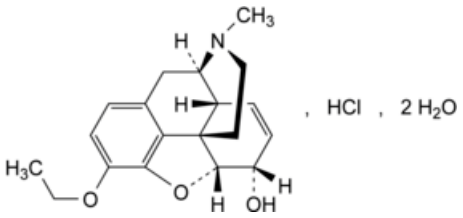
Edition: BP 2025 (Ph. Eur. 11.6 update)

Ethylmorphine Hydrochloride

General Notices

(Ph. Eur. monograph 0491)



$C_{19}H_{24}ClNO_3,2H_2O$ 385.9

Action and use

Opioid receptor agonist; analgesic.

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DEFINITION

7,8-Didehydro-4,5α-epoxy-3-ethoxy-17-methylmorphinan-6α-ol hydrochloride dihydrate.

Content

99.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Soluble in water and in ethanol (96 per cent), insoluble in cyclohexane.

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (2.2.24).

Comparison Ph. Eur. reference spectrum of ethylmorphine hydrochloride.

B. In a test-tube, dissolve 0.5 g in 6 mL of water R and add 15 mL of 0.1 M sodium hydroxide. Scratch the wall of the tube with a glass rod. A white, crystalline precipitate is formed. Collect the precipitate, wash and dissolve in 20 mL of water R heated to 80 °C. Filter and cool in iced water. The crystals, after drying *in vacuo* for 12 h, melt (2.2.14) at 85 °C to 89 °C.

C. To about 10 mg add 1 mL of sulfuric acid R and 0.05 mL of ferric chloride solution R2. Heat on a water-bath. A blue colour develops. Add 0.05 mL of nitric acid R. The colour becomes red.

D. Solution S (see Tests) gives reaction (a) of chlorides (2.3.1).

TESTS

Solution S

Dissolve 0.500 g in carbon dioxide-free water R and dilute to 25.0 mL with the same solvent.

Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution BY_6 (2.2.2, Method II).

Acidity or alkalinity

To 10 mL of solution S add 0.05 mL of methyl red solution R and 0.2 mL of 0.02 M hydrochloric acid, the solution is red. Add 0.4 mL of 0.02 M sodium hydroxide, the solution becomes yellow.

Specific optical rotation (2.2.7)

-102 to -105 (anhydrous substance), determined on solution S.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 50.0 mg of the substance to be examined in the mobile phase and dilute to 20.0 mL with the mobile phase.

Reference solution (a) Dilute 1.0 mL of the test solution to 25.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 20.0 mL with the mobile phase.

Reference solution (b) Dissolve 12.5 mg of codeine R in the mobile phase and dilute to 5.0 mL with the mobile phase.

Reference solution (c) Dilute 0.5 mL of reference solution (b) to 100.0 mL with the mobile phase.

Reference solution (d) To 1.0 mL of the test solution, add 1.0 mL of reference solution (b) and dilute to 50.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm,

— *stationary phase*: octylsilyl silica gel for chromatography R (5 µm),

— *temperature*: 30 °C.

Mobile phase Add 1.25 g of sodium heptanesulfonate R to a mixture of 12.5 mL of glacial acetic acid R and 5 mL of a 20 per cent *V/V* solution of triethylamine R in a mixture of equal volumes of methanol R and water R. Dilute to 1000 mL with water R. To 550 mL of this solution add 450 mL of methanol R.

Flow rate 1 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 10 µL.

Run time 4 times the retention time of ethylmorphine.

Relative retention With reference to ethylmorphine (retention time = about 6.2 min): impurity B = about 0.7; impurity C = about 0.8; impurity D = about 1.3; impurity A = about 2.5.

System suitability Reference solution (d):

— *resolution*: minimum 5 between the peaks due to ethylmorphine and impurity C.

Limits:

— *correction factor*: for the calculation of content, multiply the peak area of impurity D by 0.4,

— *impurities A, B, D*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent),

— *impurity C*: not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent),

— *any other impurity*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent),

— *total of impurities other than C*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent),

— *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Water (*2.5.12*)

8.0 per cent to 10.0 per cent, determined on 0.250 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.300 g in a mixture of 5 mL of *0.01 M hydrochloric acid* and 30 mL of *alcohol R*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

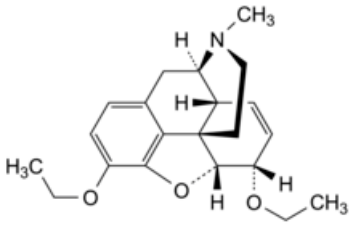
1 mL of *0.1 M sodium hydroxide* is equivalent to 34.99 mg of $C_{19}H_{24}ClNO_3$.

STORAGE

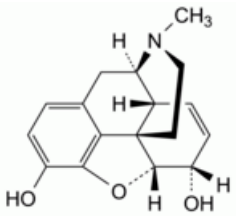
Protected from light.

IMPURITIES

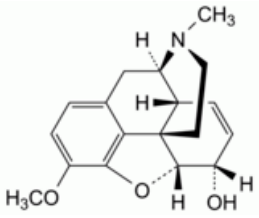
Specified impurities *A, B, C, D.*



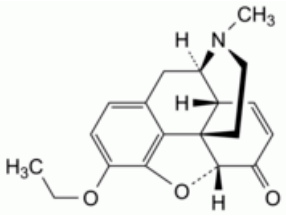
A. 7,8-didehydro-4,5α-epoxy-3,6α-diethoxy-17-methylmorphinan,



B. 7,8-didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol (morphine),



C. 7,8-didehydro-4,5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol (codeine),



D. 7,8-didehydro-4,5α-epoxy-3-ethoxy-17-methylmorphinan-6-one (ethylmorphinone).

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