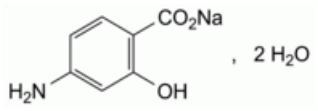
Edition: BP 2025 (Ph. Eur. 11.6 update)

Sodium Aminosalicylate Dihydrate

General Notices

(Ph. Eur. monograph 1993)



$C_7H_6NNaO_3,2H_2O$ 211.1 *6018-19-5*

Action and use

Antituberculosis drug.

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DEFINITION

Sodium 4-amino-2-hydroxybenzoate dihydrate.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder or crystals, slightly hygroscopic.

Solubility

Freely soluble in water, sparingly soluble in ethanol (96 per cent), practically insoluble in methylene chloride.

IDENTIFICATION

First identification: A, E.

Second identification: B, C, D, E.

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *sodium aminosalicylate dihydrate CRS*.

B. Introduce 0.3 g into a porcelain crucible. Cautiously heat on a small flame until vapour is evolved. Cover the crucible with a watch glass and collect the white sublimate. The melting point (2.2.14) of the sublimate is 120 °C to 124 °C.
C. To 0.1 mL of solution S (see Tests) add 5 mL of water R and 0.1 mL of ferric chloride solution R1. A reddish-brown colour develops.
D. 2 mL of solution S gives the reaction of primary aromatic amines (2.3.1).
E. 0.5 mL of solution S gives reaction (a) of sodium (2.3.1).

TESTS

Solution S

Dissolve 0.50 g in carbon dioxide-free water R and dilute to 25 mL with the same solvent.

Appearance of solution

The freshly prepared solution is clear (2.2.1) and not more intensely coloured than reference solution B_5 (2.2.2, Method II).

Dissolve 2.5 g in water R and dilute to 25 mL with the same solvent.

pH (2.2.3)

6.5 to 8.5 for solution S.

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use.*

Test solution Dissolve 50.0 mg of the substance to be examined in water R and dilute to 50.0 mL with the same solvent.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with water R. Dilute 1.0 mL of this solution to 20.0 mL with water R.

Reference solution (b) Dissolve 5 mg of 3-aminophenol R (impurity A) and 5 mg of mesalazine R (impurity B) in water R and dilute to 100 mL with the same solvent. Dilute 1 mL of the solution to 5 mL with water R.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: base-deactivated end-capped octylsilyl silica gel for chromatography R (5 µm).

Mobile phase:

— *mobile phase A*: dissolve 2.2 g of perchloric acid R and 1.0 g of phosphoric acid R in water for chromatography R and dilute to 1000 mL with the same solvent;

— *mobile phase B*: dissolve 1.7 g of perchloric acid R and 1.0 g of phosphoric acid R in acetonitrile for chromatography R and dilute to 1000 mL with the same solvent;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 15	100	0
15 - 30	100 → 40	0 → 60

Flow rate 1.25 mL/min.

Detection Spectrophotometer at 220 nm.

Injection 10 µL.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A and B.

Relative retention With reference to 4-aminosalicylate (retention time = about 17 min): impurity A = about 0.31; impurity B = about 0.39.

System suitability Reference solution (b):

— *resolution*: minimum 4.0 between the peaks due to impurities A and B.

Calculation of percentage contents:

— *correction factor*: multiply the peak area of impurity A by 0.62;

— for each impurity, use the concentration of sodium aminosalicylate dihydrate in reference solution (a).

Limits:

— *impurity A*: maximum 0.15 per cent;

— *unspecified impurities*: for each impurity, maximum 0.05 per cent;

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 0.03 per cent.

Loss on drying (*2.2.32*)

16.0 per cent to 17.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

ASSAY

Dissolve 0.150 g in 20 mL of *water R*. Add 10 mL of a 500 g/L solution of *sodium bromide R* and 25 mL of *glacial acetic acid R*. Add 5 mL of *0.1 M sodium nitrite* rapidly and continue the titration with the same titrant, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M sodium nitrite* is equivalent to 17.51 mg of $C_7H_6NNaO_3$.

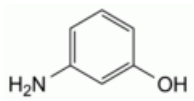
STORAGE

In an airtight container, protected from light. If the substance is sterile, the container is also sterile and tamper-evident.

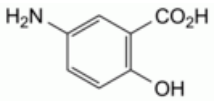
IMPURITIES

Specified impurities *A.*

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) *B.*



A. 3-aminophenol,



B. 5-amino-2-hydroxybenzoic acid (mesalazine).

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