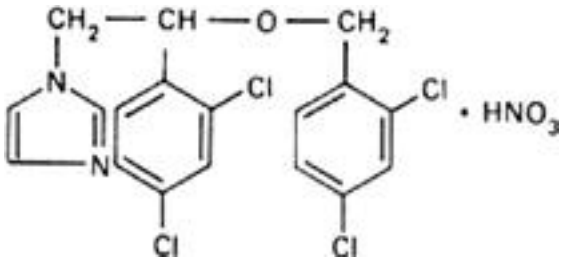
Miconazole nitrate (Miconazoli nitras)

Molecular formula. $C_{18}H_{14}Cl_4N_2O,HNO_3$

Relative molecular mass. 479.2

Graphic formula.



Chemical name. 1-[2,4-Dichloro-β-[(2,4-dichlorobenzyl)oxy]-phenethyl]imidazole mononitrate; 1-[2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)methoxy]-ethyl]-1*H*-imidazole mononitrate; CAS Reg. No. 22832-87-7.

Description. A white or almost white, crystalline powder; odourless or almost odourless.

Solubility. Very slightly soluble in water and ether R; soluble in 140 parts of ethanol (~750 g/l) TS.

Category. Antifungal drug.

Storage. Miconazole nitrate should be kept in a well-closed container, protected from light.

Additional information. Miconazole nitrate melts at about 182°C with decomposition.

Requirements

Definition. Miconazole nitrate contains not less than 98.5% and not more than 101.5% of $C_{18}H_{14}Cl_4N_2O,HNO_3$, calculated with reference to the dried substance.

Identity tests

• Either test A alone or tests B and C may be applied.

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from miconazole nitrate RS or with the *reference spectrum* of miconazole nitrate.

B. The absorption spectrum of a 0.40 mg/mL solution in a mixture of 9 volumes of methanol R and 1 volume of hydrochloric acid (0.1 mol/l) VS, when observed between 230 nm and 350 nm, exhibits maxima at about 264 nm, 272 nm, and 280 nm; the absorbances of a 1-cm layer at these wavelengths are about 0.40, 0.58, and 0.48, respectively.

C. Shake 10 mg with 5 mL of water and cool in an ice-bath. Keeping the suspension cool throughout, add 0.4 mL of potassium chloride (100 g/l) TS, 0.1 mL of diphenylamine/sulfuric acid TS, and, drop by drop with shaking, 5 mL of sulfuric acid (~1760 g/l) TS; an intense blue colour is produced.

Sulfated ash. Not more than 2.0 mg/g.

Loss on drying. Dry to constant weight at 100°C under reduced pressure (not exceeding 0.6 kPa or about 5 mm of mercury); it loses not more than 5.0 mg/g.

Related substances. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R1 as the coating substance and a mixture of 60 volumes of hexane R, 30 volumes of chloroform R, 10 volumes of methanol R, and 1 volume of ammonia (~260 g/l) TS as the mobile phase. Apply separately to the plate 50 µl of each of 2 solutions in a mixture of equal volumes of chloroform R and methanol R containing (A) 10 mg of the test substance per mL and (B) 25 µg of the test substance per mL. After removing the plate from the chromatographic chamber, allow it to dry in air, spray it with iodine/chloroform TS, and examine the chromatogram in daylight. Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B.

Assay. Dissolve about 0.35 g, accurately weighed, in 50 mL of glacial acetic acid R1 and titrate with perchloric acid (0.1 mol/l) VS, determining the end-point potentiometrically as described under 2.6 Non-aqueous titration, Method A. Each mL of perchloric acid (0.1 mol/l) VS is equivalent to 47.92 mg of $C_{18}H_{14}Cl_4N_2O,HNO_3$.