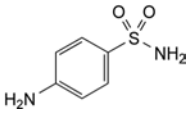
STORAGE

Protected from light.

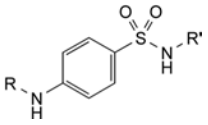
IMPURITIES

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, C, D.*

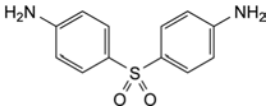


A. 4-aminobenzenesulfonamide (sulfanilamide),



B. R = CO-CH_3, R′ = H: *N*-(4-sulfamoylphenyl)acetamide,

C. R = R′ = CO-CH_3: *N*-[[4-(acetylamino)phenyl]sulfonyl]-acetamide,

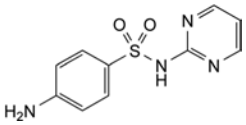


D. 4,4′-sulfonyldianiline (dapsone).

01/2008:0294
corrected 6.0

SULFADIAZINE

Sulfadiazinum



$C_{10}H_{10}N_4O_2S$ M_r 250.3
[68-35-9]

DEFINITION

Sulfadiazine contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of 4-amino-*N*-pyrimidin-2-ylbenzenesulfonamide, calculated with reference to the dried substance.

CHARACTERS

White, yellowish-white or pinkish-white, crystalline powder or crystals, practically insoluble in water, slightly soluble in acetone, very slightly soluble in alcohol. It dissolves in solutions of alkali hydroxides and in dilute mineral acids.

It melts at about 255 °C, with decomposition.

IDENTIFICATION

First identification: A, B.

Second identification: B, C, D.

A. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *sulfadiazine CRS*. Examine the substances prepared as discs.

B. Examine the chromatograms obtained in the test for related substances. The principal spot in the chromatogram obtained with test solution (a) corresponds in position and size to the principal spot in the chromatogram obtained with reference solution (a).

C. Place 3 g in a dry tube. Immerse the lower part of the tube, inclined at 45°, in a silicone oil bath and heat to about 270 °C. The substance to be examined decomposes and a white or yellowish-white sublimate is formed which, after recrystallisation from *toluene R* and drying at 100 °C, melts (*2.2.14*) at 123 °C to 127 °C.

D. Dissolve about 5 mg in 10 mL of *1 M hydrochloric acid*. Dilute 1 mL of the solution to 10 mL with *water R*. The solution, without further acidification, gives the reaction of primary aromatic amines (*2.3.1*).

TESTS

Appearance of solution. Dissolve 0.8 g in a mixture of 5 mL of *dilute sodium hydroxide solution R* and 5 mL of *water R*. The solution is not more intensely coloured than reference solution Y_5, BY_5 or GY_5 (*2.2.2, Method II*).

Acidity. To 1.25 g, finely powdered, add 25 mL of *carbon dioxide-free water R*. Heat at about 70 °C for 5 min. Cool in iced water for about 15 min and filter. To 20 mL of the filtrate add 0.1 mL of *bromothymol blue solution R1*. Not more than 0.2 mL of *0.1 M sodium hydroxide* is required to change the colour of the indicator.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution (a). Dissolve 20 mg of the substance to be examined in 3 mL of a mixture of 2 volumes of *concentrated ammonia R* and 48 volumes of *methanol R* and dilute to 5.0 mL with the same mixture of solvents.

Test solution (b). Dissolve 0.10 g of the substance to be examined in 0.5 mL of *concentrated ammonia R* and dilute to 5.0 mL with *methanol R*. If the solution is not clear, heat gently until dissolution is complete.

Reference solution (a). Dissolve 20 mg of *sulfadiazine CRS* in 3 mL of a mixture of 2 volumes of *concentrated ammonia R* and 48 volumes of *methanol R* and dilute to 5.0 mL with the same mixture of solvents.

Reference solution (b). Dilute 1.25 mL of test solution (a) to 50 mL with a mixture of 2 volumes of *concentrated ammonia R* and 48 volumes of *methanol R*.

Apply to the plate 5 µL of each solution. Develop over a path of 15 cm using a mixture of 3 volumes of *dilute ammonia R1*, 5 volumes of *water R*, 40 volumes of *nitromethane R* and 50 volumes of *dioxan R*. Dry the plate at 100 °C to 105 °C and examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with test solution (b), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.5 per cent).

Heavy metals (*2.4.8*). 1.0 g complies with limit test D for heavy metals (20 ppm). Prepare the standard using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.00 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in a mixture of 20 mL of *dilute hydrochloric acid R* and 50 mL of *water R*. Cool the solution in iced water. Carry out the determination of primary aromatic amino-nitrogen (*2.5.8*), determining the end-point electrometrically.

1 mL of *0.1 M sodium nitrite* is equivalent to 25.03 mg of $C_{10}H_{10}N_4O_2S$.

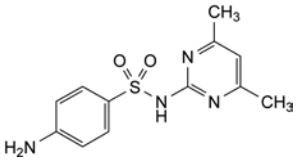
STORAGE

Store protected from light.

01/2008:0295
corrected 6.0

SULFADIMIDINE

Sulfadimidinum



$C_{12}H_{14}N_4O_2S$ M_r 278.3
[57-68-1]

DEFINITION

Sulfadimidine contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of 4-amino-*N*-(4,6-dimethylpyrimidin-2-yl)benzenesulfonamide, calculated with reference to the dried substance.

CHARACTERS

White or almost white powder or crystals, very slightly soluble in water, soluble in acetone, slightly soluble in alcohol. It dissolves in solutions of alkali hydroxides and in dilute mineral acids.

It melts at about 197 °C, with decomposition.

IDENTIFICATION

First identification: A, B.

Second identification: B, C, D.

A. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *sulfadimidine CRS*. Examine the substances prepared as discs.

B. Examine the chromatograms obtained in the test for related substances. The principal spot in the chromatogram obtained with test solution (a) corresponds in position and size to the principal spot in the chromatogram obtained with reference solution (a).

C. Place 3 g in a dry tube. Immerse the lower part of the tube, inclined at 45°, in a silicone oil bath and heat to about 270 °C. The substance to be examined decomposes and a white or yellowish-white sublimate is formed which, after recrystallisation from *toluene R* and drying at 100 °C, melts (*2.2.14*) at 150 °C to 154 °C.

D. Dissolve about 5 mg in 10 mL of *1 M hydrochloric acid*. Dilute 1 mL of the solution to 10 mL with *water R*. The solution, without further acidification, gives the reaction of primary aromatic amines (*2.3.1*).

TESTS

Appearance of solution. Dissolve 0.5 g in a mixture of 5 mL of *dilute sodium hydroxide solution R* and 5 mL of *water R*. The solution is not more intensely coloured than reference solution Y_5, BY_5 or GY_5 (*2.2.2, Method II*).

Acidity. To 1.25 g, finely powdered, add 25 mL of *carbon dioxide-free water R*. Heat at about 70 °C for 5 min. Cool in iced water for about 15 min and filter. To 20 mL of the filtrate add 0.1 mL of *bromothymol blue solution R1*. Not more than 0.2 mL of *0.1 M sodium hydroxide* is required to change the colour of the indicator.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution (a). Dissolve 20 mg of the substance to be examined in 3 mL of a mixture of 2 volumes of *concentrated ammonia R* and 48 volumes of *methanol R* and dilute to 5.0 mL with the same mixture of solvents.

Test solution (b). Dissolve 0.10 g of the substance to be examined in 0.5 mL of *concentrated ammonia R* and dilute to 5.0 mL with *methanol R*. If the solution is not clear, heat gently until dissolution is complete.

Reference solution (a). Dissolve 20 mg of *sulfadimidine CRS* in 3 mL of a mixture of 2 volumes of *concentrated ammonia R* and 48 volumes of *methanol R* and dilute to 5.0 mL with the same mixture of solvents.

Reference solution (b). Dilute 1.25 mL of test solution (a) to 50 mL with a mixture of 2 volumes of *concentrated ammonia R* and 48 volumes of *methanol R*.

Apply to the plate 5 µL of each solution. Develop over a path of 15 cm using a mixture of 3 volumes of *dilute ammonia R1*, 5 volumes of *water R*, 40 volumes of *nitromethane R* and 50 volumes of *dioxan R*. Dry the plate at 100 °C to 105 °C and examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with test solution (b), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.5 per cent).

Heavy metals (*2.4.8*). 1.0 g complies with limit test D for heavy metals (20 ppm). Prepare the standard using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.00 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in a mixture of 20 mL of *dilute hydrochloric acid R* and 50 mL of *water R*. Cool the solution in iced water. Carry out the determination of primary aromatic amino-nitrogen (*2.5.8*), determining the end-point electrometrically.

1 mL of *0.1 M sodium nitrite* is equivalent to 27.83 mg of $C_{12}H_{14}N_4O_2S$.

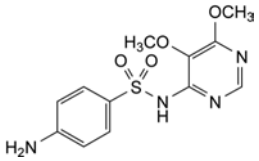
STORAGE

Store protected from light.

01/2008:0740
corrected 6.0

SULFADOXINE

Sulfadoxinum



$C_{12}H_{14}N_4O_4S$ M_r 310.3
[2447-57-6]

DEFINITION

Sulfadoxine contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of 4-amino-*N*-(5,6-dimethoxypyrimidin-4-yl)benzenesulfonamide, calculated with reference to the dried substance.

CHARACTERS

White or yellowish-white crystalline powder or crystals, very slightly soluble in water, slightly soluble in alcohol and in methanol. It dissolves in solutions of alkali hydroxides and in dilute mineral acids.

It melts at about 198 °C, with decomposition.