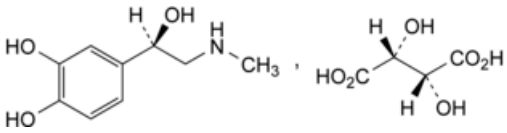
Edition: BP 2025 (Ph. Eur. 11.6 update)

Adrenaline Acid Tartrate / Epinephrine Acid Tartrate

General Notices

(Adrenaline Tartrate, Ph. Eur. monograph 0254)



$C_{13}H_{19}NO_9$ 333.3 *51-42-3*

Action and use

Adrenoceptor agonist.

Preparations

Adrenaline Injection/Epinephrine Injection

Dilute Adrenaline Injection (1 in 10,000)/Dilute Epinephrine Injection (1 in 10,000)

Adrenaline Solution/Epinephrine Solution

Adrenaline and Cocaine Intranasal Solution

Bupivacaine and Adrenaline Injection/Bupivacaine and Epinephrine Injection

Lidocaine and Adrenaline Injection/Lidocaine and Epinephrine Injection

Ph Eur

DEFINITION

(1*R*)-1-(3,4-Dihydroxyphenyl)-2-(methylamino)ethanol hydrogen (2*R*,3*R*)-2,3-dihydroxybutanedioate.

Content

98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

White or greyish-white, crystalline powder.

Solubility

Freely soluble in water, slightly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Dissolve 5 g in 50 mL of a 5 g/L solution of *sodium metabisulfite R* and make alkaline by addition of *ammonia R*. Keep the mixture at room temperature for at least 15 min and filter. Reserve the filtrate for identification test C. Wash the precipitate with 3 quantities, each of 10 mL, of *methanol R*. Dry at 80 °C. The specific optical rotation (*2.2.7*) of the residue (adrenaline base) is -53.5 to -50, determined using a 20.0 g/L solution in *0.5 M hydrochloric acid*.
B. Infrared absorption spectrophotometry (*2.2.24*).

Preparation Discs of adrenaline base prepared as described under identification test A.

Comparison Use adrenaline base prepared as described under identification test A from 50 mg of *adrenaline tartrate CRS* dissolved in 5 mL of a 5 g/L solution of *sodium metabisulfite R*. Keep the mixture at room temperature for at least 30 min. Filter through a sintered-glass filter (*2.1.2*).

C. 0.2 mL of the filtrate obtained in identification test A gives reaction (b) of tartrates (*2.3.1*).

TESTS

Appearance of solution

The solution is not more opalescent than reference suspension II (*2.2.1*) and not more intensely coloured than reference solution BY_5 (*2.2.2, Method II*).

Dissolve 0.5 g in *water R* and dilute to 10 mL with the same solvent. Examine the solution immediately.

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 then 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 R1*, solvent mixture A (130:870 *V/V*).

Test solution Dissolve 75 mg of the substance to be examined in 5 mL of *0.1 M hydrochloric acid* and dilute to 50 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 1.0 mL of the test solution and dilute to 100.0 mL with solvent mixture B.

Reference solution (c) Dissolve the contents of a vial of *adrenaline impurity mixture CRS* (impurities D and E) in 0.1 mL of *0.1 M hydrochloric acid* and 0.9 mL of solvent mixture B.

Reference solution (d) Dissolve 7.5 mg of *adrenaline tartrate with impurity A CRS* in 0.5 mL of *0.1 M hydrochloric acid* and dilute to 5.0 mL with solvent mixture B.

Blank solution *0.1 M hydrochloric acid*, solvent mixture B (1:9 *V/V*).

Column:

— *size*: *l* = 0.10 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (3 µm);

— *temperature*: 50 °C.

Mobile phase:

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

— *mobile phase B*: *acetonitrile R1*, solvent mixture A (45:55 *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 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 supplied with *adrenaline tartrate with impurity A CRS* and the chromatogram obtained with reference solution (d) to identify the peak due to impurity A.

Relative retention With reference to adrenaline (retention time = about 4 min): impurity B = about 0.8; impurity C = about 1.3; impurity A = about 3.2; 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;

— *impurity A*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent);

— *impurities B, C*: 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 6 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.6 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).

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* for 18 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.300 g in 50 mL of *anhydrous acetic acid R*, heating gently if necessary. Titrate with *0.1 M perchloric acid* until a bluish-green colour is obtained, using 0.1 mL of *crystal violet solution R* as indicator.

1 mL of *0.1 M perchloric acid* is equivalent to 33.33 mg of $C_{13}H_{19}NO_9$.

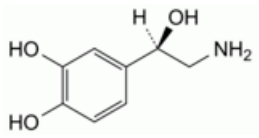
STORAGE

In an airtight container, or preferably in a sealed tube under vacuum or under an inert gas, protected from light.

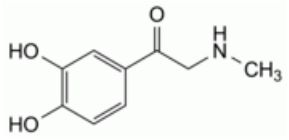
IMPURITIES

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

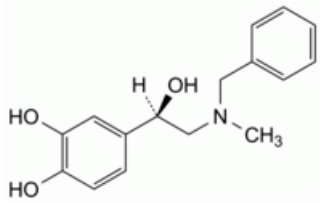
A. unknown structure,



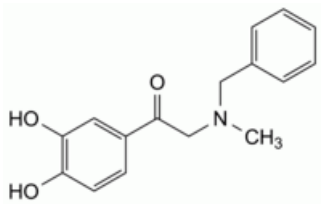
B. (1*R*)-2-amino-1-(3,4-dihydroxyphenyl)ethanol (noradrenaline),



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



D. 4-[(1*R*)-2-(benzylmethylamino)-1-hydroxyethyl]benzene-1,2-diol,



E. 2-(benzylmethylamino)-1-(3,4-dihydroxyphenyl)ethanone.

Ph Eur