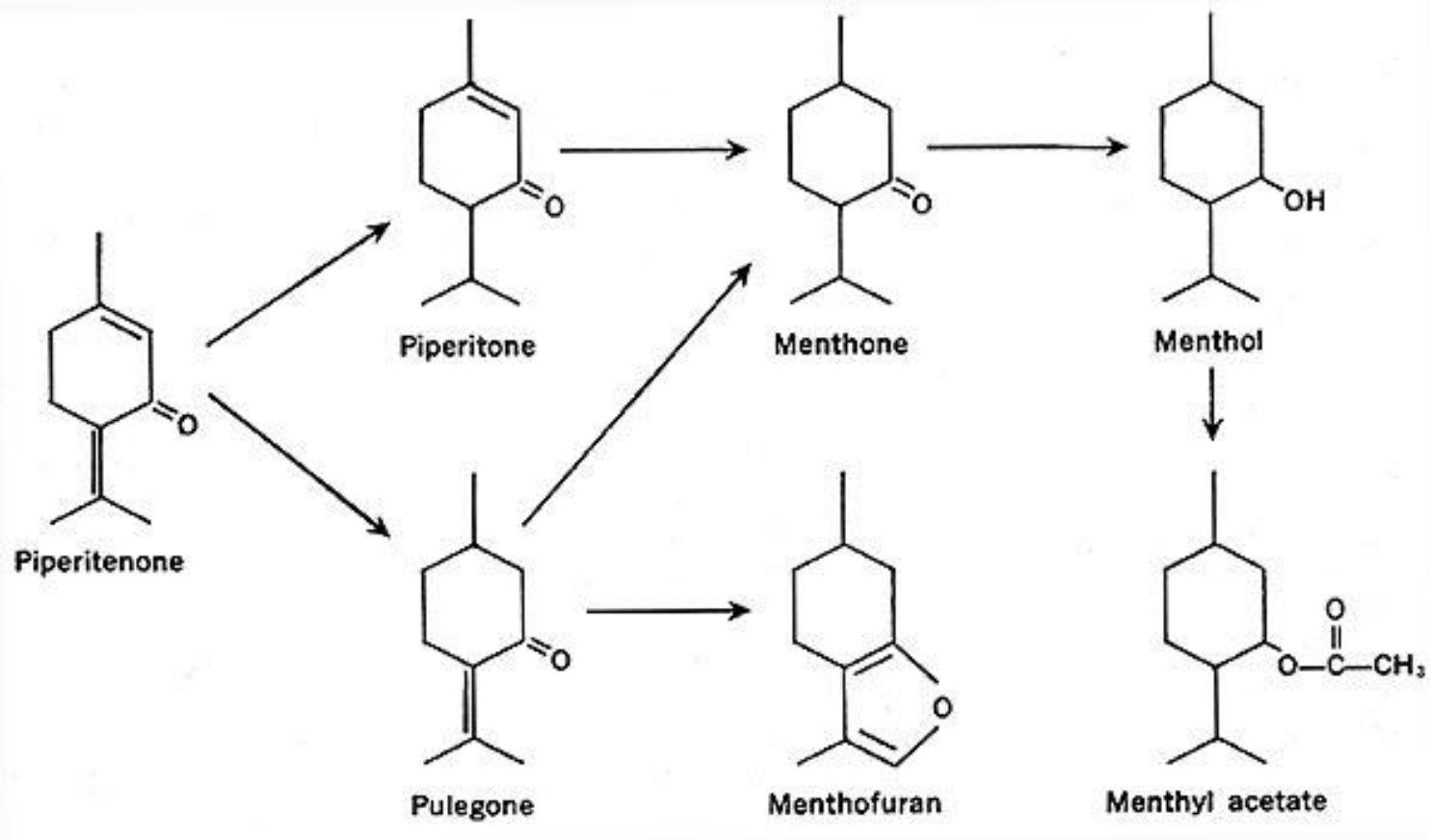
(-)-Isomenthol



(-)-Neomenthol



(-)-Neoisomenthol


Piperitenone
Piperitone
Pulegone
Menthone
Menthofuran
Menthol
Menthyl acetate
O
OH
O—C—CH₃

Uses : Menthol has been presented as a nasal decongestant for over a century : empirically, it has been abundantly demonsrated that this reflects a purely subjective sensation, linked to the cool sensation thought to be due to the stimulation of the nasal cavity thermoreceptors. Menthol vapors inhibit respiration (like cold air) and may cause very transient apnea in very young children. The risk is minimal, yet the direct application of peppermint oil or menthol on the nasal mucosa of very young children is discouraged. Application of menthol on the skin can induce a cold sensation, but menthol is neither antipruriginous nor analgesic.

The drug is devoid of toxicity, and is traditionally used orally for the symptomatic treatment of functional dyspepsia, including epigastric bloating, impaired digestion, eructations and flatulence. It is also traditionally used orally 1. as an adjunctive therapy for the painful component of functional dyspepsia, 2. to enhance urinary and digestive elimination functions, 3. in functional dyspepsia when it is attributed to a hepatic origin. Topically, it is traditionally used to relieve nasal congestion in the common cold, as an antalgic for diseases of the mouth, pharynx, or both.

The German Commission E monograph specifies that peppermint is used for gastrointestinal, gallbladder, and biliary tract spasms.

Mint Oils

Peppermint Oil (Menthae aetheroleum)

The essential oil must contain 30-55% menthol, 14-32% menthone, 1-9% menthofuran, 2.8-10% menthyl acetate, not more than 4% pulegone, and not more than 1% carvone. It must also contain 1-5% limonene, 3-5% cineole, and 1.5-10% isomethone; the cineole(%)/limonene(%) ratio must be more than 2.

Peppermint oil is probably not completely devoid of toxicity : administration of high doses (40-100 mg/kg) to rats induces histopathological changes in the brain. Menthone, like pulegone, produces similar effects.

Peppermint oil is used as a flavor in medications, as well as in pharmaceutical, hygiene, and other products. Food technology is the chief consumer for liquors, sodas, concentrated syrups, confectionery (candy, chewing gums, chocolates).

It should never be forgotten that peppermint oil, especially menthol, can cause severe allergic reactions in some individuals!!! Menthol allergy is not very seldom.

Spearmint Oil

The spearmint oil is “obtained by steam disttillation of the aerial parts recently harvested form *Mentha spicata*. The official oil must contain from 55 to 67% carvone and from 2 to 25% limonene. The concentration of the other constituents (menthone, isomenthone, menthol, menthofuran, menthyl acetate, and cineole) must be less than 2%; the level of pulegone must be not more than 0.5%.

Cornmint Oil :

Cornmint oil is partially dementholated essential oil of *Mentha arvensis* var. *piperascens* and var. *glabrata.* The average composition of the essential oil after menthol removal is outlined: menthol (30-45%), menthone (17-35%), isomenthone (5-13%), menthyl acetate (2-7%), and limonene (1.5-7%).

The essential oil of *Mentha arvensis* contains normally 70-80% menthol

Menthol

Only one of the stereoisomers of menthol is used, (-)-(1*R*,3*R*,4*S*) menthol, easier to refer as (-)-menthol, and sometimes called levorotatory menthol. Although it is the chief constituent of peppermint oil, menthol is generally not extracted from it. Several approaches are in use to obtain this monoterpenoid alcohol.

Mentholated essential Oils : Menthol is crystallized by freezing the essential oil of *Mentha arvensis,* which is very rich in menthol.
Menthol can also be obtained by semisynthesis or total synthesis.

Menthol is in pharmacy an ingredient of itch-relieveing creams and of preparations designed to decongest the upper respiratory tract in case of rhinitis; it is also an aroma. It is incorporated in oral hygiene products and shaving products.

Mentha pulegium, M. rotundifolia, M. longifolia and *M. aquatica* grow widespread in Turkey, but their esential oils contain menthol in very less amounts.

Mentha spicata *M. longifolia*

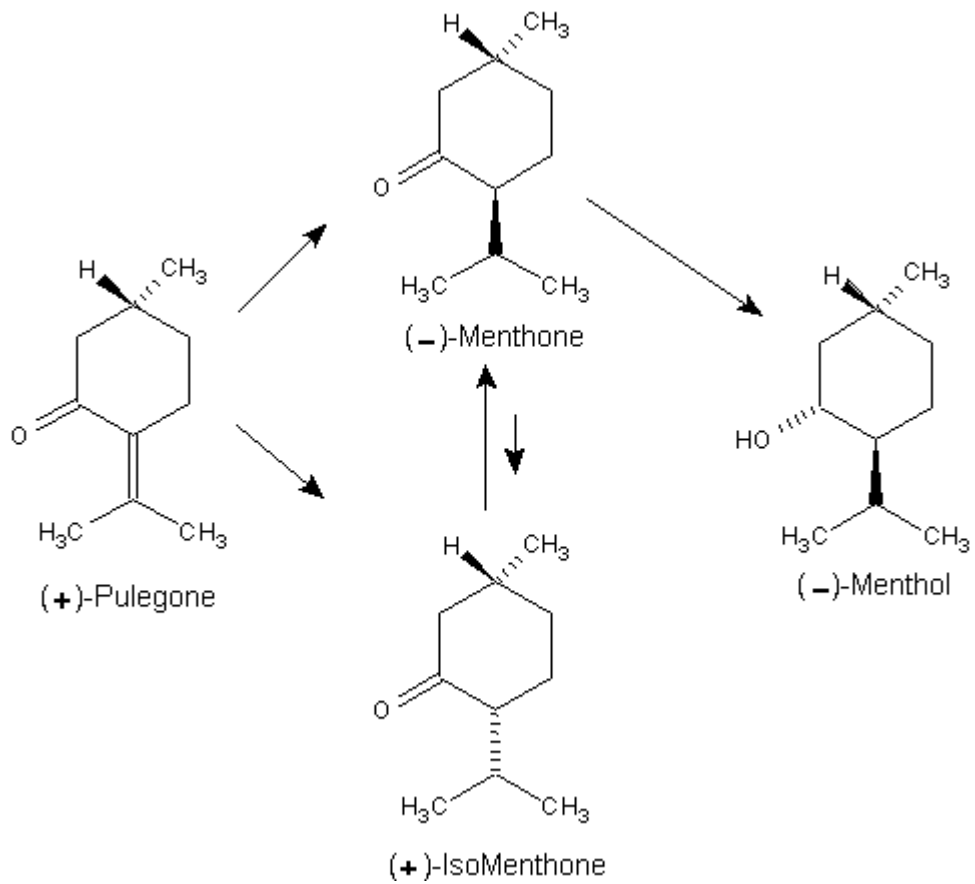
Both species grow wildly in Cyprus

Mentha pulegium, widespread in Cyprus

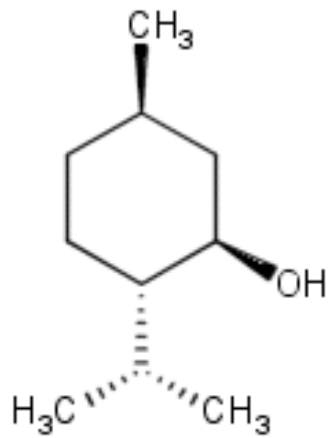
CALAMINT **CALAMINTHAE FLOS**

Calamintha sylvatica **Lamiaceae**

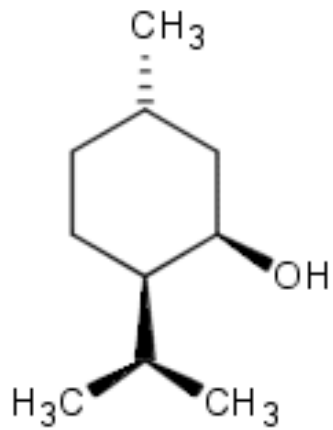
The official plant grows in Europe also in Turkey. The dried flowering tops of calamint produce a small amount of essential oil (not less than 6 ml/kg in the case of the officinal drug), containing neomenthol, pulegone, menthone, isomenthone, and other monoterpenes.


H
CH3
O
H3C
CH3
(–)-Menthone
H
CH3
O
H3C
CH3
(+)-Pulegone
H
CH3
O
H3C
CH3
(+)-IsoMenthone
H
CH3
HO
H3C
CH3
(–)-Menthol

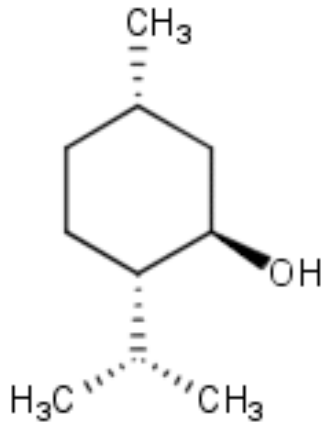
The Four Menthol Stereoisomers



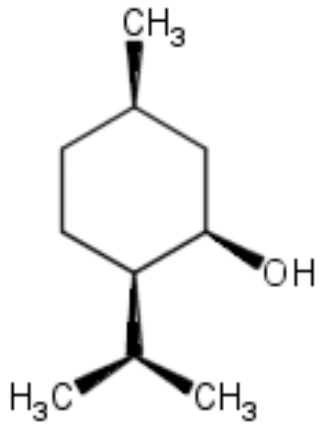
(-)-Menthol



(+)-Neomenthol



(+)-Isomenthol



(+)-Neoisomenthol

The drug (flowering tops) is traditionally used for the symptomatic treatment of gastrointestinal disturbances (epigastric bloating, impaired digestion, eructations, flatulence) and as an adjunctive therapy for the painful component of functional dyspepsia. Around the Mediterranean, a related species is used in folk medicine, namely *Calamintha nepeta* which occurs as many different chemotypes, including chemotypes with pulegone, piperitone, carvone and cineole.

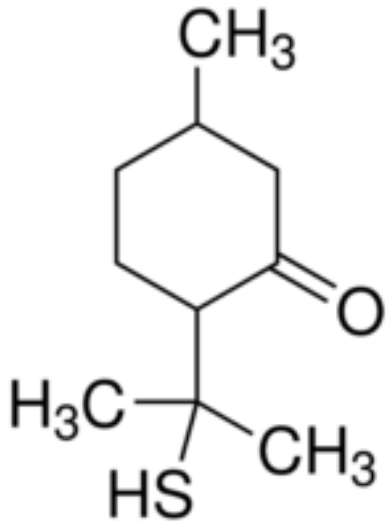
BUCHU **AGATHOSMAE FOLIUM**

***Agathosma betulina* (*Barosma betulina*)**

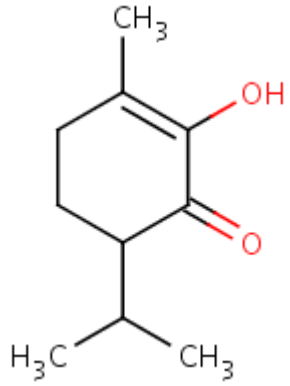
Rutaceae

The plant is a small shrub widespread at high altitudes around Cape Town (South Africa).

Chemical Composition : The leaves of buchu contain flavonoids (diosmin and other glycosides), mucilage, and an essential oil (10-20 ml/kg) containing primarily ketones with a *p*-menthane skleton : (-)-isomenthone, (+)-menthone, and less than 4.5% (-)-pulegone. Buchu oil also contains bifunctional derivatives, namely diosphenols. Its specific odor is due to sulfur-containing compounds (*p*-menthane-8-thiol-3-one). Another important compound in the essential oil is diosphenol.

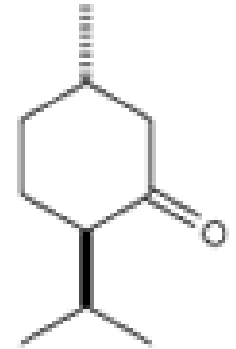


p-menthane-8-thiol-3-on

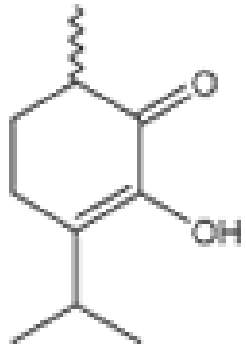


diosphenol

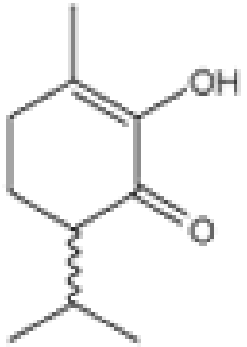
1. *Agathosma betulina*



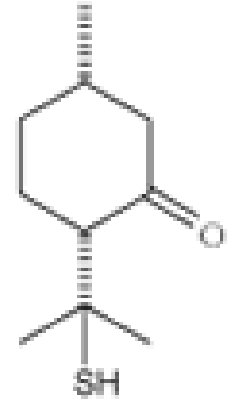
(+) - Menthone



ψ –diosphenol



diosphenol



8-mercapto -*p*- menthan-3-one

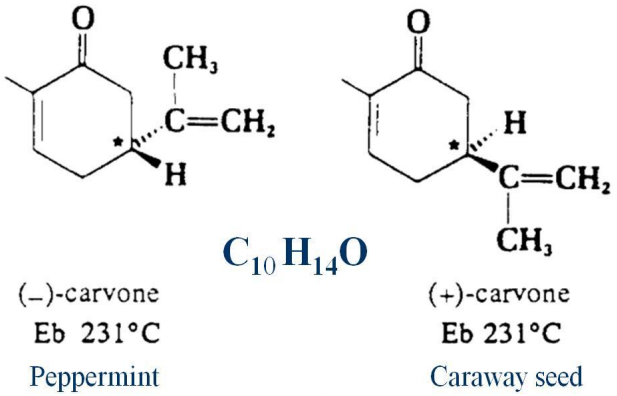
The drug must contain not less than 13 ml/kg essential oil. Buchu is thought to be a urinary antiseptic. It is traditionally used orally to enchance the renal elimination of water and as an adjunctive treatment to increase diuresis in benign urinary disorders. Because buchu oil is rich in pulegone, its use in aromatherapy must be discouraged. Pregnancy is a contraindication.

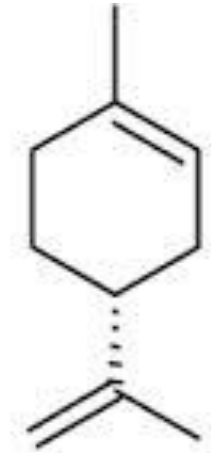
CARAWAY (kimyon)

CARVI FRUCTUS **CARVI AETHEROLEUM**

Carum carvi **Apiaceae**

The dried fruit must contain not less than 30 ml/kg essential oil. The essential oil is mainly composed of (S)-(+)-carvone (50-55%), and (R)-(+)-limonene (35-45%).





R(+)-limonene

S(-)-limonene

The drug has been considered to be a galactogogue, expectorant, and carminative and used by the oral route for its digestive indications. Carvi fructus is also a very well known spice.

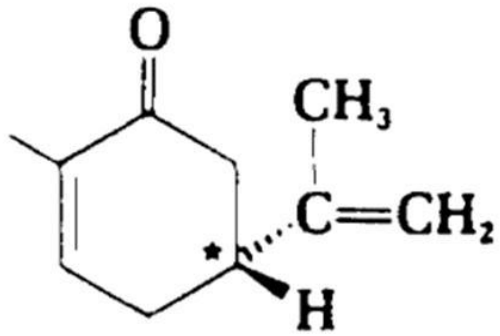
DILL (dere otu)

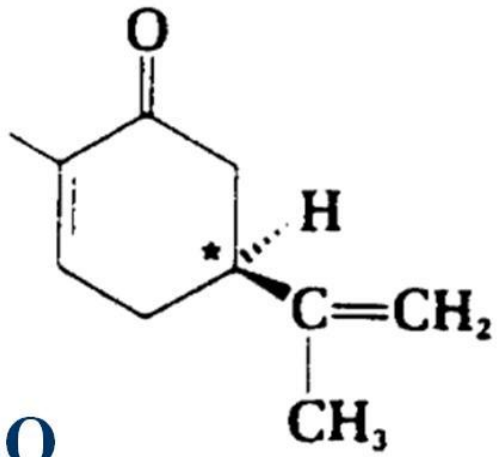
ANETHI FRUCTUS **ANETHI AETHEROLEUM**

Anethum graveolens **Apiaceae**

The dried fruit must contain not less than 25 ml/kg essential oil.

The essential oil in which (S)-(+)-carvone and (R)-(+)-limonene are the major constituents , owes its characteristic odor to dill-ether. The whole plant essential oil contains 20-50% (S)-(+)-α- phellandrene.





$C_{10}H_{14}O$

(–)-carvone

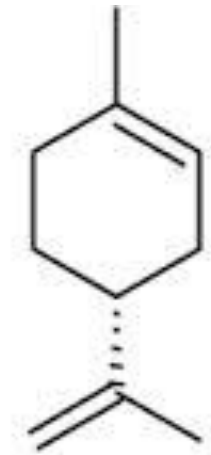
Eb 231°C

Peppermint

(+)-carvone

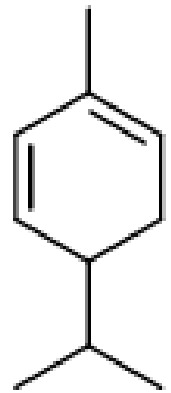
Eb 231°C

Caraway seed

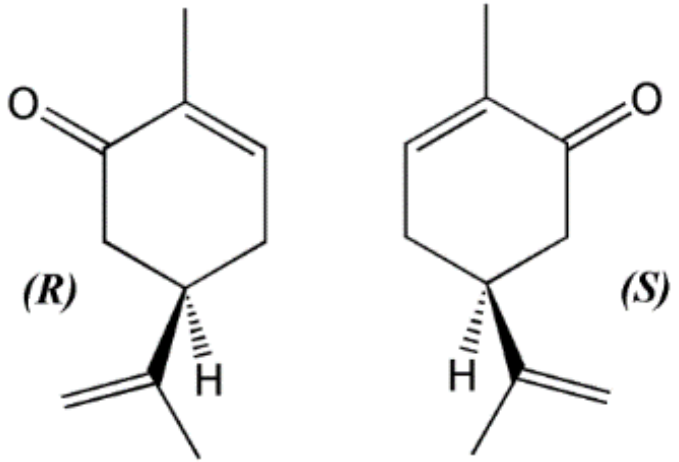


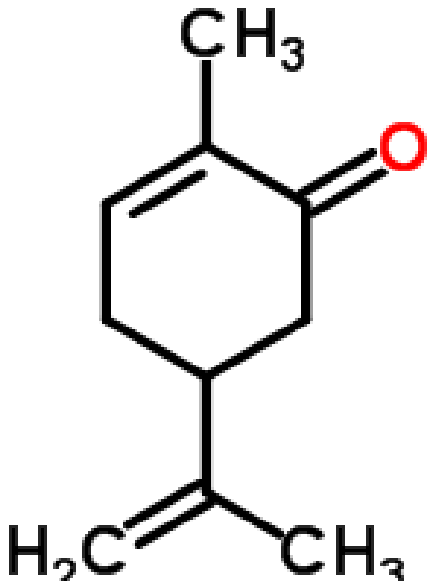
R(+)-limonene

S(-)-limonene



α- Phellandrene





Carvone

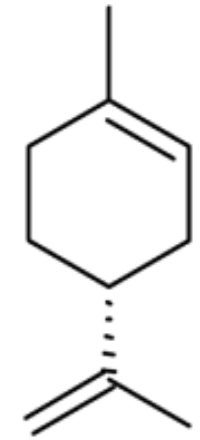
WILD CELERY (kereviz)

APII FRUCTUS **APII AETHEROLEUM**

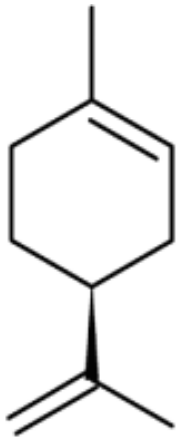
Apium graveolens

Apiaceae

The celery fruit contains 20-30 ml/kg essential oil that includes mostly hydrocarbons (limonene, selinene, p-cymene), dihydrocarvone, α-terpineol and phthalides. The celery fruit also contains flavonoids, phenolic acids, and numerous coumarins, isoprenylcoumarins, and furanocoumarins (bergapten and derivatives, free and as glycosides). The celery fruit is a diuretic in animals and a weak antispasmodic (phthalides). The phototoxicity of the furanocoumarins and the risk of allergic reaction are well documented for celery.

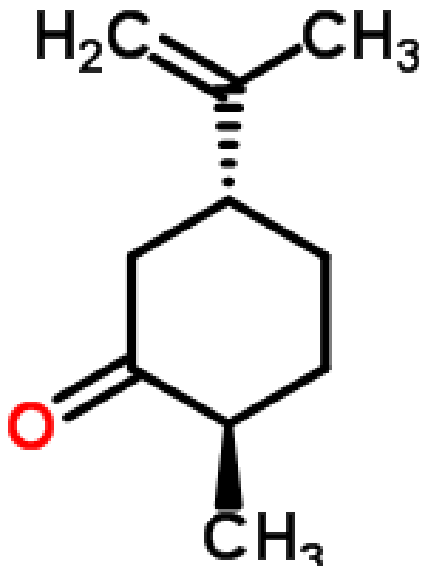


R(+)-limonene

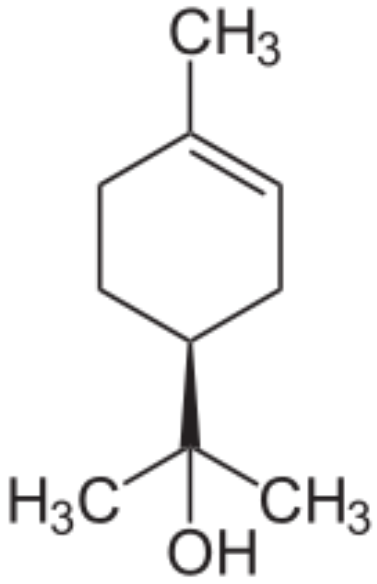


S(-)-limonene

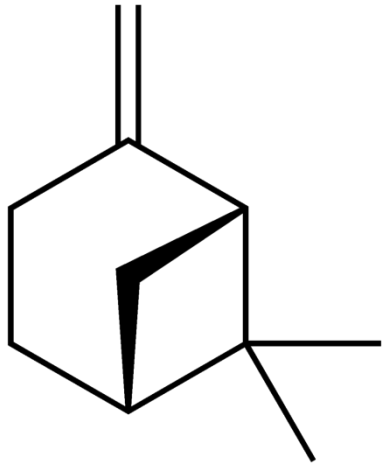
1



dihydrocarvone



α- terpineol



β-pinene

TEA TREE MELALEUCAE ALTERNIFOLIAE FOLIUM

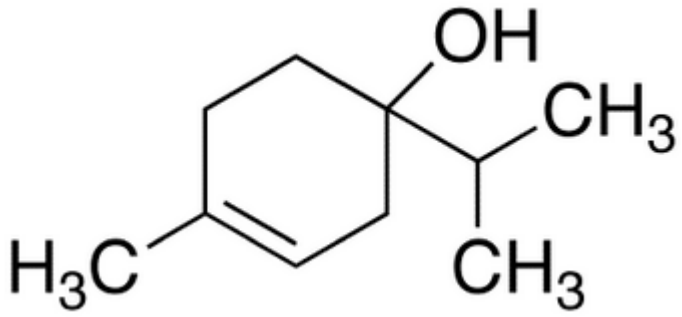
Melaleuca alternifolia

Myrtaceae

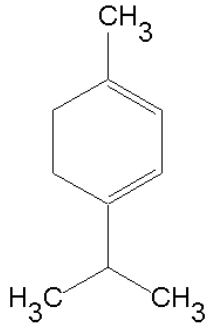
(çay ağacı)

The name “tea tree” causes much confusion. Confusion with tea (*Camellia sinensis*) of course but also with other Myrtaceae, bacause in Australia, the term tea tree is used for other species of the genus *Melaleuca*, as well as for species of a closely related genus *Leptospermum*. The tea tree is native to the northeast of New South Wales where its leaves are harvested to produce essential oil. The major constituents are generally terpin-1-en-4-ol, but some clones produce an essential oil in which the cineole concentration can reach 60%. The essential oil must contain not more than 15% cineole and not less than 30% terpin-1-en-4-ol.

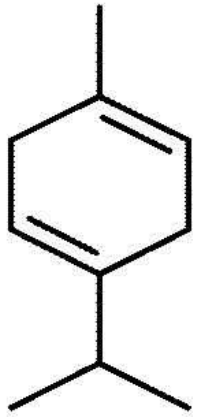
The other compounds in the essential oil are γ- terpinene 10-28%, *p*-cymene 0.5-2%, α-terpinene



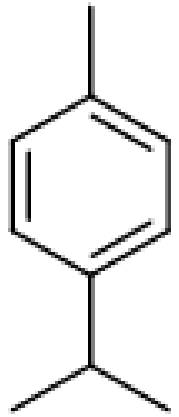
terpin-1-en-4-ol



α-terpinene



γ- terpinene



p-Cymene

The antibacterial reputation of the essential oil is consistent with *in vitro* tests that show its activity, as well as that of terpinen-4-ol and other constituents, against various strains (*Staphilococcus aureus, Escherichia coli*) but also against *Candida albicans* or against *Aspergillus niger.*

It is because of its antiseptic properties that the tea tree oil is used. It is now an ingredient, and not only in Australia, of gels, creams, lotions, and shampoos for human and animal use, foot care products, soaps, toothpastes, insect repellents, and air fresheners. It is frequently used in phytotherapy and can cutaneous irritation in very rare cases.

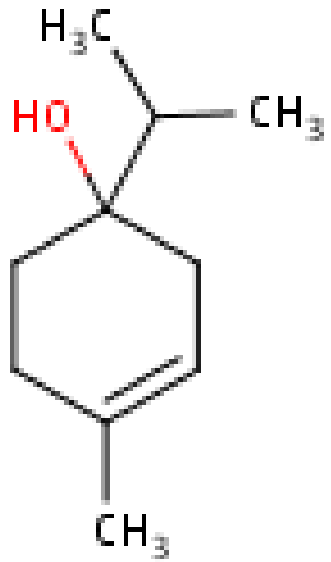
SWEET MARJORAM ORIGANI MAJORANAE HERBA

Origanum majorana

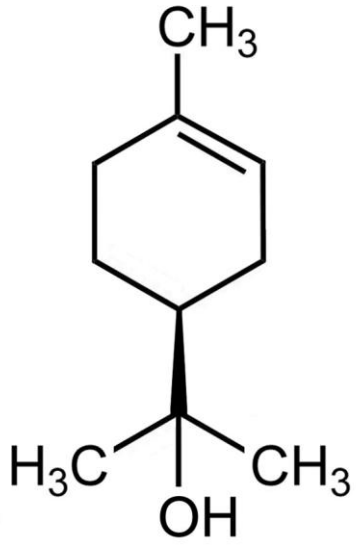
Lamiaceae

Growing also in Cyprus

Originally from the Orient, marjoram is widespread in all the Mediterranean basin (production : Egypt). It contains 7-30 ml/kg essential oil with terpin-1-en-4-ol, α-terpineol, sabinene hydrates and linalool.



Terpin-1-en-4-ol



α-Terpineol

The leaves and flowering tops are used traditionally for the symptomatic treatment of gastrointestinal disturbances (epigastric bloating, impaired digestion, eructations, flatulence) and to treat acute benign bronchial disease. Marjoram is used locally to relive the symtoms of the common cold, such as nasal congestion, and in mouthwashes for oral hygiene.

Reference Books :

Main Book

Bruneton, J., Pharmacognosy, Phytochemistry, Medicinal Plants, TEC & DOC Editions, Paris 1999

Other Books

- Hänsel, R., Sticher, O., Pharmakognosie – Phytopaharmazie, Springer Medizin Verlag, Heidelberg 2010
- Evans, W.C., Trease and Evans Pharmacognosy, Elsevier Limited, Edinburgh, London 2002
- Baytop, T., Farmakognozi I-II, İstanbul Üniv. Yay. No. 2783, Eczacılık Fak. No.29, İstanbul 1980
- Tanker, M., Tanker N., Farmakognozi I-II, Ankara Üniv. Eczacılık Fak. Yay. No. 63, Ankara 1990