



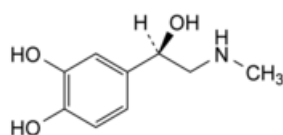
Edition: BP 2025 (Ph. Eur. 11.6 update)

Adrenaline / Epinephrine



[General Notices](#)

(Ph. Eur. monograph 2303)



C₉H₁₃NO₃ 183.2 51-43-4

Action and use

Adrenoceptor agonist.

Preparations

[Adrenaline Eye Drops/Epinephrine Eye Drops](#)

[Dilute Adrenaline Injection \(1 in 10,000\)/Dilute Epinephrine Injection \(1 in 10,000\)](#)

Ph Eur

DEFINITION

4-[(1*R*)-1-Hydroxy-2-(methylamino)ethyl]benzene-1,2-diol.

Synthetic product.

Content

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

CHARACTERS

Appearance

White or almost white crystalline powder, becoming coloured on exposure to air and light.

Solubility

Practically insoluble in water, in ethanol (96 per cent) and in methylene chloride. It dissolves in hydrochloric acid.

IDENTIFICATION

A. Infrared absorption spectrophotometry ([2.2.24](#)).

Comparison [adrenaline CRS](#).

B. Specific optical rotation (see Tests).

TESTS

Solution S

Dissolve 1.000 g in a 25.75 g/L solution of [hydrochloric acid R](#) and dilute to 50.0 mL with the same solvent. Examine the solution immediately.

Appearance of solution

Solution S is not more opalescent than reference suspension II ([2.2.1](#)) and not more intensely coloured than reference solution BY₅ ([2.2.2, Method II](#)).

[Specific optical rotation](#) ([2.2.7](#))

-54.0 to -50.0 (anhydrous substance), determined on solution S.

Related substances

Liquid chromatography ([2.2.29](#)). *Prepare the solutions protected from light.*

Solvent mixture A Dissolve 5.0 g of [potassium dihydrogen phosphate R](#) and 2.6 g of [sodium octanesulfonate R](#) in [water for chromatography R](#) and dilute to 1000 mL with the same solvent (it is usually necessary to stir for at least 30 min to achieve complete dissolution). Adjust to pH 2.8 with [phosphoric acid R](#).

Solvent mixture B [acetonitrile R](#), solvent mixture A (13:87 V/V).

Solvent mixture C 10.3 g/L solution of [hydrochloric acid R](#), solvent mixture B (10:90 V/V).

Test solution Dissolve 40.0 mg of the substance to be examined in 5 mL of a 10.3 g/L solution of [hydrochloric acid R](#) and dilute to 50.0 mL with solvent mixture B.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with solvent mixture B. Dilute 1.0 mL of this solution to 10.0 mL with solvent mixture B.

Reference solution (b) Dissolve 1.5 mg of [noradrenaline tartrate CRS](#) (impurity B) and 1.5 mg of [adrenalone hydrochloride R](#) (impurity C) in solvent mixture B, add 1 mL of the test solution and dilute to 100 mL with solvent mixture B.

Reference solution (c) Dissolve the contents of a vial of [adrenaline impurity mixture CRS](#) (containing impurities D and E) in 1 mL of solvent mixture C.

Reference solution (d) Dissolve the contents of a vial of [adrenaline impurity F CRS](#) in 1 mL of a 10.3 g/L solution of [hydrochloric acid R](#).

Column:

— size: $l = 0.10$ m, $\varnothing = 4.6$ mm;

— stationary phase: [base-deactivated end-capped octadecylsilyl silica gel for chromatography R](#) (3 μ m);

— temperature: 50 °C.

Mobile phase:

— mobile phase A: [acetonitrile R1](#), solvent mixture A (5:95 V/V);

Time (min)	Mobile phase A (per cent V/V)	Mobile phase B (per cent V/V)
0 - 15	92 → 50	8 → 50
15 - 20	50 → 92	50 → 8
20 - 25	92	8

Flow rate 2.0 mL/min.

Detection Spectrophotometer at 210 nm.

Injection 20 µL.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peaks due to impurities B and C; use the chromatogram supplied with [adrenaline impurity mixture CRS](#) and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities D and E; use the chromatogram obtained with reference solution (d) to identify the peak due to impurity F.

Relative retention With reference to adrenaline (retention time = about 4 min): impurity F = about 0.2; impurity B = about 0.8; impurity C = about 1.3; impurity D = about 3.3; impurity E = about 3.7.

System suitability Reference solution (b):

— [resolution](#): minimum 3.0 between the peaks due to impurity B and adrenaline.

Limits:

— *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity D = 0.7; impurity E = 0.6;

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

— *impurities D, E*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);

— *unspecified 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 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 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).

[Water \(2.5.32\)](#)

Maximum 0.4 per cent, determined on 0.300 g using the evaporation technique at 130 °C.

[Sulfated ash \(2.4.14\)](#)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.150 g in 50 mL of [anhydrous acetic acid R](#). Titrate with [0.1 M perchloric acid](#), determining the end-point potentiometrically ([2.2.20](#)).

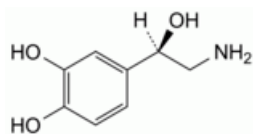
1 mL of [0.1 M perchloric acid](#) is equivalent to 18.32 mg of C₉H₁₃NO₃.

STORAGE

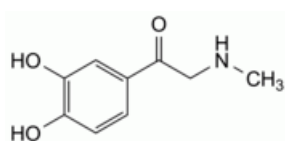
Under nitrogen, protected from light.

IMPURITIES

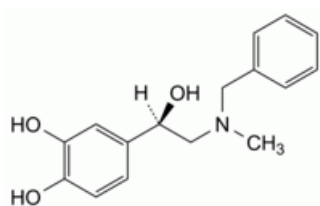
Specified impurities B, C, D, E, F.



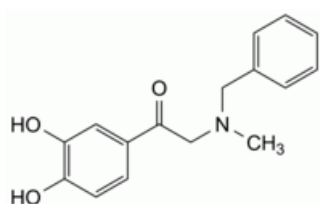
B. 4-[(1R)-2-amino-1-hydroxyethyl]benzene-1,2-diol (noradrenaline),



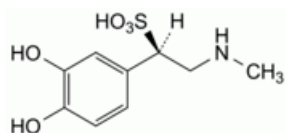
C. 1-(3,4-dihydroxyphenyl)-2-(methylamino)ethan-1-one (adrenalone),



D. 4-[(1R)-2-[benzyl(methyl)amino]-1-hydroxyethyl]benzene-1,2-diol,



E. 2-[benzyl(methyl)amino]-1-(3,4-dihydroxyphenyl)ethan-1-one,



F. (1R)-1-(3,4-dihydroxyphenyl)-2-(methylamino)ethane-1-sulfonic acid.

