



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

Dihydrocodeine Oral Solution

[General Notices](#)

Action and use

Opioid receptor agonist; analgesic.

DEFINITION

Dihydrocodeine Oral Solution is a solution of Dihydrocodeine Tartrate in a suitable flavoured vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

Content of dihydrocodeine tartrate, $C_{18}H_{23}NO_3$, $C_4H_6O_6$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Carry out the following procedure protected from light. To a volume of the oral solution containing 20 mg of Dihydrocodeine Tartrate add 10 mL of [water](#) and extract with two 25-mL quantities of [cyclohexane](#). Discard the cyclohexane extracts, add 3 mL of 5M [sodium hydroxide](#) to the aqueous layer, mix and extract with 25 mL of [cyclohexane](#). Wash the cyclohexane layer with 10 mL of [water](#), shake with [anhydrous sodium sulfate](#) and filter. Wash the filter with [cyclohexane](#) and evaporate the combined filtrate and washings to dryness. Dissolve the residue in 1 mL of [dichloromethane](#) and apply 0.2 mL dropwise on to the surface of a disc prepared using 0.3 g of [potassium bromide](#), allowing the solvent to evaporate between applications, and dry the disc at 50° for 2 minutes. The [infrared absorption spectrum, Appendix II A](#), is concordant with the [reference spectrum](#) of dihydrocodeine ([RS 102](#)).

TESTS

Related substances

Carry out the following test protected from light. Carry out the method for [liquid chromatography, Appendix III D](#), using the following solutions in the mobile phase.

- (1) Dilute a quantity of the oral solution to produce a solution containing 0.1% w/v of Dihydrocodeine Tartrate.
- (2) Dilute 1 volume of solution (1) to 200 volumes.
- (3) 0.04% w/v each of [dihydrocodeine tartrate BPCRS](#) and [codeine phosphate BPCRS](#).
- (4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (25 cm × 4.6 mm) packed with [octylsilyl silica gel for chromatography](#) (5 µm) (Hypersil Gold C8 is suitable).
- (b) Use gradient elution and the mobile phase described below.
- (c) Use a flow rate of 1 mL per minute.

- (d) Use an ambient column temperature.
- (e) Use a detection wavelength of 284 nm.
- (f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A To 1.0 g of [sodium heptanesulfonate](#), add 10 mL of [glacial acetic acid](#) and 4 mL of a solution containing 5 mL of [triethylamine](#) diluted to 25 mL with a mixture of equal volumes of [acetonitrile](#) and [water](#). Add 170 mL of [acetonitrile](#) and dilute to 1000 mL with [water](#).

Mobile phase B [acetonitrile](#)

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-20	100	0	isocratic
20-25	100→20	0→80	linear gradient
25-40	20	80	isocratic
40-45	20→100	80→0	linear gradient
45-50	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the retention relative to dihydrocodeine (retention time about 11 minutes) of codeine is about 1.1.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the [resolution](#) between the peaks due to dihydrocodeine and codeine is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to codeine is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any other [secondary peak](#) is not greater than 0.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%).

the sum of the areas of any [secondary peaks](#) is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

Carry out the following procedure protected from light. Carry out the method for [liquid chromatography, Appendix III D](#), using the following solutions.

- (1) Disperse a weighed quantity of the oral solution containing 25 mg of Dihydrocodeine Tartrate in 25 mL of mobile phase A and filter. Dilute 1 volume to 10 volumes with mobile phase A.
- (2) 0.01% w/v of [dihydrocodeine tartrate BPCRS](#) in [water](#).
- (3) 0.04% w/v each of [dihydrocodeine tartrate BPCRS](#) and [codeine phosphate BPCRS](#) in mobile phase A.

CHROMATOGRAPHIC CONDITIONS

Use the conditions described under Related substances.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the [*resolution*](#) between the peaks due to dihydrocodeine and codeine is at least 2.0.

DETERMINATION OF CONTENT

Determine the [*weight per mL*](#) of the oral solution, [Appendix V G](#), and calculate the content of $C_{18}H_{23}NO_3$, $C_4H_6O_6$, weight in volume, using the declared content of $C_{18}H_{23}NO_3$, $C_4H_6O_6$ in [*dihydrocodeine tartrate BPCRS*](#).

STORAGE

Dihydrocodeine Oral Solution should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Dihydrocodeine Tartrate.