Chlorides (*2.4.4*): maximum 0.5 per cent.

Dilute 1 ml of solution S to 15 ml with *water R*.

Heavy metals (*2.4.8*): maximum 20 ppm.

1.0 g complies with test C. Prepare the reference solution using 2 ml of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 7.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulphated ash (*2.4.14*): maximum 1.6 per cent, determined on 1.0 g using a platinum crucible.

LABELLING

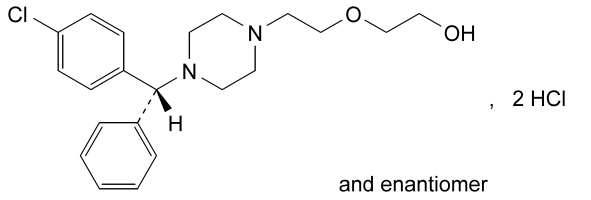
The label states:

- the apparent viscosity in millipascal seconds for a 2 per cent *m/m* solution,
- for a product of low viscosity, the concentration of the solution to be used and the apparent viscosity in millipascal seconds,
- where applicable, that the substance contains silica.

01/2008:0916
corrected 6.0

HYDROXYZINE HYDROCHLORIDE

Hydroxyzini hydrochloridum



$C_{21}H_{29}Cl_3N_2O_2$ M_r 447.8
[2192-20-3]

DEFINITION

(*RS*)-2-[2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]ethanol dihydrochloride.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, hygroscopic, crystalline powder.

Solubility: freely soluble in water and in ethanol (96 per cent), very slightly soluble in acetone.

mp: about 200 °C, with decomposition.

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *hydroxyzine hydrochloride CRS*.

B. Thin-layer chromatography (*2.2.27*).

Solvent mixture: *methanol R, methylene chloride R* (50:50 *V/V*).

Test solution. Dissolve 0.50 g of the substance to be examined in the solvent mixture and dilute to 10 ml with the solvent mixture.

Reference solution (a). Dissolve 0.50 g of *hydroxyzine hydrochloride CRS* in the solvent mixture and dilute to 10 ml with the solvent mixture.

Reference solution (b). Dissolve 0.50 g of *meclozine hydrochloride R* in the solvent mixture and dilute to 10 ml with the solvent mixture. Dilute 1 ml of this solution to 2 ml with reference solution (a).

Plate: *TLC silica gel G plate R*.

Mobile phase: *concentrated ammonia R, ethanol (96 per cent) R, toluene R* (1:24:75 *V/V/V*).

Application: 2 µl.

Development: over a path of 15 cm.

Drying: in air.

Detection: spray with *potassium iodobismuthate solution R2*.

System suitability: reference solution (b):

- the chromatogram shows 2 clearly separated principal spots.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a).

C. Dissolve 0.1 g in *ethanol (96 per cent) R* and dilute to 15 ml with the same solvent. Add 15 ml of a saturated solution of *picric acid R* in *ethanol (96 per cent) R*. Allow to stand for 15 min. A precipitate is formed. Filter. Recrystallise from *ethanol (96 per cent) R*. Initiate crystallisation, if necessary, by scratching the wall of the tube with a glass rod. The crystals melt (*2.2.14*) at 189 °C to 192 °C.

D. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 2.0 g in *water R* and dilute to 20.0 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_7 (*2.2.2, Method II*).

Optical rotation (*2.2.7*): – 0.10° to + 0.10°, determined on solution S.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 10.0 mg of the substance to be examined in the mobile phase and dilute to 10.0 ml with the mobile phase.

Reference solution (a). Dissolve 10.0 mg of *hydroxyzine hydrochloride CRS* in the mobile phase and dilute to 10.0 ml with the mobile phase.

Reference solution (b). Dilute 3.0 ml of the test solution to 200.0 ml with the mobile phase. Dilute 5.0 ml of this solution to 25.0 ml with the mobile phase.

Column:

- *size*: *l* = 0.15 m, Ø = 4.6 mm;
- *stationary phase*: *base-deactivated octadecylsilyl silica gel for chromatography R* (3 µm).

Mobile phase: dissolve 0.5 g of *sodium methanesulphonate R* in a mixture of 14 ml of *triethylamine R*, 300 ml of *acetonitrile R* and 686 ml of *water R*, then adjust to pH 2.7 with *sulphuric acid R*.

Flow rate: 1 ml/min.

Detection: spectrophotometer at 230 nm.

Injection: 20 µl.

Run time: 2.5 times the retention time of hydroxyzine.

System suitability: reference solution (a):

– *peak-to-valley ratio*: minimum 10, where H_p = height above the baseline of the peak immediately before the peak due to hydroxyzine and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to hydroxyzine.

Limits:

– *any impurity*: for each impurity, not more than 1/3 of the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent);

– *total*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);

– *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.03 per cent).

Heavy metals (*2.4.8*): maximum 10 ppm.

12 ml of solution S complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 5.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

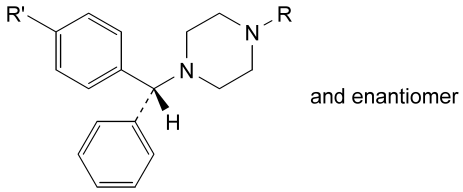
Dissolve 0.200 g in 10 ml of *anhydrous acetic acid R*. Add 40 ml of *acetic anhydride R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M perchloric acid* is equivalent to 22.39 mg of $C_{21}H_{29}Cl_3N_2O_2$.

STORAGE

In an airtight container, protected from light.

IMPURITIES



and enantiomer

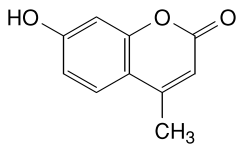
A. R = H, R′ = Cl: (*RS*)-1-[(4-chlorophenyl)phenylmethyl]-piperazine,

B. R = CH_2-CH_2-O-CH_2-CH_2-OH, R′ = H: 2-[2-[4-(diphenylmethyl)piperazin-1-yl]ethoxy]ethanol (decloxizine).

01/2008:1786
corrected 6.0

HYMECROMONE

Hymecromonum



$C_{10}H_8O_3$ M_r 176.2
[90-33-5]

DEFINITION

7-Hydroxy-4-methyl-2*H*-1-benzopyran-2-one.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: almost white crystalline powder.

Solubility: very slightly soluble in water, sparingly soluble in methanol, slightly soluble in methylene chloride. It dissolves in dilute solutions of ammonia.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *hymecromone CRS*.

TESTS

Absorbance (*2.2.25*). Dissolve 50 mg in 10 ml of *ammonium chloride buffer solution pH 10.4 R* and dilute to 100.0 ml with *water R*. To 1.0 ml of the solution, add 10 ml of *ammonium chloride buffer solution pH 10.4 R* and dilute to 100.0 ml with *water R*. Examined between 200 nm and 400 nm, the solution shows 2 absorption maxima, at 229 nm and 360 nm, and an absorption minimum at 276 nm. The specific absorbance at the maximum at 360 nm is 1020 to 1120.

Related substances. Liquid chromatography (*2.2.29*).

Buffer solution. To 280 ml of a 1.56 g/l solution of *sodium dihydrogen phosphate R*, add 720 ml of a 3.58 g/l solution of *disodium hydrogen phosphate R*. Adjust to pH 7 with a 100 g/l solution of *phosphoric acid R*.

Test solution. Dissolve 10 mg of the substance to be examined in the mobile phase and dilute to 10.0 ml with the mobile phase.

Reference solution (a). Dissolve 20 mg of *hymecromone CRS*, 10 mg of *hymecromone impurity A CRS* and 10 mg of *hymecromone impurity B CRS* in the mobile phase and dilute to 100.0 ml with the mobile phase.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 200.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4 mm,

– *stationary phase*: spherical *octadecylsilyl silica gel for chromatography R* (10 µm).

Mobile phase: *methanol R*, buffer solution (465:535 *V/V*).

Flow rate: 1.0 ml/min.

Detection: spectrophotometer at 270 nm.

Injection: 20 µl.

Run time: 1.5 times the retention time of hymecromone.

Relative retention with reference to hymecromone (retention time = about 6 min): impurity A = about 0.5; impurity B = about 0.7.

System suitability: reference solution (a):

– *resolution*: minimum of 2 between the peaks due to impurity A and to impurity B and minimum of 3 between the peaks due to impurity B and to hymecromone.

Limits:

– *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.05 per cent),

– *impurity B*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.05 per cent),

– *any other impurity*: not more than the area of the peak due to hymecromone in the chromatogram obtained with reference solution (b) (0.1 per cent),