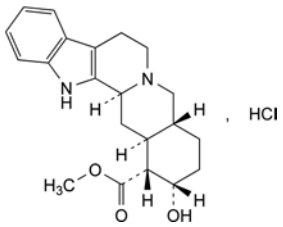
01/2008:2172

YOHIMBINE HYDROCHLORIDE

Yohimbini hydrochloridum



$C_{21}H_{27}ClN_2O_3$ M_r 390.9
[65-19-0]

DEFINITION

Methyl 17α-hydroxyyohimban-16α-carboxylate hydrochloride.

Content: 97.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance: white or slightly yellowish, crystalline powder.

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

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *yohimbine hydrochloride CRS*.

B. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 0.500 g in *carbon dioxide-free water R* with heating, allow to cool to room temperature and dilute to 50.0 mL with the same solvent.

pH (*2.2.3*): 3.5 to 5.5 for solution S.

Specific optical rotation (*2.2.7*): + 101.0 to + 105.0 (dried substance), determined on solution S.

Related substances. Liquid chromatography (*2.2.29*). *Prepare the solutions protected from light.*

Test solution. Dissolve 10.0 mg of the substance to be examined in *methanol R* and dilute to 50.0 mL with the same solvent.

Reference solution (a). Dissolve 5.0 mg of *yohimbine hydrochloride CRS* (containing impurities A, F and G) in *methanol R* and dilute to 25.0 mL with the same solvent.

Reference solution (b). Dilute 1.0 mL of reference solution (a) to 100.0 mL with *methanol R*.

Reference solution (c). Dilute 1.0 mL of reference solution (b) to 10.0 mL with *methanol R*.

Column:

– *size*: *l* = 0.125 m, Ø = 4.0 mm;
– *stationary phase*: *octylsilyl silica gel for chromatography R* (4 μm);
– *temperature*: 40 °C.

Mobile phase: mix 50 mL of a 9.08 g/L solution of *potassium dihydrogen phosphate R*, 100 mL of an 11.88 g/L solution of *disodium hydrogen phosphate dihydrate R*, 285 mL of *acetonitrile R*, 4.0 g of *sodium laurilsulfate R* and 355 mL of *water R*.

Flow rate: 1.5 mL/min.

Detection: spectrophotometer at 229 nm.

Injection: 10 μL.

Run time: 3 times the retention time of yohimbine.

Relative retention with reference to yohimbine (retention time = about 7 min): impurity F = about 0.65; impurity G = about 0.70; impurity A = about 0.75.

System suitability: reference solution (a):

– *peak-to-valley ratio*: minimum 1.3, where H_p = height above the baseline of the peak due to impurity G and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity A; and minimum 1.3, where H_p = height above the baseline of the peak due to impurity G and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity F.

Limits:

– *sum of impurities A and G*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent);
– *impurity F*: not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.4 per cent);
– *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.10 per cent);
– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (2.0 per cent);
– *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.05 per cent).

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

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

Injection: test solution and reference solution (a).

Calculate the percentage content of $C_{21}H_{27}ClN_2O_3$ from the declared content of *yohimbine hydrochloride CRS*.

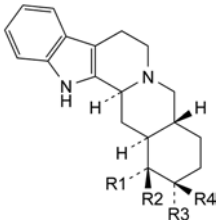
STORAGE

In an airtight container, protected from light.

IMPURITIES

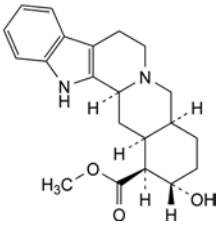
Specified impurities: *A, F, G*.

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*): *B, C, D, E*.

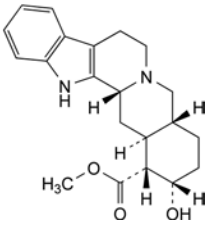


A. R1 = CO-OCH_3, R2 = R3 = H, R4 = OH: methyl 17β-hydroxyyohimban-16α-carboxylate (β-yohimbine),

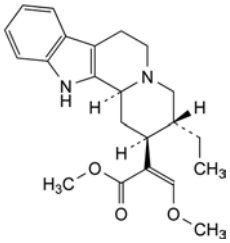
C. R1 = R4 = H, R2 = CO-OCH_3, R3 = OH: methyl 17α-hydroxyyohimban-16β-carboxylate (corynantheine),



B. methyl 17α-hydroxy-20α-yohimban-16β-carboxylate (α-yohimbine),



D. methyl 17α-hydroxy-3β-yohimban-16α-carboxylate (pseudo-yohimbine),



E. methyl (2*Z*)-2-[(2*S*,3*R*,12b*S*)-3-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizin-2-yl]-3-methoxyprop-2-enoate,

F. unknown structure,

G. unknown structure.