An Aroma Chemical Profile

Thymol

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The name *thymol* comes from the name of the herb thyme from which the aroma chemical was originally isolated, and, in turn, from the Greek word *Thymos* meaning positive disposition, elan, soul or spirit.

Our reference for organoleptic descriptions is based upon our cultural experiences. Those materials and products we encounter in our culture and the uses they find in our own world determine the vocabulary we use to describe the aroma chemicals and essential oils we utilize.

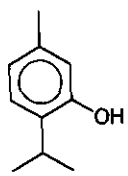
Thymol, because of its antiseptic properties, has found its major niche in the aroma chemical world in oral hygiene products that have medicinal value. Hence, the organoleptic description employed for thymol inevitably contains a reference to that use; that is, thymol is best defined as a sweet phenolic-herbal-medicinal odor with a similar taste description. Natural thymol that has been isolated from essential oil invariably is tinged with notes of carvacrol, a material that is described as being more dry-medicinal-phenol-tarry than thymol itself. Very little, if any, natural thymol is produced today as its price would be about ten-fold higher than the synthetic product available.

Until the 1940s, the world supply of thymol was mainly from natural sources, but with the advent of modern petrochemical catalysis, the situation rapidly changed so that all the thymol marketed today is of synthetic origin.

The commercially available material is all synthetic and all offerings are of such high purity that few problems occur in reproducibility of lots, unless inadvertent contamination has occurred in shipping or storage. As with many powdered materials, thymol will tend to collect foreign odors.

Thymol's major use in oral hygiene products is based upon its antiseptic properties. It is a strong antiseptic with a much lower toxicity than phenol, the original antiseptic of the English surgeon Joseph Lister; that is, the LD_{50} for rats is 980 mg/kg for thymol versus 530 mg/kg for phenol. Thymol also has strong fungicidal and anti-parasitic properties and was used in the past to prevent mold (such as on canvas for tents), to de-worm animals and humans, and as a

Thymol



Mwt 150 $C_{10}H_{14}O$
FEMA-GRAS 3066
CAS 89-83-8

Classification:
Dialkyl substituted phenol, found in nature chiefly in the plants of the species *Thymus* and *Monarda*. Displays fungicidal, antiseptic and anti-parasitic properties.

Additional Names:[1-3]
2-hydroxy-1-isopropyl-4-methyl benzene
5-methyl-2-isopropyl-1-phenol
5-methyl-2-isopropyl-1-hydroxy benzene
meta-thymol
3-para-cymenol
3-hydroxy-p-cymene
thyme camphor
p-isopropyl-m-cresol
French: Thymol *German:* Thymol
Portuguese: Timol *Spanish:* Timol

Physical Data:

Appearance:	white crystals
Boiling point:	@233°C
Melting point:	49-51.5°C
Flash point (TCC):	101°C
LD_{50} oral, rats:	980 mg/kg
Flavor threshold PPB:	50[4]

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Table I. Plant essential oils and thymol content

Plant essential oils	Thymol content
Monarda punctata	64-80%
Satureja montana	trace-66%
Origanum vulgare	0.4-65%
Ajowan seed	6-62%
Thymus vulgaris	25-58%
Marjoram Egyptian	21%
Mandarin oil	trace-15%

preservative for anatomical specimens. In oral hygiene products, it inhibits plaque formation.

Thymol currently finds its major use in such medicinal mouthwashes as Listerine,* usually in conjunction with eucalyptol, menthol and methyl salicylate. Minor applications for thymol are found in cough drops, toothpaste and as a flavor-touch additive in herbals, mints and citrus formulations. But these uses are very minor and isolated. Its use in fragrances, due to its hospital smell, only appears in such products as Absorbine Jr.** where it provides a marketing plus. Thymol is available in one standard grade N.F.

Natural Sources

Thymol is not widely prevalent in the plant kingdom and where it appears in practical amounts in a species, often subspecies of the plant will show widely divergent concentrations. Table I reports the species where the most thymol is encountered and the observed thymol concentration ranges.

Various industrial literature sources report that thymol was obtained by caustic (NaOH) extractions of the essential oils of *Thymus vulgaris* (common thyme), ajowan seed and *Ocimum gratissimum* (a basil subspecies). The basic process was to extract the oils with aqueous sodium hydroxide, which removed all the phenols and acids as their water-soluble sodium salts, and then release the organics from solution by acidification. The collected organics were then crystallized from various solvents including petroleum ether and ethanol. A good deal of the thymol thus produced was impure and displayed melting points of 43-48°C, whereas pure thymol melts at 49.5-51.5°C. The accompanying impurity was usually its isomeric phenol, carvacrol.

History

Impure thymol was isolated from *Thymus vulgaris* as early as 1719 by Neumann. However, the discovery is credited to Arppe who isolated and characterized it from horsemint (*Monarda sylvestris*) in 1846.[5] The use of thymol developed slowly because thymol's effect could be elicited by the use of thyme oil or Spanish origanum oil in both flavor and fragrance formulations.

*Trade name of Warner-Lambert Company
**Trade name of W. F. Young, Inc.

Table II. Essential oils as bactericides versus phenol (rated 1)[6]

Essential oil	Relative bactericidal effectiveness	Dominant aroma chemical
Oil of thyme	12.2	Thymol
Oil of clove	9.2	Eugenol
Oil of cinnamon	7.8	Cinnamic aldehyde
Oil of rose	7.0	Phenethyl alcohol
Oil of rue	6.4	Undecanone
Oil of rosemary	5.4	Cineol
Oil of lavender	4.4	Linalyl acetate
Oil of ylang-ylang	2.8	Benzyl acetate

In 1867, Joseph Lister began the then controversial practice of using phenol (carbolic acid) as an antiseptic in surgery and to treat wounds. Phenol was effective, but the painful irritation it caused prompted others to seek more potent and painless agents. This search led to the use of thymol, ethanol and iodine tinctures to treat wounds. Once the antiseptic nature of thymol was established, thymol, as well as other essential oils and their derivatives, were harnessed for the commercial production of medicinal preparations, which eventually led to thymol's use—along with eucalyptol, menthol and methyl salicylate—in oral hygiene products. The antiseptic properties of these aroma chemicals have been found to control the germs that cause plaque in the human mouth. Many of these antiseptic materials were referred to, at the time, as Lister agents.

Essential oils, in general, are bacteriostats, preventing the growth of bacteria. Many are also bactericides, actually killing bacteria. The bactericidal effectiveness of some selected essential oils (compared to phenol) is presented in Table II, along with the dominant aroma chemical found in each oil. Note that the bactericidal action often is a result of more than one constituent, and combinations of materials have been shown to be synergistic.

Thyme oil was used before the mid-1800s in fragrance compositions (such as the millefleurs popular in France in the 1600-1700s), but the changing application for thyme resulted in its gradual decline in use.

The use of thymol as a medicinal-preservative reflected itself in a distinct prejudice toward the material as to its use in fragrances and flavors. One frequently encounters the smell of thymol in a hospital setting—with all its negative emotional connotations. Humans naturally want to avoid such experiences and the secondary impressions associated with them. The hospital smell is hardly romantic or palate-appealing.

Piesse[7] states in 1891 that thymol has practically no use in perfumery except for medicinal soaps and that its main use is for its antiseptic properties. Mann[8] remarks in 1911 that its use is mainly relegated to toothpaste and mouthwash as aroma chemical, and in soap via the use of white thyme

Table III. 1995 World consumption of thymol in MTons (estimated)

Uses	MTons
Spices, direct	40
Essential oils	30
Flavors	90
Chemical intermediates	1900
Total	**2060**

Table IV. 1995 Regional consumption of thymol in MTons from all sources (estimated)

Regions	MTons
North America	57
Europe	1865
Asia	123
Other	15
Total	**2060**

oil. The Polak and Schwartz catalog of 1927 states that "on account of its antiseptic properties, it is used in dentrifices, cosmetics and in the medicine." Gebhardt (1931) gives some formula usage in mouthwash and toothpaste.[9] Only Poucher[10] lists a use in a now forgotten cologne named "Eau de Berlin" at a 2% formula level. More recent reports indicate that thymol's direct use in fragrances has literally disappeared; where that particular note is needed, such as in men's "country" type colognes, the need is filled by the use of thyme oil itself.

The use of thyme oil in oral hygiene products and pharmaceuticals created a demand for a more soluble thyme note, which resulted in the use of the purified main ingredient, thymol, obtained from thyme oil or ajowan seed oil via caustic extraction. These oils were the major source of thymol until WWII, because no economical, viable synthetic method of production had yet been developed.

The shortage of menthol that developed about 1940 in the US led firms to explore the possibility of producing synthetic menthol from thymol. In particular, Givaudan and Heyden-Newport, now part of Reichold Chemical, developed viable processes for the production of synthetic thymol in order to supply racemic menthol to the pharmaceutical industry. Their production of thymol also satisfied the needs for thymol in that market. In the 1970s, Haarmann & Reimer began offering thymol produced from Bayer's by-product meta cresol by vapor phase catalytic alkylation using propylene. The bulk of this thymol production is used to produce menthol products, and the excess capacity is available to the world market as synthetic thymol N.F.

World Consumption

Total world consumption of thymol from both natural and synthetic sources is estimated at 2,060 MTons for 1995 (Tables III and IV).

Pricing

Synthetic thymol N.F. grade is readily available as a fine powder exceeding 99% purity, priced in the $3.50-4.00/lb range.

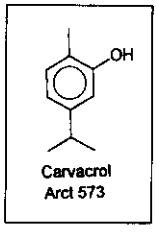
Supply and Current Producers

Of the current market suppliers for synthetic thymol, the

largest by far is Haarmann & Reimer GmbH with a production capacity estimated at more than 2500 MTons per year. Over the past 12 years, Schering AG, Sumitomo and Osaka have offered thymol, but they all now appear to have withdrawn from the market.

Substitutes, Analogues and Isomers

There are no true substitutes for thymol which possess its rather distinct phenolic medicinal notes. The closest product having thymol-like organoleptic properties is its isomer carvacrol, which can readily be made synthetically from p-cymene.



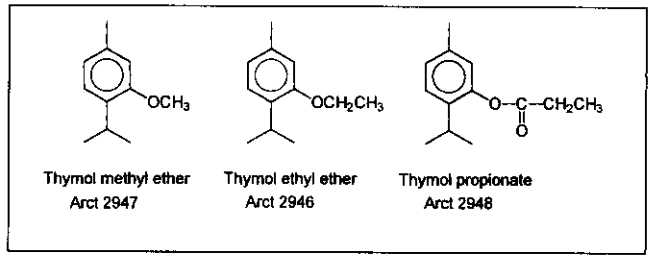
Carvacrol
Arct 573

The few derivatives of thymol available to the flavor and fragrance industry are seldom used and, if so, only in a minor way.

The acetate of thymol is listed in the Merck Index 9247 with the warning it is an irritant as well as an antiseptic.

Derivatives

Some derivatives of thymol have been used by the chemical and pharmaceutical industries over the years. The most interesting of these was probably the thymol-based pH indicators. Until the 1950s, the main laboratory method



Thymol methyl ether
Arct 2947

Thymol ethyl ether
Arct 2946

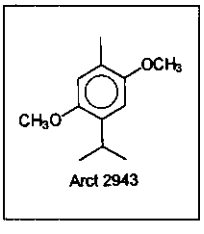
Thymol propionate
Arct 2948

Table V. Thymol-based pH indicators

Indicator	pH Range	Color change
acid-thymol blue	1.2-2.8	red to yellow
brom-thymol blue	6.0-7.6	yellow to blue
thymol blue	8.0-9.6	yellow to blue

of determining the acidity-basicity (pH) of an aqueous system was by the use of standard pH indicators, as the pH-meter was not yet a commercial product. A standard set of some 16 indicators allowed the estimation of the approximate pH of aqueous systems over the range 1.0 to 14.0. It was necessary to use buffer solutions (Clark and Lubs buffers) to standardize the analysis, and thymol itself was added to the buffer solution to prevent the growth of mold. In addition, thymol furnished the basis of two of these standard indicators: thymol blue (thymol sulfonphthalein) and brom-thymol blue, which in turn provided pHs to be determined by their color changes (Table V).

The derivative thymol hydroquinone dimethyl ether is reported to have a fennel-like odor and is found in a native US *Liatris* plant called dog fennel or Mayweed.



Arct 2943

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