Volatile oils Containing Bicyclic Monoterpenes as Active Constituents

Prof. Dr. Ali H. Meriçli

SAGE (adaçayı) **SALVIAE FOLIUM**

***Salvia* ssp. (*Salvia officinalis*,**
S. sclarea (clary), *S. lavandulifolia*,
***S. fruticosa* (*S. triloba*)** **Lamiaceae**

Salvia officinalis

Salvia sclarea

Salvia lavandulifolia

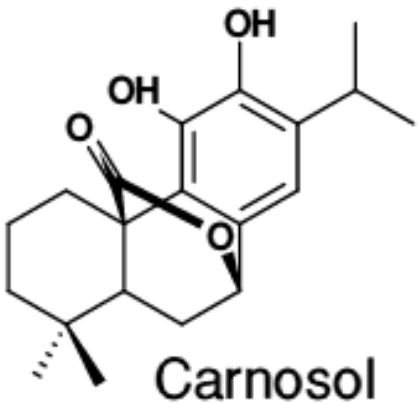
Salvia fruticosa (*S. triloba*)

Growing also in Cyprus

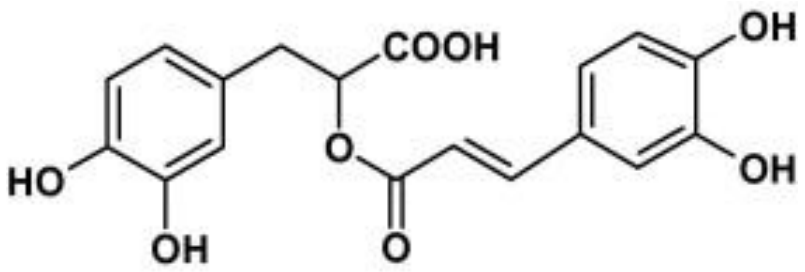
Gall on *S. fruticosa*

Salvia officinalis

Chemical Composition : The leaf is rich (1-3%) in flavonoids (apigenin, luteolin, 6-methoxylated flavonoids and their 7-O-glycosids), triterpenes (chiefly ursolic acid) and diterpenes (carnosol), and phenolic acids (rosmarinic acid).

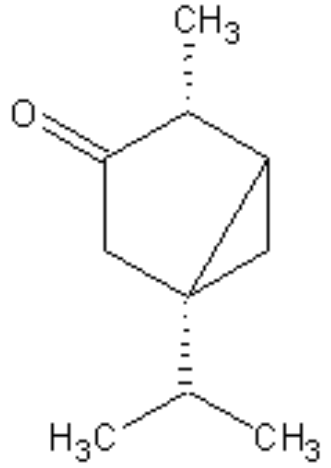


Carnosol

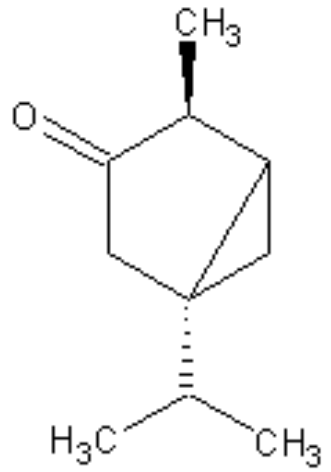


Rosmarinic acid (RA)

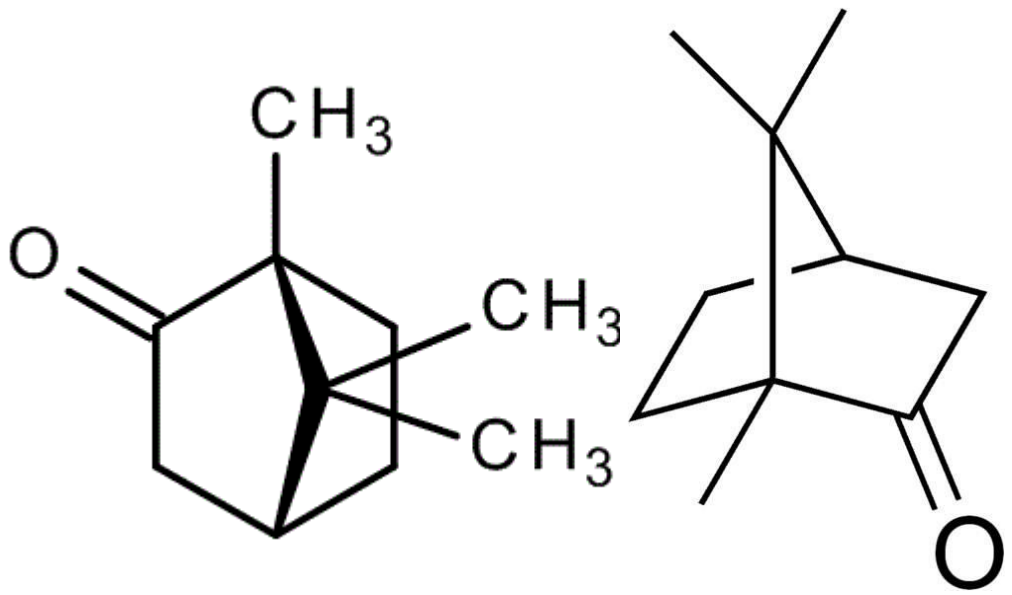
The essential oil of *Salvia officinalis* (8-25 ml/kg) is characterized by camphor, cineole, and bicyclic monoterpenoid ketones : the thujones (α- and β- thujones). These may represent up to 60% of the essential oil, which α-thujone almost always accounting for the major part. The profile defined by standard official sage oil is α-thujone (18-43%), β-thujone (3.8-5%), camphor (4.5-24.5%), cineole (5.5-13%), humulene (0-12%), α-pinene ((1-6.5%), camphene (1.5-7%), limonene (0.5-3%), linalool, free and esterified (1% maximum) and bornyl acetate (2.5% maximum).



α-Thujon



ß-Thujon



Camphor

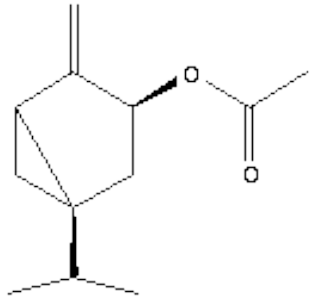
Tests : The identification is completed by observing the red color developed by a hexane extract in the presence of sodium hydroxide (thujones). The assay includes a quantitation of the essential oil (required concentration 20-30 ml/kg) and a TLC analysis.

Pharmacological Properties : Sage enjoys a reputation for being a panacea. Although experimental work does not confirm all of the virtues that are attributed to it, it does prove the antispasmodic properties : small doses of essential oil inhibit the isolated guinea pig ileum contractions induced by electrical stimulation. The hydroalcoholic extract also displays spasmolitic properties against the spasms induced by acetylcholine or seretonin (possible role of polymethoxylated flavones). The antioxidant properties have long been applied to food preparation, have also been demonstrated, and the are linked to the presence of diterpenes.

In contrast to sage, its aqueous preparations, and its hydroalcoholic extracts, which seem to have little toxicity, the essential oil is neurotoxic : its ingestion causes convultions preceted by hypersalivation and vomiting, and interrupted by periods of obnubilation, hyporeflexia, and hypotonia. The action is central origin and seems linked to the ketones (thujones), and to a lesser extent, to camphor.

Uses : Sage-based phytomedicines –official sage, clary, *Salvia lavandulifolia*- for oral administration may only claim one indication : traditionally used for the symptomatic treatment of gastrointestinal disturbances (epigastric bloating, impaired digestion, eructations, flatulence). Topically, all three species are traditionally used in mouthwashes for oral hygiene. In addition clary may be used for minor wounds after thorough cleansing.

The essential oil of *Salvia lavandulifolia* : It contains no or almost no thujones. Camphor (11-36%), and cineole (11-25%) are the most abundant elements. The profiles also covers α-pinene (4-11%), sabinene, limonene, linalool, borneol, linalyl acetate, and terpin-1-en-4-ol. Most commercial samples contain sabinyl acetate, which is toxic; a systematic quantitation of it seems indicated.



Sabinyl acetate

Clary sage oil : is rich in linalool (10-20%), and linalyl acetate (45-75%), which occur alongside (-)-germacrene D and (-)-caryophyllene.

The concrete essence contains mainly (-)-sclareol (70%) and its C-13 epimer. Sclareol is a diterpen concentrated in the calyx. It is a raw material for the perfume industry. Clary oil comes mainly from Russia. It is also producted in France, China and Bulgaria.

The essential oil of *Salvia fruticosa* (*S. triloba*) : chiefly contains cineole (60%), camphor, borneol, terpineol, and about 7% thujones. This species of strong and pungent odor is listed in some pharmacopoeias. It is characteristic by a leaf blade with one or two small lateral lobes at the base, shaped aproximately like ears. It contains tannins, flavonoids, and diterpenes.

Salvia triloba *(syn:* ***Salvia fruticosa***)

Sometimes galls occur on the branches of *Salvia fruticosa*, these galls are named as **“apple”** in folk medicine .

Galls also contain essential oil, that’s why the essential oil obtained from this plant is known as “apple oil”. The principal constituents of “apple oil” have some differences from the essential oil obtained from the leaves. In some provinces, the young galls can be eaten.

In Turkey, there are more than 70 *Salvia* species grow wildly, including *S. fruticosa* and *S. sclarea.* Almost in all parts of Turkey, *Salvia fruticosa* is used as sage.

Salvia cryptantha (endemic) is another *Salvia* species growing especially in Central Anatolia, its essential oil contains cineole (25-30%), geranyl acetate (15-20%), camphor (12-17%), borneole (5-10%) and only 1% thujones.

Salvia candidissima *Salvia palaestina*

86 *Salvia* species and 94 taxa grow in Turkey;
33 of them are endemic plants.

Especially in south-western Turkey some *Sideritis* species (*Sideritis libanotica, S. congesta*…) (dağ çayı) have been used like sage for the preparation of herbal teas. The essential oil of these species also contain cineole and camphor as major components.

Sideritis libanotica

S. congesta

Sideritis species

Lamiaceae

Sideritis montana

Sideritis perfoliata

Sideritis species are known in Turkey as “mountain sage”

Sideritis cypria –endemic-

DORYSTOECHAS HASTATAE FOLIUM

Dorystoechas hastata **Lamiaceae**

A monotypic genus for Turkey (monotypic = genus with only one species and endemic). This plant grows only in region Antalya.

Dorystoechas hastata is a woody shrub possessing an inflorescence, which is an erect sylindrical spike with many flowered verticillasters. The plant is used like sage in the region for the preparation of a herbal tea.

The leaves contain like sage flavonoids (apigenin, luteolin, 6-methoxylated flavonoids and their 7-O-glycosids), and diterpenes (rosmanol, carnosol). The drug contains 2-2.5ml/kg of an essential oil, and the major constituents of this oil are cineole,α-pinene, borneole, guaiole and camphor. Only 1% thujones are present in the essential oil.

ROSEMARY **(biberiye, kuş dili)** **ROSMARINI FOLIUM**

Rosmarinus officinalis

Lamiaceae

Growing also in Cyprus

The drug contains 10 to 25 ml/kg of an essential oil in which the principal constituents are camphor (15-25%), cineole (15-50%), α-pinene (10-25%), and borneol, free and esterified.

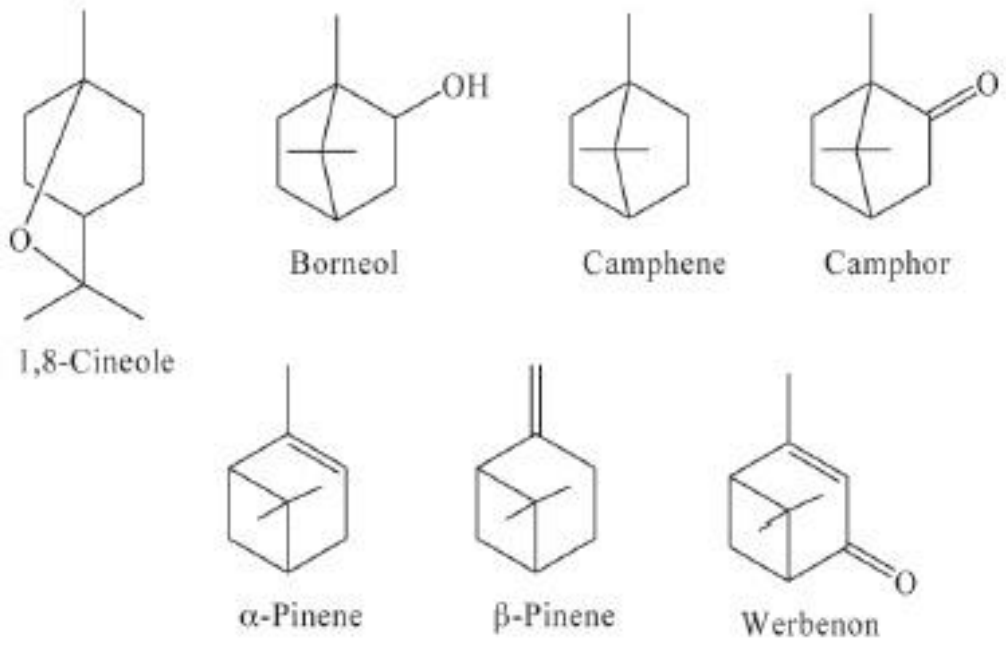


Fig. 1. Main components of rosemary oil

Since the composition of the essential oil depends on several factors, including source (Spanish type and Moroccan-Tunisian type). Obtained by steam distillation from native plants, the two essential oils differ slightly by physical characteristics and mostly by their compositions; cineole represents 38-58% of the Moroccan-Tunisian type oil, but only 16-25% of the Spanish type oil.The Spanish type is characterized by a large proportion of hydrocarbons (18-26 α-pinene and 8-12 camphene whereas the Moroccan-Tunisian type contains 9-14% and 2.6-6%, respectively.

The Moroccan-Tunisian type can contain little camphor (5-15%), whereas the Spanish type always contains a fair amount (13-18%).

Rosmary oil (Rosmarini aetheroleum), like mint and sage oil, is a spasmolitic.

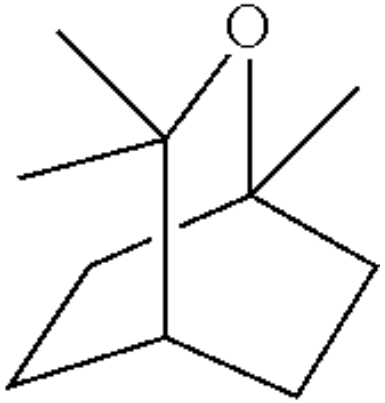
EUCALYPTUS (ökaliptus) EUCALYPTI FOLIUM

Eucalyptus globulus

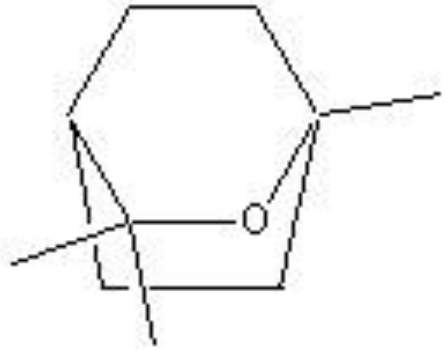
Myrtaceae

With the exception of Papua New Guinea and a few nearby islands, the genus *Eucalyptus* is native only to Australia.

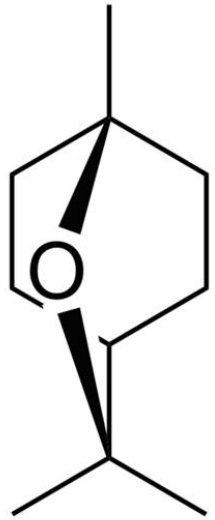
One of the assets of this genus is the diversity in the composition of the leaf essential oil, made even greater by the frequent occurence of chemotypes. Thus the following essential oil types are known with 1,8-cineole (eucalyptol) 70-80% *Eucalyptus globulus,* with piperitone and phellandrene 40-45% *E. dives,* with phellendrene 60-80% *E. radiata*, with geranyl acetate 45-55 % *E. macarthuri*, with citronellal 65-85% *E. citriodora*, with citral up to 63% *E. staigerana*.

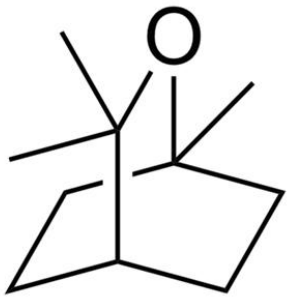


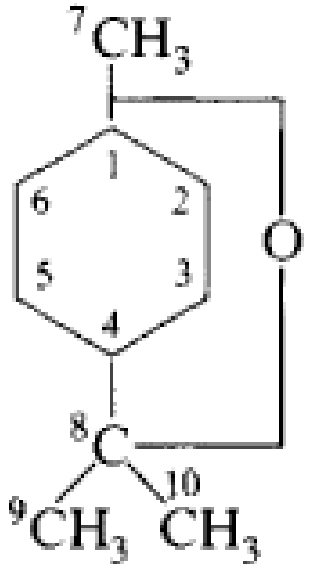
Cineole



1,8-cineole







Eucalyptol,
1,3,3-trimethyl- 2-oxabicyclo[2,2,2]octane
1,8-Cineole

1,8-cineole = eucalyptol

According to the European Pharmacopoeia the drug must contain not less than 70% 1,8-cineole (eucalyptol).

Chemical composition : The essential oil concentration ranges from 5 to 35 ml/kg. The major constituent (70-80%) is 1,8-cineole (=eucalyptol); the other constituents are chiefly terpenoids. The other compounds in the leaves are phenolics, common phenolic acids, and flavonoids (rutin, hyperin, and methylated flavones in the epicuticular wax.

Pharmacological Activity : Eucalyptus oil (Eucalypti aetheroleum) has antiseptic properties. Cineole is readily absorbed by the digestive route, as well as by the cutaneous or rectal route, and is eliminated by pulmonary or renal excretion. It is widely accepted that eucalyptus oil (0.05-0.2 ml/day) has expectorant and mucolytic properties, and stimulates the bronchial epithelium. Eucalyptus oil, like menthol, is believed to “decongest” the upper respiratory tract in case of a common cold. At high doses eucalyptus oil is neurotoxic (LD_{50} = 1.7 ml/kg, rat, IP).

Uses : Eucalyptus oil and cineole, both products are ingredients of many proprietary drugs because of their antiseptic and “decongestant” activity : syrups, lozenges, nasal drops, preparations for inhalation. In preparations for external use, cineole can be used to facilitate the transcutaneous absorbtion of other substances.

Pharmaceuticals based on eucalyptus leaves are traditionally used to treat acute benign bronchial disease (oral route and local use), and locally, to relieve nasal congestion in the common cold.

Eucalyptus is also used in Germany for catarrh of the upper respiratory tract for bronchitis. There, package inserts must list 1. the contraindications (no use *per os* in case of gastrointestinal or biliary tract inflammation, or in case of severe liver disease), 2. the (rare) side effects (vomiting, diarrhea), 3. a warning not to use eucalyptus in children under age of two. The recommendation to drink the infusion slowly is based on the notion that the tannins in the drug exert an astringent effect on the inflamed mucous membranes of the throat.

Eucalytus deglupta = Rainbow Eucalyptus
(Phylipinne Islands)

NIAOULI **MELALEUCAE QUINQUENERVIAE FOLIUM**

NIAOULI AETHEROLEUM

Melaleuca quinquenervia **Myrtaceae**

Niaouli is a small tree native to the Mollucas. It grows in Austraila, southwest Asia and in Madagascar. The leaf essential oil “Niaouli aetheroleum” contains cineole as the most common major compound. Niaouli oil is an antiseptic and is still an ingredient of combinations proposed for the adjunctive treatment of rhinitis and bronchial infections.

CAJEPUT MELALEUCAE KAJEPUTI FOLIUM

KAJEPUTI AETHEROLEUM

Melaleuca kajeputi

Myrtaceae

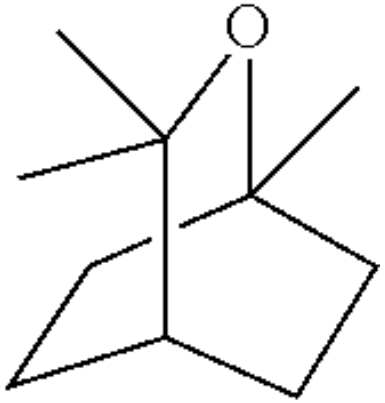
Cajeput is a tree that grows in Australia, India, and southeast Asia. The leaf essential oil (5-25 ml/kg), contains, depending on the source, up to 65% cineole. Cajeput oil, which is traditionally used used in southeast Asia, China, and Indenosia to treat infected cutaneous lesions and by inhalation for respiratory tract disorders, is an antibacterial *in vitro*. It is sometimes used in aromatherapy and it is an ingredient of antipruriginous ointments.

LAUREL (defne) **LAURI FOLIUM**

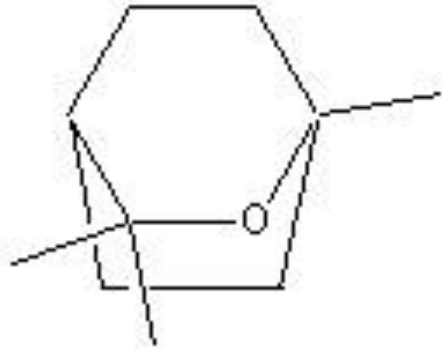
Laurus nobilis

Lauraceae

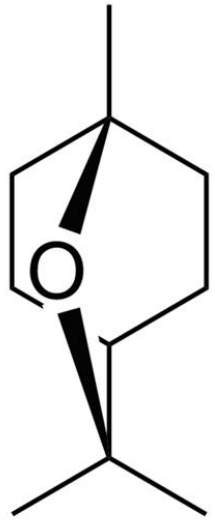
The bay laurel or noble laurel is a dioecious tree native to western Europe. It also grows in Turkey and Cyprus wildly. By steam distillation, bay leaves yield about 10-30% ml/kg of an essential oil in which cineole is always the major compound (25-60%). Bay leaf is traditionally used orally to treat the symptoms of gastrointestinal problems such as epigastric bloating, impaired digestion, eructations, and flatulence.

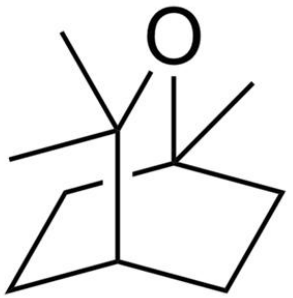


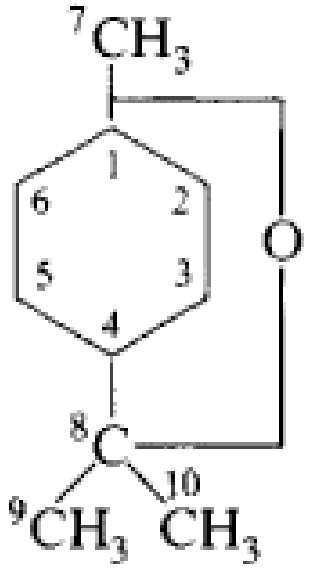
Cineole



1,8-cineole







Eucalyptol,
1,3,3-trimethyl- 2-oxabicyclo[2,2,2]octane
1,8-Cineole

1,8-cineole = eucalyptol

MYRTLE (mersin, mırt) **MYRTI FOLIUM**

MYRTOL, MYRTI AETHEROLEUM

Myrtus communis

Myrtaceae

Myrtle is a little tree, growing in the Mediterranean region, also including Turkey and Cyprus. Myrtol, an essential oil with pleasant odor reminiscent of turpentine oil and eucalyptus oil. The drug product has the following manufacturer-listed ingredients : not less than 25% limonene, 25% cineole, and 6.7% α-pinene. The chemical composition of myrtol is similar to that of eucalyptus oil. The pharmacologic profile of myrtol features mucolytic properties that are supplemented by antioxidative and anti-inflammatory actions.

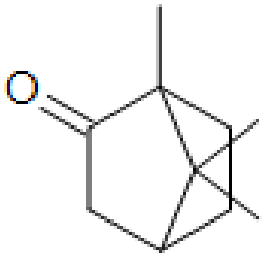
Strictly speaking, since myrtol is a artificial mixture derived from specific essential oils (Commercial myrtol is a by 160-180 ^{o}C boiling fraction of *Myrtus communis* essential oil), it is not classified as a phytomedicine, but belongs to the group of essential oils and essential oil derived compounds, and, as such, is approved in Germany for use in “acute and chronic bronchitis and sinusitis”.

CAMPHOR TREE (kafur) **CAMPHORA**

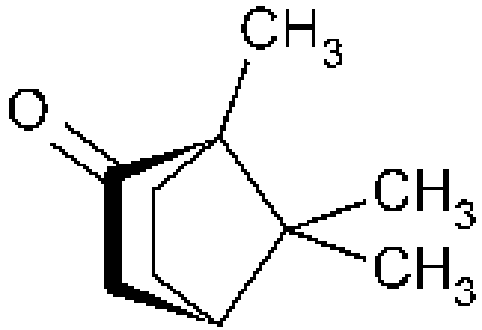
Cinnamomum camphora

Lauraceae

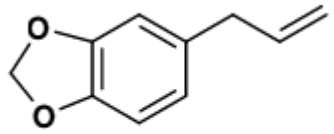
The camphor tree is a tall Asian tree (Taiwan, China) which has long been exploited for the production of (+)-(1*R*)-camphor, obtained by cooling and distilling the essential oil found in the wood. Racemic camphor, a cardiac and respiratory analeptic, is easy to synthesize. After camphor has crystallized and has been filtered out, the essential oil (camphor oil) can be distilled into three fractions : light, medium (80% safrole), and heavy (sesquiterpene rich). These three fractions are known as white, brown, and blue camphor oil, respectively.



Camphor



camphor



Safrole

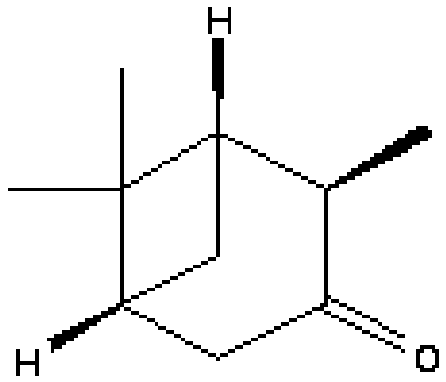
HYSSOP HYSSOPAE HERBA

Hyssopus officinalis

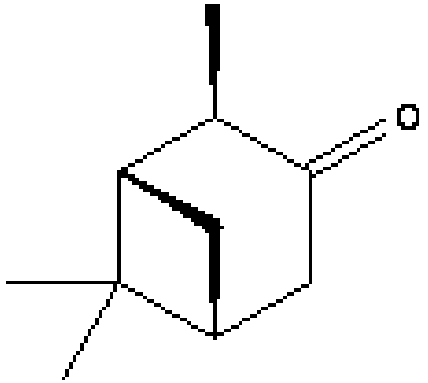
Lamiaceae

This species is a small Mediterranian plant, common on piles of rocks and old walls. The drug consists of the leaves and flowering tops (herba).

The drug contains phenolics (rosmarinic acid, flavonoids), di- and triterpenes (marrubiin, oleanolic acid), and an essential oil (3-10 ml/kg). The main oil constituents are the ketones isopinocamphone (34.5-50%), and pinocamphone (5.5-17.5%), alongside mono- and sesquiterpenoid hydrocarbons (β-pinene, 13.5-23%, limonene 1-4%, and sabinene 2-3%).



isopinocamphone



pinocamphone

The drug is used as expectorant, antiseptic and stimulant (essential oil). The essential oil of hyssop is neurotoxic : pinocamphone and isopinocamphone are considered responsible for its epileptogenic activity; the neurotoxicity could be linked to the inhibitory action of the ketones on cell respiration. The drug is advised in very small doses.

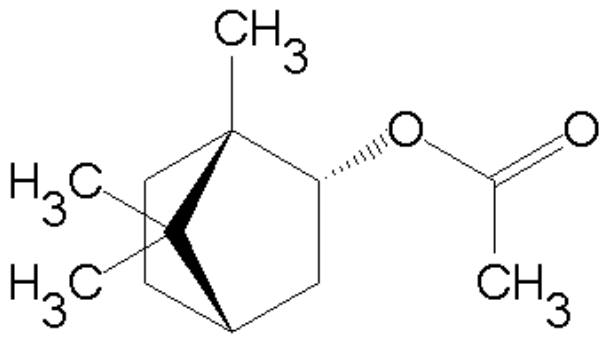
PRODUCTS FROM CONIFERS

Needle Oils (Aetheroleum) (Pine, Spruce, Fir) (çam, ladin, göknar) Pinaceae

Various industries (perfumes, soaps, air fresheners) use pine (or spruce, or fir) needle oil obtained by steam distillation of fresh leaves (needles). Pharmacy sometimes uses them in the formulation of praparations for inhalation. The essential oils from pine (*Pinus*), fir (*Abies*), and spruces (*Picea*) contain monoterpenoid hydrocarbons; their odor is due to esters, chiefly represented by (-)-bornyl acetate.

Pinus pinea (Cyprus)

Abies alba



Picea abies

Bornyl acetate

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