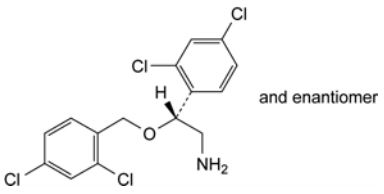
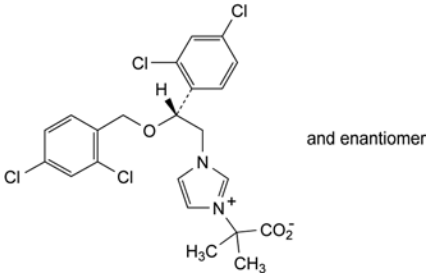


C. (2*RS*)-2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethanamine,

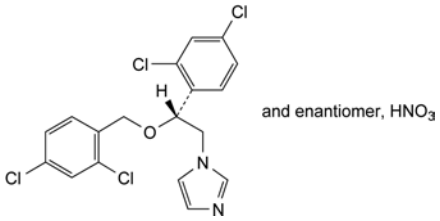


E. 2-[1-[(2*RS*)-2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazol-3-io]-2-methylpropanoate.

01/2008:0513
corrected 6.0

MICONAZOLE NITRATE

Miconazoli nitras



$C_{18}H_{15}Cl_4N_3O_4$ M_r 479.1
[22832-87-7]

DEFINITION

1-[(2*RS*)-2-[(2,4-Dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)-ethyl]-1*H*-imidazole nitrate.

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

CHARACTERS

Appearance: white or almost white powder.

Solubility: very slightly soluble in water, sparingly soluble in methanol, slightly soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 178 °C to 184 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs of *potassium bromide R.*

Comparison: *miconazole nitrate CRS.*

C. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 30 mg of the substance to be examined in the mobile phase and dilute to 5 mL with the mobile phase.

Reference solution (a). Dissolve 30 mg of *miconazole nitrate CRS* in the mobile phase and dilute to 5 mL with the mobile phase.

Reference solution (b). Dissolve 30 mg of *miconazole nitrate CRS* and 30 mg of *econazole nitrate CRS* in the mobile phase, then dilute to 5 mL with the mobile phase.

Plate: *TLC octadecylsilyl silica gel plate R.*

Mobile phase: *ammonium acetate solution R, dioxan R, methanol R* (20:40:40 *V/V/V*).

Application: 5 µL.

Development: over a path of 15 cm.

Drying: in a current of warm air for 15 min.

Detection: expose to iodine vapour until the spots appear and examine in daylight.

System suitability: reference solution (b):

– the chromatogram shows 2 clearly separated spots.

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

D. It gives the reaction of nitrates (*2.3.1*).

TESTS

Solution S. Dissolve 0.1 g in *methanol R* and dilute to 10 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_7 (*2.2.2, Method II*).

Optical rotation (*2.2.7*): – 0.10° to + 0.10°, determined on solution S.

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 10.0 mL with the mobile phase.

Reference solution (a). Dissolve 2.5 mg of *miconazole nitrate CRS* and 2.5 mg of *econazole nitrate CRS* in the mobile phase, then dilute to 100.0 mL with the mobile phase.

Reference solution (b). Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 5.0 mL of this solution to 20.0 mL with the mobile phase.

Column:

– *size*: *l* = 0.10 m, Ø = 4.6 mm;

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (3 µm).

Mobile phase: dissolve 6.0 g of *ammonium acetate R* in a mixture of 300 mL of *acetonitrile R*, 320 mL of *methanol R* and 380 mL of *water R.*

Flow rate: 2 mL/min.

Detection: spectrophotometer at 235 nm.

Equilibration: with the mobile phase for about 30 min.

Injection: 10 µL.

Run time: 1.2 times the retention time of miconazole.

Retention time: econazole = about 10 min; miconazole = about 20 min.

System suitability: reference solution (a):

– *resolution*: minimum 10 between the peaks due to econazole and miconazole; if necessary, adjust the composition of the mobile phase.

Limits:

– *impurities A, B, C, D, E, F, G*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.25 per cent);

– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

– *disregard limit*: 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent); disregard any peak due to the nitrate ion.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2 h.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.350 g in 75 mL of *anhydrous acetic acid R*, with slight heating if necessary. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*). Carry out a blank titration.

1 mL of *0.1 M perchloric acid* is equivalent to 47.91 mg of $C_{18}H_{15}Cl_4N_3O_4$.

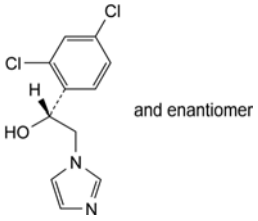
STORAGE

Protected from light.

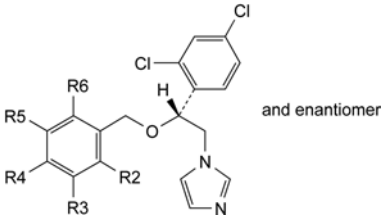
IMPURITIES

Specified impurities: A, B, C, D, E, F, G.

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*): *H, I.*



A. (1*RS*)-1-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-yl)ethanol,



B. R2 = R3 = R5 = R6 = H, R4 = Cl: 1-[(2*RS*)-2-[(4-chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole,

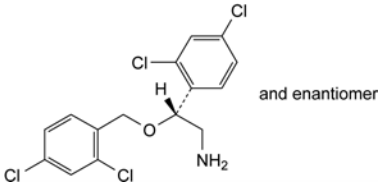
D. R2 = R6 = Cl, R3 = R4 = R5 = H: 1-[(2*RS*)-2-[(2,6-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole,

F. R2 = R5 = R6 = H, R3 = R4 = Cl: 1-[(2*RS*)-2-[(3,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole,

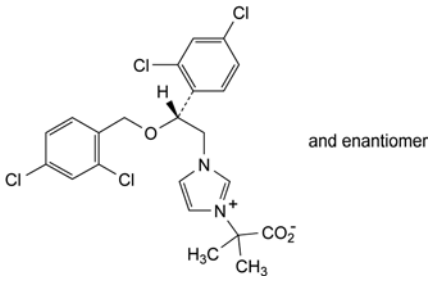
G. R2 = R5 = Cl, R3 = R4 = R6 = H: 1-[(2*RS*)-2-[(2,5-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole,

H. R2 = R3 = R4 = R5 = R6 = H: 1-[(2*RS*)-2-benzyloxy-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole,

I. R2 = Cl, R3 = R4 = R5 = R6 = H: 1-[(2*RS*)-2-[(2-chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole,



C. (2*RS*)-2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethanamine,



E. 2-[1-[(2*RS*)-2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazol-3-io]-2-methylpropanoate.

01/2008:2050
corrected 7.0

MICROCRYSTALLINE CELLULOSE AND CARMELLOSE SODIUM

Cellulosum microcristallinum et carmellosum natricum

DEFINITION

Colloid-forming, powdered mixture of *Microcrystalline Cellulose (0316)* with 5 per cent to 22 per cent of *Carmellose sodium (0472)*.

Content: 75.0 per cent to 125.0 per cent of the nominal amount of carmellose sodium (dried substance).

CHARACTERS

Appearance: white or off-white, coarse or fine powder.

Solubility: dispersible in water producing a white, opaque colloidal dispersion; practically insoluble in organic solvents and in dilute acids.

IDENTIFICATION

A. Mix 6 g with 300 mL of *water R* and stir at 18 000 r/min for 5 min. A white opaque dispersion is obtained which does not produce a supernatant liquid.

B. Add several drops of the dispersion obtained in identification A to a 10 per cent *V/V* solution of *aluminium chloride R*. Each drop forms a white, opaque globule which does not disperse on standing.

C. Add 2 mL of *iodinated potassium iodide solution R* to the dispersion obtained in test A. No blue or purplish colour is produced.

D. It complies with the limits of the assay.

TESTS

Solubility. Add 50 mg to 10 mL of *ammoniacal solution of copper tetrammine R* and shake. It dissolves completely leaving no residue.

pH (*2.2.3*): 6.0 to 8.0 for the dispersion obtained in identification A.

Loss on drying (*2.2.32*): maximum 8.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*): maximum 7.4 per cent, determined on 2.0 g.

ASSAY

Heat 2.00 g with 75 mL of *anhydrous acetic acid R* under a reflux condenser for 2 h, cool and 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 29.6 mg of carmellose sodium.

LABELLING

The label states the nominal percentage *m/m* of carmellose sodium.

Monographs M