

Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

Menthol

Published on: 07 February, 2024

Last date for comments: 22 March, 2024

This draft proposal contains monograph text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to revisions before publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

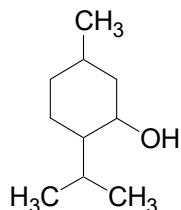
Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

Description	Details
Document version	1.0
First draft published on IPC website for public comments	February 7, 2024
Last date for comments	March 22, 2024
Monograph revisions proposed for inclusion in	IP 2026
Tentative effective date of monograph revisions	July, 2026
Draft revision published on IPC website for public comments	--
Further follow-up action as required.	

Menthol. Page 2857

Change to: **Menthol**



C₁₀H₂₀O

Mol. Wt.156.3

Menthol is cyclohexanol, 5-methyl-2-(1-methylethyl). It is an alcohol obtained from oils derived from a variety of mints or prepared synthetically. Menthol may be levorotatory (-) from natural or synthetic sources, or racemic (±).

Menthol contains not less than 98.0 per cent and not more than 102.0 per cent of C₁₀H₂₀O.

Category. Topical antipruritic.

Description. A colourless, hexagonal or needle-like crystals, or infused masses or a crystalline powder; has a pleasant, peppermint-like odour.

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *menthol IPRS* or with the reference spectrum of menthol.

B. Dissolve 10 mg in 1 ml of *sulphuric acid* and add 1 ml of 1 per cent w/v solution of *vanillin* in *sulphuric acid*, an orange-yellow colour is produced. Add 1 ml of *water*, the colour changes to violet (distinction from thymol).

C. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Tests

Appearance of solution. Dissolve 1.0 g in 10 ml of *ethanol (95 per cent)*. The solution is not more opalescent than opalescence standard OS4 (2.4.1), and not more intensely coloured than reference solution RS6 (2.4.1).

Acidity. To 1.0 g in a 100-ml glass-stoppered conical flask, add 20 ml of *water*, boil until dissolution is complete, cool, stopper the flask and shake vigorously for 1 minute. Add a few crystals of the substance under examination to initiate crystallisation, shake vigorously for 1 minute and filter. To 5 ml of the filtrate, add 0.05 ml of *methyl red solution* and 0.05 ml of 0.01M *sodium hydroxide*; the solution is yellow.

Specific optical rotation (2.4.22). (for (-)-menthol) -51° to -45°, (for (±)-menthol) -2° to +2°, determined in a 10.0 per cent w/v solution in *ethanol (95 per cent)*.

Congearing range (2.4.10). (for (±)-menthol) 27.0° to 28.0°, on prolonged stirring, the temperature rises 30.5° to 32°.

Melting range of (-) menthol. 41°– 44°.

Related substances. Determine by gas chromatography (2.4.13).

Internal standard solution. A 1.0 per cent w/v solution of *1-butanol IPRS* in *hexane*.

Test solution. Dissolve 0.1 g of the substance under examination in internal standard solution and dilute to 10.0 ml with internal standard solution.

Reference solution. A 1.0 per cent w/v solution of *menthol IPRS* in internal standard solution.

Chromatographic system

- a fused silica capillary column 20 m x 0.18 mm, coated with polyethylene glycol compound (Average Mol. Wt. about 15000) film thickness 0.18 μm , (Such as DB-Heavy WAX),
- temperature:
 - column 60° to 110° @ 20° per minute and hold at 110° for 10 minutes,
- injection port at 250° and the detector at 260°,
- flame ionization detector,
- split ratio: 50:1,
- flow rate: 0.9 ml per minute, using hydrogen as the carrier gas,
- injection volume: 0.5 μl

The relative retention time with reference to menthol, for internal standard solution is about 0.27.

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections the ratio of menthol to internal standard solution is not more than 2.0 per cent.

Inject the test solution. The area of any peak corresponding to isomenthol (relative retention time is about 1.08) from synthetic racemic menthol from natural and synthetic menthol is not more than 0.5 per cent and the sum of the areas of all the secondary peaks is not more than 2.0 per cent, calculated by area normalization.

Readily Oxidizable Substances in (\pm) Menthol.

Transfer 0.5 g of \pm menthol to a dry test tube and add 10 ml of 3 per cent v/v solution of 0.1 M *potassium permanganate*.

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 seconds, and mix quickly by shaking. The purple colour of potassium permanganate is still apparent after 5 minutes.

Residue on evaporation. Evaporate 2.0 g in a tarred open porcelain dish on a steam-bath and dry the residue at 105° for 1 hour. The residue weighs not more than 1.0 mg (0.05 per cent).

Assay. Determine by gas chromatography (2.4.13), as described under Related substances.

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $\text{C}_{10}\text{H}_{20}\text{O}$.

Storage. Store protected from moisture at a temperature not exceeding 30°.

Labelling. The label states whether it is levorotatory or racemic menthol.