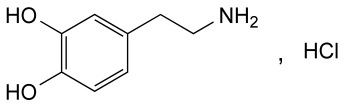
01/2008:0664

DOPAMINE HYDROCHLORIDE

Dopamini hydrochloridum



$C_8H_{12}ClNO_2$ M_r 189.6
[62-31-7]

DEFINITION

4-(2-Aminoethyl)benzene-1,2-diol hydrochloride.

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

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: freely soluble in water, soluble in ethanol (96 per cent), sparingly soluble in acetone and in methylene chloride.

IDENTIFICATION

First identification: B, E.

Second identification: A, C, D, E.

A. Ultraviolet and visible absorption spectrophotometry (*2.2.25*).

Test solution. Dissolve 40.0 mg in *0.1 M hydrochloric acid* and dilute to 100.0 ml with the same acid. Dilute 10.0 ml of this solution to 100.0 ml with *0.1 M hydrochloric acid.*

Spectral range: 230-350 nm.

Absorption maximum: at 280 nm.

Specific absorbance at the absorption maximum: 136 to 150.

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *dopamine hydrochloride CRS.*

C. Dissolve about 5 mg in a mixture of 5 ml of *1 M hydrochloric acid* and 5 ml of *water R*. Add 0.1 ml of *sodium nitrite solution R* containing 100 g/l of *ammonium molybdate R*. A yellow colour develops which becomes red on the addition of *strong sodium hydroxide solution R*.

D. Dissolve about 2 mg in 2 ml of *water R* and add 0.2 ml of *ferric chloride solution R2*. A green colour develops which changes to bluish-violet on the addition of 0.1 g of *hexamethylenetetramine R*.

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

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution B_6 or Y_6 (*2.2.2, Method II*).

Dissolve 0.4 g in *water R* and dilute to 10 ml with the same solvent.

Acidity or alkalinity. Dissolve 0.5 g in *carbon dioxide-free water R* and dilute to 10 ml with the same solvent. Add 0.1 ml of *methyl red solution R* and 0.75 ml of *0.01 M sodium hydroxide*. The solution is yellow. Add 1.5 ml of *0.01 M hydrochloric acid*. The solution is red.

Related substances. Liquid chromatography (*2.2.29*). *Protect the solutions from light.*

Buffer solution. Dissolve 21 g of *citric acid R* in 200 ml of *1 M sodium hydroxide* and dilute to 1000 ml with *water R*. To 600 ml of this solution add 400 ml of *0.1 M hydrochloric acid.*

Test solution. Dissolve 50 mg of the substance to be examined in mobile phase A and dilute to 25 ml with mobile phase A.

Reference solution (a). Dilute 1.0 ml of the test solution to 100.0 ml with mobile phase A. Dilute 1.0 ml of this solution to 10.0 ml with mobile phase A.

Reference solution (b). Dissolve 10 mg of *3-O-methyldopamine hydrochloride R* (impurity B) and 10 mg of *4-O-methyldopamine hydrochloride R* (impurity A) in mobile phase A and dilute to 100 ml with mobile phase A. Dilute 6 ml of this solution to 25 ml with mobile phase A.

Column:

– *size*: *l* = 0.15 m, Ø = 3.9 mm;
– *stationary phase*: spherical *end-capped octadecylsilyl silica gel for chromatography R* (4 µm).

Mobile phase:

– *mobile phase A*: dissolve 1.08 g of *sodium octanesulphonate R* in 880 ml of the buffer solution and add 50 ml of *methanol R* and 70 ml of *acetonitrile R*;
– *mobile phase B*: dissolve 1.08 g of *sodium octanesulphonate R* in 700 ml of the buffer solution and add 100 ml of *methanol R* and 200 ml of *acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 5	90	10
5 - 20	90 → 40	10 → 60
20 - 25	40	60

Flow rate: 1.0 ml/min.

Detection: spectrophotometer at 280 nm.

Injection: 10 µl.

Retention time: dopamine = about 5 min.

System suitability: reference solution (b):

– *resolution*: minimum 5.0 between the peaks due to impurities B and A.

Limits:

– *unspecificied impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);
– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
– *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

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 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2 h.

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

ASSAY

In order to avoid overheating in the reaction medium, mix thoroughly throughout the titration and stop the titration immediately after the end-point has been reached.

Dissolve 0.150 g in 10 ml of *anhydrous formic acid R*. Add 50 ml of *acetic anhydride R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

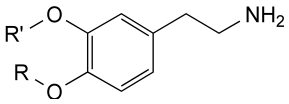
1 ml of *0.1 M perchloric acid* is equivalent to 18.96 mg of $C_8H_{12}ClNO_2$.

STORAGE

In an airtight container, under nitrogen, 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.*



A. R = CH_3, R′ = H: 5-(2-aminoethyl)-2-methoxyphenol (4-*O*-methyldopamine),

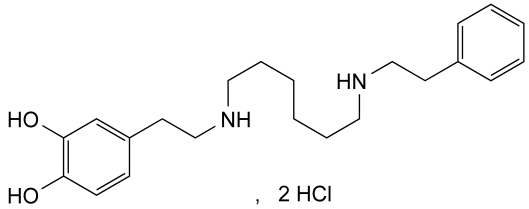
B. R = H, R′ = CH_3: 4-(2-aminoethyl)-2-methoxyphenol (3-*O*-methyldopamine),

C. R = R′ = CH_3: 2-(3,4-dimethoxyphenyl)ethanamine.

01/2008:1748

DOPEXAMINE DIHYDROCHLORIDE

Dopexamini dihydrochloridum



$C_{22}H_{34}Cl_2N_2O_2$ M_r 429.4
[86484-91-5]

DEFINITION

4-[2-[[6-[(2-Phenylethyl)amino]hexyl]amino]ethyl]benzene-1,2-diol dihydrochloride.

Content: 98.5 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: soluble in water, sparingly soluble in ethanol (96 per cent) and in methanol, practically insoluble in acetone.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *dopexamine dihydrochloride CRS*.

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

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution BY_7 (*2.2.2, Method II*).

Dissolve 0.10 g in *0.1 M hydrochloric acid* and dilute to 10 ml with the same acid.

pH (*2.2.3*): 3.7 to 5.7.

Dissolve 0.20 g in *carbon dioxide-free water R* and dilute to 20 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.100 g of the substance to be examined in mobile phase A and dilute to 10.0 ml with mobile phase A.

Reference solution (a). Dilute 1.0 ml of the test solution to 100.0 ml with mobile phase A. Dilute 1.0 ml of this solution to 10.0 ml with mobile phase A.

Reference solution (b). Dissolve 5 mg of the substance to be examined and 5 mg of *dopexamine impurity B CRS* in mobile phase A and dilute to 10.0 ml with mobile phase A.

Reference solution (c). Dissolve 5 mg of *dopexamine impurity F CRS* in mobile phase A and dilute to 100 ml with mobile phase A.

Column:

– *size*: *l* = 0.15 m, Ø = 4.6 mm;
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm);
– *temperature*: 45 °C.

Mobile phase:

– *mobile phase A*: mix 5 volumes of *buffer solution pH 2.5 R* and 95 volumes of *water R*;
– *mobile phase B*: mix 5 volumes of *buffer solution pH 2.5 R* and 95 volumes of a 60 per cent *V/V* solution of *acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 10	81 → 77	19 → 23
10 - 25	77 → 50	23 → 50
25 - 30	50	50
30 - 31	50 → 81	50 → 19
31 - 39	81	19

Flow rate: 1 ml/min.

Detection: spectrophotometer at 280 nm.

Preconditioning of the column: rinse for 5 min with a mixture of 19 volumes of mobile phase B and 81 volumes of mobile phase A.

Injection: 20 µl.

Relative retention with reference to dopexamine (retention time = about 5 min): impurity A = about 0.5; impurity B = about 2.0; impurity C = about 2.3; impurity D = about 2.8; impurity E = about 2.9; impurity F = about 3.0; impurity I = about 3.6; impurity J = about 5.0; impurity K = about 5.9.

System suitability: reference solution (b):

– *resolution*: minimum 2 between the peaks due to dopexamine and impurity B.

Limits:

– *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 1.4; impurity F = 0.7;
– *impurities A, B, C, D, E, F, I, K*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);