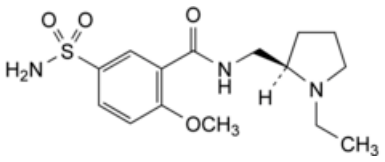
Edition: BP 2025 (Ph. Eur. 11.6 update)

Sulpiride

General Notices

(Ph. Eur. monograph 1045)



and enantiomer

$C_{15}H_{23}N_3O_4S$ 341.4 *15676-16-1*

Action and use

Dopamine receptor antagonist; neuroleptic.

Preparation

Sulpiride Tablets

Ph Eur

DEFINITION

N-[[(2*RS*)-1-Ethylpyrrolidin-2-yl)]methyl]-2-methoxy-5-sulfamoylbenzamide.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, sparingly soluble in methanol, slightly soluble in ethanol (96 per cent) and in methylene chloride. It dissolves in dilute solutions of mineral acids and alkali hydroxides.

IDENTIFICATION

First identification: B.

Second identification: A, C, D.

A. Melting point (2.2.14): 177 °C to 181 °C.
B. Infrared absorption spectrophotometry (2.2.24).

Comparison sulpiride CRS.

C. Examine the chromatograms obtained in the test for impurity A.

Detection Examine in ultraviolet light at 254 nm.

Results The principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).

D. To about 1 mg in a porcelain dish, add 0.5 mL of sulfuric acid R and 0.05 mL of formaldehyde solution R. Examined in ultraviolet light at 365 nm, the solution shows blue fluorescence.

TESTS

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution Y_6 (2.2.2, Method I).

Dissolve 1.0 g in dilute acetic acid R and dilute to 10 mL with the same acid.

Impurity A. Thin-layer chromatography (2.2.27)

Test solution (a) Dissolve 0.20 g of the substance to be examined in methanol R, sonicate until dissolution is complete and dilute to 10.0 mL with the same solvent.

Test solution (b) Dilute 1.0 mL of test solution (a) to 10.0 mL with methanol R.

Reference solution (a) Dissolve 20 mg of sulpiride CRS in methanol R and dilute to 10.0 mL with the same solvent.

Reference solution (b) Dissolve 5.0 mg of sulpiride impurity A CRS in methanol R and dilute to 25.0 mL with the same solvent. Dilute 1.0 mL of the solution to 10.0 mL with methanol R.

Plate TLC silica gel F_{254} plate R.

Mobile phase concentrated ammonia R, dioxan R, methanol R, methylene chloride R (2:10:14:90 *V/V/V/V*).

Application 10 µL.

Development Over 1/2 of the plate.

Drying In air.

Detection Examine in ultraviolet light at 254 nm for identification test C and then spray with ninhydrin solution R; heat at 100-105 °C for 15 min and examine in daylight.

Limit Test solution (a):

— *impurity A*: any spot due to impurity A is not more intense than the corresponding spot in the chromatogram obtained with reference solution (b) (0.1 per cent).

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 0.100 g of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

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

Reference solution (b) Dissolve 5 mg of the substance to be examined and 5 mg of *sulpiride impurity B CRS* in the mobile phase and dilute to 50.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

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

Mobile phase Mix 10 volumes of *acetonitrile R*, 10 volumes of *methanol R* and 80 volumes of a solution containing 6.8 g/L of *potassium dihydrogen phosphate R* and 1 g/L of *sodium octanesulfonate R*, previously adjusted to pH 3.3 with *phosphoric acid R*.

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 240 nm.

Injection 10 µL.

Run time Twice the retention time of sulpiride.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peak due to impurity B.

Relative retention With reference to sulpiride (retention time = about 15 min): impurity B = about 0.7.

System suitability Reference solution (b):

— *resolution*: minimum 2.5 between the peaks due to impurity B and sulpiride.

Calculation of percentage contents:

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

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.3 per cent;

— *reporting threshold*: 0.05 per cent.

Chlorides (*2.4.4*)

Maximum 100 ppm.

Shake 1.0 g with 20 mL of *water R*. Filter through a sintered-glass filter (40) (*2.1.2*). To 10 mL of the filtrate add 5 mL of *water R*.

Iron (*2.4.9*)

Maximum 10 ppm.

Ignite 1.0 g in a silica crucible. To the residue add 1 mL of *1 M hydrochloric acid*, 3 mL of *water R* and 0.1 mL of *nitric acid R*. Heat on a water-bath for about 5 min. Place the solution in a test-tube. Rinse the crucible with 4 mL of *water R*. Collect the rinsings in the test-tube and dilute to 10 mL with *water 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.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

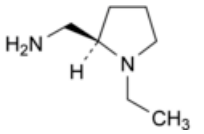
Dissolve 0.250 g in 80 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 34.14 mg of $C_{15}H_{23}N_3O_4S$.

IMPURITIES

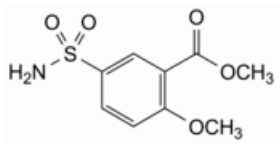
Specified impurities *A.*

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, E, F, G.*

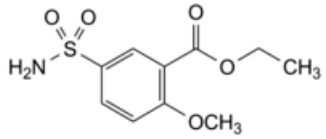


and enantiomer

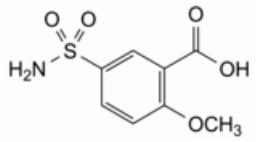
A. [(2*RS*)-1-ethylpyrrolidin-2-yl]methanamine,



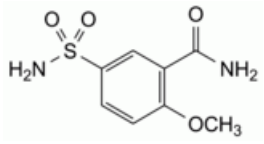
B. methyl 2-methoxy-5-sulfamoylbenzoate,



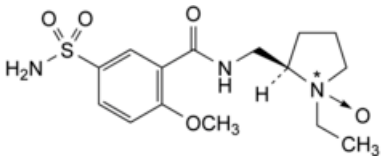
C. ethyl 2-methoxy-5-sulfamoylbenzoate,



D. 2-methoxy-5-sulfamoylbenzoic acid,

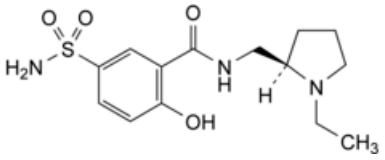


E. 2-methoxy-5-sulfamoylbenzamide,



and enantiomer

F. *N*-[[(2*RS*)-1-ethyl-1-oxidopyrrolidin-2-yl]methyl]-2-methoxy-5-sulfamoylbenzamide,



and enantiomer

G. *N*-[[(2*RS*)-1-éthylpyrrolidin-2-yl]méthyl]-2-hydroxy-5-sulfamoylbenzamide.

Ph Eur