Eucalyptol

By George Clark, Cameron & Stuart, Easton, MD

Table 1. Eucalyptol statistics

Classification: Bicyclic internal monoterpenoid ether

Additional names:[1,2,3] 1,3,3-Trimethyl-2-oxabecyclo[2.2.2} octane; 1,8 - Oxido-p-menthane; 1,8 – Epoxy-p-menthane; 1,8 – Cineole; Anhydride of Menthame-1,8-diol; Cajuputol; Cajeputol; Kajeputol.

Physical data:[4,5,6]

Appearance: Clear, colorless mobile liquid

Specific gravity at 25°C / 25°C: 0.921-0.924

Melting point: 1.3°C

Congealing point: Not less than 0°C

Boiling point: 176- 177°C

Refractive index at 20°C: 1.455 - 1.460

Flash point: 47-48°C

Odor threshold: 12 ppb

Solubility: Only sparingly soluble in water: 0.35 wt% at 25°C. Very soluble in most organic solvents, esters, aliphatic and aromatic alcohols, ketones, essential oils, fixed oils, chlorinated solvents, DEP, and hydrocarbons. Poorly soluble in organic diols; glycerin.

Stability: Very stable to air, but fairly volatile. Can be stored for long periods in contact with air without serious deterioration. Stable to contact with water over a broad pH range (2-12). Attacked by strong acids, such as hydrochloric acid.

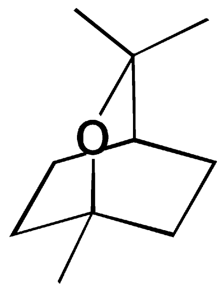

Figure 1. Eucalyptol: Mwt 15; HT Nr. 2909.20; $C_{10}H_{18}O$; CAS #470-82-6; FEMA-GRAS #2465

Natural has been the rage of the flavor and fragrance industry over the last decade. However, in retrospect, one might well refer to the 20th century as the era of synthetic organic chemicals. Thus, at the beginning of the new millennium, it is surprising to find that the supply of a number of common, commercially available aroma chemicals remains largely or solely of natural in origin (i.e. eugenol, l-menthol, menthone and eucalyptol). Eucalyptol shares with eugenol the rare distinction of being one of two large-volume aroma chemicals whose supply is totally natural. No synthetic counterpart of these two materials is offered commercially. The basis for this reality is economic. Mother Nature can produce these materials far more economically than can the chemist.

Eucalyptol's basic impression is medicinal-camphoraeous. Small amounts of Eucalyptus fractions or Eucalyptol can twist a floral material, such as linalool or Aprol® 100 into a lavender. The term "medicinal" is used as a nebulous descriptive modifier for a number of aroma chemicals whose overall organoleptic profile have little in common;

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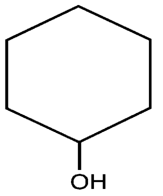
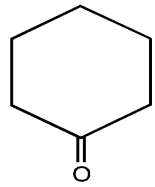
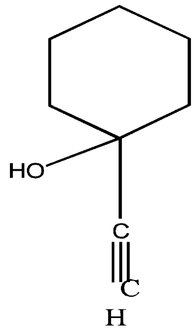


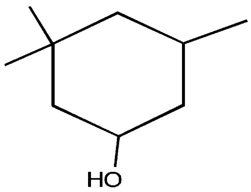
Cyclohexanol



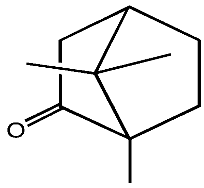
Cyclohexanone



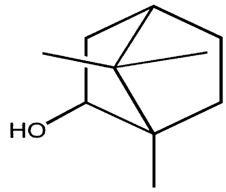
Ethynyl Cyclohexanol



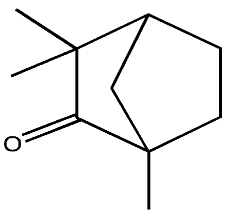
Cyclonol



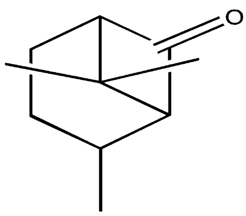
Camphor



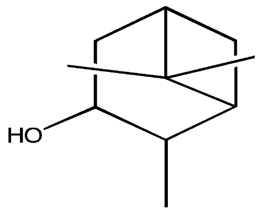
isoBorneol



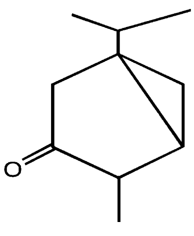
Fenchone



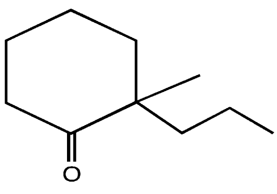
Chrsanthenone



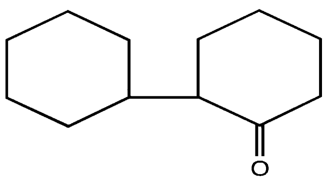
Pinocampheol



Thujone



Freskomenth



Givmenthe

Figure 2. Materials with a camphoraceous odor

Table 2. Contents of Vicks Vaporub (1989)

Cedar leaf Oil	0.75%	
Camphor		4.7-5%
Eucalyptus Oil	1.2-1.5%	
Menthol		2.6-2.8%
Nutmeg Oil		0.75%
Thymol		0.25%
Turpentine		5%

camphor, carvcarol, methyl salicylate, thymol, eucalyptol. This relatively negative term is a result of their use as disinfectants in hospitals and "rooms of the infirm". The six to seven percent eucalyptol content of the pine oil these cleaners contain dominates the impression of these "disinfectants". Many of these products have a strong, ethereal impact and their use can invoke unpleasant memories; hence the negative reaction. Their use as bacteriostats and bacteriocides grew out of folk medicine and their efficacy has been confirmed through modern research.[7] Often the combination of a number of essential oils displayss synergism in its bacteriostatic and bacteriocidal activity. A side development has been their use in aromatherapy, which itself is little more than an extension of folk medicine. That the term "medicinal" is used to describe eucalyptol and these other items should not be surprising, because their major applications involve medicines. These include cough drops and syrup, aromatic balms, tiger balm, and mouthwash. The mixtures used to create these medicines show an interesting similarity around the globe. Even in today's guides on aromatherapy, we find eucalyptol and *eucalyptus globulus* listed for antiseptic and rubefacient usage. A good representative for the type of mixture found in this group is Vicks Vaporub (Table 2).

This medicinal view of eucalyptol remains valid, despite the latest craze for eucalyptus-menthol candies. Possibly the most perplexing facet of this subject is the general negative impression the public has of the combination of menthol and eucalyptol as a flavor. Angelich reported in an article that older North American consumers list the menthol-eucalyptus flavor in hard candies in the five most-disliked flavor categories[8] A 1992 Wall Street Journal article reported that the major brands of mouthwash, which contain eucalyptol, are all losing market share.[9]

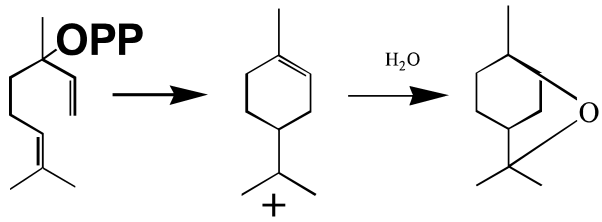


Figure 3. The biosynthesis of eucalyptol from linalyl pyrophosphate

Regarding the term camphoraceous, there are a large number of substituted cyclohexanols and derivatives that fall in this category (see Figure 2). The camphoraceous effect seems to shift over into a woody-pine effect, often with all three tones existing to one degree or another simultaneously in many materials. Because of its wide use and exposure, the terms cineole and eucalyptol are often used to denote a medicinal-camphoraceous quality. The word "eucalyptol" gives most people a rather ill-defined and broad impression. This is most likely due to a lack of interest in these materials in an economic and theoretical sense. Unlike musks, they peak no one's serious attention or curiosity. Because this category is vague, Figure 2 is presented to help highlight the impression, which includes facets of green and mint in its nature.

Natural Sources

It is safe to say that eucalyptol is found only in the natural plant kingdom. There is no known record of it having been found in the bio-systems of animals. What is perplexing is its absence in eucalyptus flower honey.[10] Just how eucalyptol arises in plant metabolism is still unclear, but it is thought to result from the quenching of the terpinyl cation by water, yielding a proton and eucalyptol (1,8-Cineole) (Figure 3). This explanation is in agreement with the fact that eucalyptol is found in almost every plant system in large and trace amounts.

It may well be that eucalyptol is a biosynthetic dead end in many systems, such as the eucalyptus species, thus allowing large quantities to build up in the plant. Eucalyptol has been found in artemisia oils, basil oils, betel leaves (2-3%), black pepper oil, bois-de-rose oil, cardamom oil, carrot leaf oil, cinnamon bark and leaf oils, cistus oil, elsholtzia banda, eucalyptus species (7-92%), eucalyptus globulus (40-92%), firs oil, geranium oil, ginger oil, lavender oil (trace- 67.7%), lemongrass oil, lime oil, litsea cubeba, lotus flowers (0.26%), melaleuca cajeputi (0-50 %), mentha species (0- 16.7%), mentha piperita (2 - 5%), musk melons, narcssus absolute (1.5%), palmarosa oil, passion fruit, pine oil (6.5%), rose oil, rosemary oil (0.1-70%), rue oil, sage oil (5-40%), spruce oil, tea tree (Melaleuca alternnafloia; trace-57%), verbena-lemon type (12%), woodworm oil (trace-13%), and yarrow oil. The highest concentrations of eucalyptol discovered to date have been found in eucalyptus globulus oil,[11] thus making this oil the prime target for the commercial production of this natural aroma chemical.

History

Eucalyptol is widely found in nature, but seldom in high concentrations. The modern commercial availability of Eucalyptol is from a number of sub-species of trees from the family, myrtle (myrtaceae), which includes both the species eucalyptus and melaleuca. Eucalyptol was discovered in 1833 by Blanchet[12] in cajuput oil, a member of the melaleuca family from East India (Indonesia). The exact chemical structure of eucalyptol was a difficult challenge to 19th century chemists and was worked on by many teams, each of which unveiled only part of the secret. The work was clouded by a new problem. Eucalyptol formed an azeotrope when distilled with the terpene, p-cymene, which was present in all the oils being investigated. Initially workers did not realize there was a problem, resulting in confusing and contradictory reports for molecular weight and formula values. Once the problem was recognized, methods to remove this hydrocarbon had to be developed before pure eucalyptol could be obtained. By 1885, Ritter[13] finally put all the pieces together and proposed the structure we recognize today as eucalyptol. The oil that eucalyptol was found in was obtained from a number of related melaleuca species throughout South Asia. These oils are collectively is known as cajuput oil. Cajuput oil was the original source of eucalyptol until the introduction of species of eucalyptus globulus, which was discovered in by colonists in Australia in 1788, and by Labilladiere in Tasmania in 1792.[14] The medicinal properties of these oils, collectively known as Sidney Peppermint, were recognized as early as 1788. In 1852, a German pharmacist, Baron Sir Ferdinand von Müller, recommended that the oil be distilled on a commercial scale. The first commercial production of eucalyptus oil was accomplished by Joseph Bosisto in Victoria, Australia in 1854.

The eucalyptus species, a hardy, rapidly growing evergreen tree, is native to Tasmania and Australia. Young trees will grow 6-8ft/year. Thus, they are sometimes cultivated as a bush, with the annual growth being cut, chipped and distilled to yield the oil. This growth provides a large amount of biomass and provides eucalyptus oil in a ~1% yield. The oil is in such a free state in the wood that one can smell it 50 ft away. Groves of trees can perfume large areas. Eucalyptus globulus trees will attain a height of 50 ft in ten years and will eventually reach a height of over 200 ft. The eucalyptus species approaches in height the Great Sequoia of the US Pacific Northwest. This rapid growth and bushy-evergreen factor has resulted in eucalyptus trees being planted alongside roads in Israel in the area of the Golan Heights to shield the roads from hostile fire.

The tree's rapid growth, evergreen branches for shade, hardy nature in all but northern climes, useful wood and oil, made it a prime candidate to be transplanted around the world. Thus, areas and nations never thought of as suppliers of eucalyptus oil and eucalyptol have entered the market since the tree was discovered in 1788. The commercial sources of eucalyptol before 1900 were the various European and North American wormseed oils and cajuput oils from South Asia and India. By 1900, Australia produced eucalyptus globulus and eucalyptol, and entered the world market. Because of this, cajuput oil entered a slow decline and disappeared from the market in the US by the 1930's. The eucalyptol content of these new oils was the force behind cajuput oil's decline. Australia was the major producer of eucalyptol and eucalyptus globulus on a commercial basis until just after World War II. Since then, Brazil, Columbia, Spain, South Africa, Paraguay, Portugal, China and India have entered the market and Australia has greatly reduced its production. China also began producing a eucalyptus oil from the roots of the camphor tree. By 1980, China had become the dominant supplier of eucalyptus oils. As China's standard of living improves, the supply chain will again change. Look to India and Vietnam as the next commercial source of these products.

Producers and Capacity

It is estimated that the world production of eucalyptus oils and eucalyptol will reach 2500 Mtons and 800 Mtons, respectively, in 2000. The question of just how much eucalyptol could be produced is probably impossible to answer. More over, any estimate would be a guess. Because the production of eucalyptol is dependant upon the availability of eucalyptus globulus oil, that oil is the limiting factor for the production. The crude distillation units needed for the distillation of eucalyptus oil from wood chips are simple and low-cost. The capital investment is not a limiting factor. The eucalyptus tree grows in many areas of the world and in the wild, so the availability of biomass for the production of the oil is not the limiting factor. The only critical variable seems to be the price of eucalyptus oil on the open market. Once the price falls below a value where the local producer cannot hope to cover costs, they drop out of the market. Thus, the production has shifted over the years as rising

Table 3

ACEDSA		Spain
Bordas	Spain	
Cembracom		Brazil
Shanghai Native Prduce		China
Jindaldrugs		India
Keith Harris		Australia
Munoz	Spain	

Table 4. A comparison of eucalyptol and eucalyptus globulus oil prices, 1986-1997, in US$/lb

Year	Eucalyptol	Eucalyptus globulus oil
1986	3.65	2.40
1987	4.50	3.30
1988	6.50	4.85
1989	5.50	3.85
1990	5.75	3.75
1991	4.45	2.65
1992	5.20	3.00
1994	5.00	2.50
1993	5.20	2.90
1995	2.70	1.60
1996	3.85	2.35
1997	3.85	2.40

standards of living and stagnant prices have forced producers to stop production. The market is continuing to shift to always favor the lowest-cost producer. The trend will continue until the market price of eucalyptol reaches a level that favors its production by synthetic routes. The number of producers is many and the supply in excess of demand. Table 3 lists some of the major producers of pure eucalyptol.

Pricing

Eucalyptol prices parallel those of eucalyptus globulus oil. Both have remained low compared to other aroma-chemical prices over the past 50 years. The prices fluctuate, as do most natural products. The period 1986-1997 is typical of the eucalyptus market. In January, 2000, we see the prices at US$4 and US$2.25, respectively. The price of eucalyptus oil goes up and down in unpredictable cycles, but has always remained relatively low in comparison to other essential oils. In 1976 it was US1.77/lb. See Table 4 for a comparison.

Imports

The US has no producer of eucalyptol or eucalyptus globulus oil, thus everything used there is imported from some-

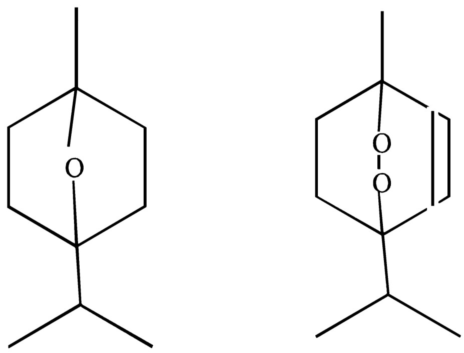


Figure 4. 1,4-Cineole and Ascaridole

where. Over the years, imports of both eucalyptol and eucalyptus globulus oil have shown only mild growth and stagnation in application of use in the US. In 1976, approximately 225,000 kilos of both materials were imported by the US. By the early 1990s, that volume had only grown to 350,000 kilos of both. Exact annual consumption figures are impossible to gage because imports vary widely year to year by 100,000kg or more. The stagnated growth rate is due to many factors; the decline in usage of liniments containing eucalyptol, the decline of its use in oral hygiene products, the growth of herbal cough drops and a shift of production of eucalyptus type cough drops globally.

Substitutes and Analogs

As far as direct chemical analogs are concerned, very little is available in this area. The isomer 1,4-Cineole, for example, is harder to come by and has a less desirable organoleptic profile. The peroxide ascaridole is found in nature in chenopodium (wormseed) oil and is considered a derivative of 1,4-Cineole (Figure 4).

The flavor area has little choice for a eucalyptus tone. In fragrances, eucalyptol's basic medicinal-camphoraeous impression can be mimicked by other materials. There are a large number of substituted cyclohexanol and derivatives that fall in this medicinal-camphoraeous category (see Figure 2).

Derivatives

There are many derivatives that a synthetic organic chemist could prepare in the laboratory, but none have been reported. Possibly because there is no commercial incentive to do so. Mother Nature has also been reluctant to provide derivatives of eucalyptol.

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