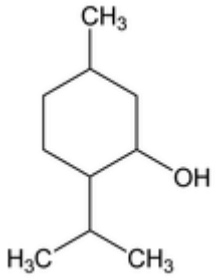
Menthol



$C_{10}H_{20}O$ 156.27
Cyclohexanol, 5-methyl-2-(1-methylethyl)- CAS RN®: 1490-04-6.

DEFINITION

Menthol is an alcohol obtained from oils derived from a variety of mints or prepared synthetically. Menthol may be levorotatory (*l*-menthol) from natural or synthetic sources, or racemic (*dl*-menthol). It contains NLT 98.0% and NMT 102.0% of menthol ($C_{10}H_{20}O$).

IDENTIFICATION

- **A.** The retention time of the major peak from the *Sample solution* corresponds to that of the menthol peak from the *Standard solution*, as obtained in the *Assay*.
- **B.** It meets the requirements in the test for *Optical Rotation*.

ASSAY

Change to read:

- **Procedure**

▲Internal standard solution: 10 mg/mL of 1-butanol in hexanes▲ (USP 1-Dec-2022)
Standard solution: 10 mg/mL of USP Menthol RS in ▲the *Internal standard solution*▲ (USP 1-Dec-2022)
Sample solution: 10 mg/mL of Menthol in ▲the *Internal standard solution*▲ (USP 1-Dec-2022)
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: GC
Detector: Flame ionization
Column: 0.18-mm × 20-m fused silica; coated with a 0.18-µm film of stationary phase G16
Temperatures
Injection port: 250°
Detector: 260°
Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
60	20	110	10

Carrier gas: Hydrogen
Flow rate: 0.9 mL/min
Injection volume: 0.5 µL
Injection type: Split ratio, 50:1
System suitability
Sample: *Standard solution*
▲ [NOTE—The relative retention times for the internal standard and menthol are about 0.27 and 1.00, respectively.]▲ (USP 1-Dec-2022)
Suitability requirements
Relative standard deviation: NMT 2.0% for ▲the ratio of menthol to internal standard peak responses▲ (USP 1-Dec-2022) in replicate injections
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of menthol ($C_{10}H_{20}O$) in the portion of Menthol taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak ▲response ratio▲ (USP 1-Dec-2022) of menthol ▲to the internal standard▲ (USP 1-Dec-2022) from the *Sample solution*
r_S = peak ▲response ratio▲ (USP 1-Dec-2022) of menthol ▲to the internal standard▲ (USP 1-Dec-2022) from the *Standard solution*
C_S = concentration of USP Menthol RS in the *Standard solution* (mg/mL)
C_U = concentration of Menthol in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0%

IMPURITIES

- **Limit of Nonvolatile Residue**

Analysis: Evaporate 2 g, accurately weighed, in a tared open porcelain dish on a steam bath, and dry the residue at 105° for 1 h.
Acceptance criteria: NMT 0.05%

Change to read:

- **Related Compounds**

▲Internal standard solution,▲ (USP 1-Dec-2022) Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Analysis
Sample: *Sample solution*
Calculate the percentage of each individual impurity in the portion of Menthol taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak area of each impurity from the *Sample solution*
r_T = sum of the peak areas from the *Sample solution*

Acceptance criteria
Individual impurities: NMT 0.5% for isomenthol (relative retention time is 1.08) from synthetic racemic menthol and 0.3% for all other impurities from natural and synthetic menthol
Total impurities: NMT 2.0%

- **Readily Oxidizable Substances in *dl*-Menthol**

Sample solution: Place 500 mg of *dl*-menthol in a clean, dry test tube. Add 10 mL of a solution of potassium permanganate, prepared by diluting 3 mL of 0.1 N potassium permanganate with water to 100 mL.
Analysis: Place the test tube in a beaker with water at a temperature between 45° and 50°. Remove the tube from the bath at intervals of 30 s, and mix quickly by shaking.
Acceptance criteria: The purple color of potassium permanganate is still apparent after 5 min.

SPECIFIC TESTS

- **Congealing Range of *dl*-Menthol**

(See *Congealing Temperature* ⟨651⟩.)

Official

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[NOTE—Perform this test preferably in a room with a temperature below 30° and a relative humidity below 50%.]

Sample: 10 g of *dl*-menthol, previously dried in a desiccator over silica gel for 24 h

Analysis: Place the *Sample* in a dry test tube with an internal diameter of 18–20 mm, and melt the contents at a temperature of about 40°. Suspend the test tube in water at a temperature of 23°–25°, and stir the contents of the tube continually with a thermometer, keeping the bulb of the thermometer immersed in the liquid.

Acceptance criteria: *dl*-Menthol congeals at a temperature between 27° and 28°. Shortly after the temperature has stabilized at the congealing point, add a few milligrams of dried *dl*-menthol to the congealed mass, and continue stirring. After a few min, the temperature of the mass quickly rises to 30.5°–32.0°.

- **MELTING RANGE OF *l*-MENTHOL** (See *Melting Range or Temperature* ⟨741⟩.)
  Acceptance criteria: 41°–44°
- **OPTICAL ROTATION** ⟨781S⟩**,** *Procedures, Specific Rotation*
  Sample solution: 100 mg/mL in alcohol
  Acceptance criteria
  ***l*-Menthol:** –45° to –51°
  ***dl*-Menthol:** –2° to +2°

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, preferably at controlled room temperature.
- **LABELING:** Label it to indicate whether it is levorotatory or racemic.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Menthol RS

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