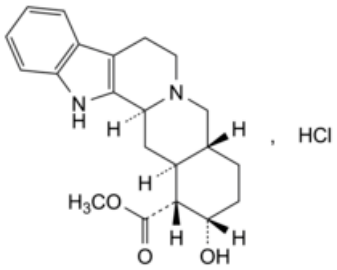
Edition: BP 2025 (Ph. Eur. 11.6 update)

Yohimbine Hydrochloride

General Notices

(Ph. Eur. monograph 2172)



$C_{21}H_{27}ClN_2O_3$ 390.9 *65-19-0*

Action and use

Alpha2-adrenoceptor antagonist.

Ph Eur

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 mg of *yohimbine for system suitability CRS* (containing impurities A, F and G) in *methanol R* and dilute to 25 mL with the same solvent.

Reference solution (b) Dilute 1.0 mL of the test solution 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*.

Reference solution (d) Dissolve 5.0 mg of *yohimbine hydrochloride CRS* in *methanol R* and dilute to 25.0 mL with the same solvent.

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 for chromatography R*, 4.0 g of *sodium laurilsulfate R* and 355 mL of *water for chromatography R*.

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 229 nm.

Injection 10 µL of the test solution and of reference solutions (a) (b) and (c).

Run time 3 times the retention time of yohimbine.

Identification of impurities Use the chromatogram supplied with *yohimbine for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A, F and G.

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; 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 (d).

Calculate the percentage content of $C_{21}H_{27}ClN_2O_3$ taking into account the assigned content of *yohimbine hydrochloride CRS*.

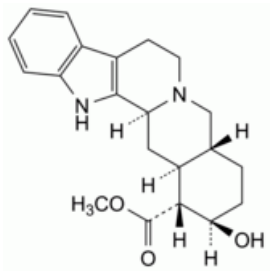
STORAGE

In an airtight container, protected from light.

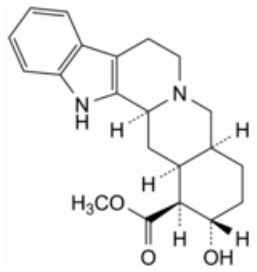
IMPURITIES

Specified impurities *A, F, G*.

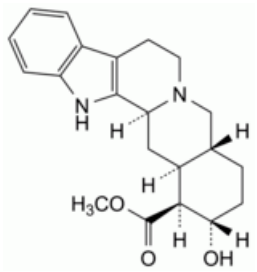
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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*.



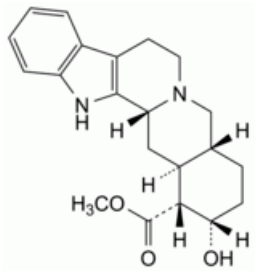
A. methyl 17β-hydroxyyohimban-16α-carboxylate (β-yohimbine),



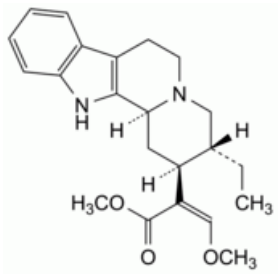
B. methyl 17α-hydroxy-20α-yohimban-16β-carboxylate (α-yohimbine),



C. methyl 17α-hydroxyyohimban-16β-carboxylate (corynantheine),



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.

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