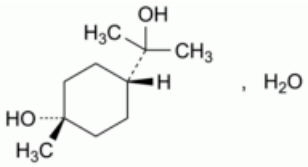
Edition: BP 2025 (Ph. Eur. 11.6 update)

Terpin Monohydrate

General Notices

(Ph. Eur. monograph 2940)



$C_{10}H_{20}O_2,H_2O$ 190.3 *2451-01-6*

Action and use

Expectorant.

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DEFINITION

(1*s*,4*s*)-4-(2-Hydroxypropan-2-yl)-1-methylcyclohexan-1-ol monohydrate.

Content

98.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Slightly soluble in water, soluble in ethanol (96 per cent), slightly soluble in methylene chloride.

mp

About 117 °C.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *terpin monohydrate CRS*.

B. Water (see Tests).

TESTS

Solution S

Dissolve 2.50 g in *ethanol (96 per cent) R* and dilute to 50.0 mL with the same solvent.

Appearance of solution

Solution S is clear (2.2.1) and colourless (2.2.2, Method II).

Acidity or alkalinity

To 10 mL of solution S add 0.1 mL of *bromothymol blue solution R1*. Not more than 0.2 mL of *0.02 M sodium hydroxide* or *0.02 M hydrochloric acid* is required to change the colour of the indicator.

Related substances

Gas chromatography (2.2.28): use the normalisation procedure.

Internal standard solution Dissolve 0.500 g of *biphenyl R* in 1 mL of *methylene chloride R* and dilute to 25.0 mL with *methanol R*.

Test solution (a) Dissolve 0.375 g of the substance to be examined in *methanol R* and dilute to 25.0 mL with the same solvent.

Test solution (b) Dissolve 85.0 mg of the substance to be examined in *methanol R*, add 2.0 mL of the internal standard solution and dilute to 100.0 mL with *methanol R*.

Reference solution (a) Dissolve the contents of a vial of *terpin impurity D CRS* in 1 mL of test solution (a).

Reference solution (b) Dissolve 85.0 mg of *terpin monohydrate CRS* in *methanol R*, add 2.0 mL of the internal standard solution and dilute to 100.0 mL with *methanol R*.

Column:

— *material*: fused silica;

— *size*: *l* = 30 m, Ø = 0.32 mm;

— *stationary phase*: *methylpolysiloxane R* (film thickness 1.0 µm).

Carrier gas *helium for chromatography R*.

Flow rate 1 mL/min.

Split ratio 1:10.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 11	180
	11 - 14	180 → 270
	14 - 15	270
Injection port		220

	Time (min)	Temperature (°C)
Detector		300

Detection Flame ionisation.

Injection 1 µL of test solution (a) and reference solution (a).

Relative retention With reference to terpin (retention time = about 6.3 min): impurity D = about 1.05; internal standard = about 1.2.

System suitability Reference solution (a):

— *peak-to-valley ratio*: minimum 3, where H_p = height above the baseline of the peak due to impurity D and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to terpin.

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.3 per cent;

— *reporting threshold*: 0.05 per cent.

Water (*2.5.12*)

8.0 per cent to 10.0 per cent, determined on 0.200 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Gas chromatography (*2.2.28*) as described in the test for related substances with the following modification.

Injection 0.5 µL of test solution (b) and reference solution (b).

Calculate the percentage content of terpin using the following expression:

$$\frac{\text{———————}}{\text{———————}}$$

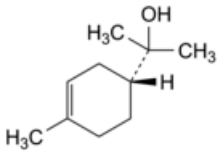
A_1	=	area of the peak due to terpin in the chromatogram obtained with test solution (b);
A_2	=	area of the peak due to terpin in the chromatogram obtained with reference solution (b);
A_3	=	area of the peak due to the internal standard in the chromatogram obtained with test solution (b);
A_4	=	area of the peak due to the internal standard in the chromatogram obtained with reference solution (b);
m_1	=	mass of the substance to be examined used to prepare test solution (b), in milligrams;
m_2	=	mass of *terpin monohydrate CRS* used to prepare reference solution (b), in milligrams.

STORAGE

In an airtight container, protected from light.

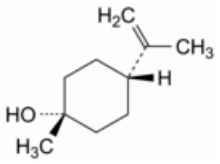
IMPURITIES

Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *A, B, C, D.*

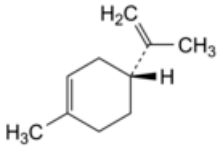


and enantiomer

A. 2-[(1*RS*)-4-methylcyclohex-3-en-1-yl]propan-2-ol (α-terpineol),

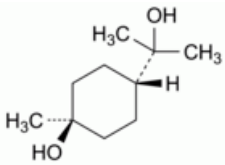


B. (1*s*,4*s*)-1-methyl-4-(prop-1-en-2-yl)cyclohexan-1-ol (*cis*-β-terpineol),



and enantiomer

C. (4*RS*)-1-methyl-4-(prop-1-en-2-yl)cyclohex-1-ene (limonene),



D. (1*r*,4*r*)-4-(2-hydroxypropan-2-yl)-1-methylcyclohexan-1-ol (*trans*-terpin).

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