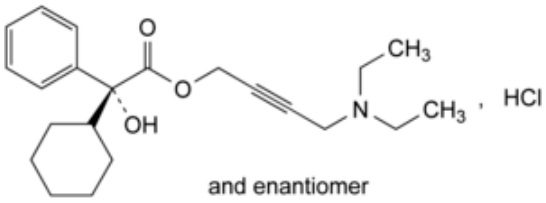
Edition: BP 2025 (Ph. Eur. 11.6 update)

Oxybutynin Hydrochloride

General Notices

(Ph. Eur. monograph 1354)



$C_{22}H_{32}ClNO_3$ 394.0 *1508-65-2*

Action and use

Anticholinergic.

Preparations

Oxybutynin Oral Solution

Oxybutynin Tablets

Oxybutynin Prolonged-release Tablets

Ph Eur

DEFINITION

4-(Diethylamino)but-2-yn-1-yl (*RS*)-cyclohexyl(hydroxy)phenylacetate hydrochloride.

Content

99.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Freely soluble in water and in ethanol (96 per cent), soluble in acetone, practically insoluble in cyclohexane.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 124 °C to 129 °C.
B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *oxybutynin hydrochloride CRS*.

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

Test solution Dissolve 50 mg of the substance to be examined in *ethanol (96 per cent) R* and dilute to 10 mL with the same solvent.

Reference solution Dissolve 10 mg of *oxybutynin hydrochloride CRS* in *ethanol (96 per cent) R* and dilute to 2 mL with the same solvent.

Plate *TLC silica gel plate R*.

Mobile phase *methanol R*.

Application 5 µL.

Development Over 2/3 of the plate.

Drying In air.

Detection Expose to iodine vapour for 30 min.

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 the reference solution.

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

TESTS

Solution S

Dissolve 2.00 g in *water R* and dilute to 20.0 mL with the same solvent.

Appearance of solution

Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution BY_5 (*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 50.0 mg of the substance to be examined in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution (a) Dissolve 5.0 mg of oxybutynin hydrochloride CRS and 5.0 mg of oxybutynin impurity A CRS in the mobile phase and dilute to 10.0 mL with the mobile phase. Dilute 5.0 mL of this solution to 50.0 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 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (c) Dissolve 5 mg of oxybutynin hydrochloride for system suitability CRS (containing impurities C, D and F) in 1 mL of the mobile phase.

Column:

— *size*: *l* = 0.15 m, Ø = 3.9 mm;

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

— *temperature*: 35 °C.

Mobile phase Mix 49 volumes of a solution containing 3.4 g/L of potassium dihydrogen phosphate R and 4.36 g/L of dipotassium hydrogen phosphate R and 51 volumes of acetonitrile R1.

Flow rate 1 mL/min.

Detection Spectrophotometer at 210 nm.

Injection 10 µL.

Run time Twice the retention time of oxybutynin.

Identification of impurities Use the chromatogram obtained with reference solution (a) to identify the peak due to impurity A; use the chromatogram supplied with oxybutynin hydrochloride for system suitability CRS and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities C, D and F.

Relative retention With reference to oxybutynin (retention time = about 15 min): impurity D = about 0.08; impurity F = about 0.7; impurity C = about 0.8; impurity A = about 1.6.

System suitability Reference solution (c):

— resolution: minimum 2.0 between the peaks due to impurities F and C.

Calculation of percentage contents:

— *correction factor*: multiply the peak area of impurity D by 0.6;

— for impurity A, use the concentration of impurity A in reference solution (a);

— for impurities other than A, use the concentration of oxybutynin hydrochloride in reference solution (b).

Limits:

— *impurity A*: maximum 1.5 per cent;

— *impurities C, D, F*: for each impurity, maximum 0.15 per cent;

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

— *sum of impurities other than A*: maximum 0.5 per cent;

— *reporting threshold*: 0.05 per cent.

Loss on drying (*2.2.32*)

Maximum 3.0 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 0.300 g in a mixture of 5.0 mL of *0.01 M hydrochloric acid* and 50 mL of *ethanol (96 per cent) R*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 mL of *0.1 M sodium hydroxide* is equivalent to 39.40 mg of $C_{22}H_{32}ClNO_3$.

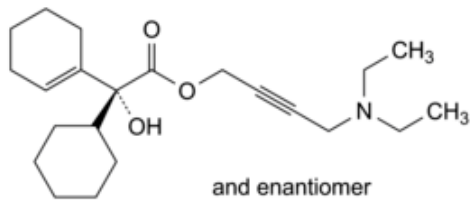
STORAGE

Protected from light.

IMPURITIES

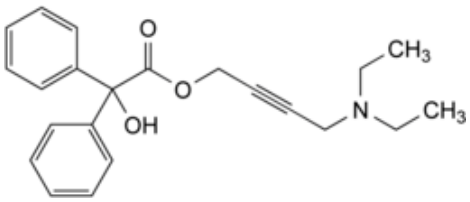
Specified impurities *A, C, D, F.*

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, E.*

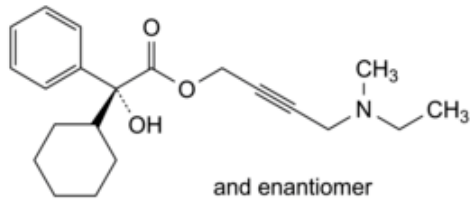


and enantiomer

A. 4-(diethylamino)but-2-yn-1-yl (*RS*)-(cyclohex-1-en-1-yl)(cyclohexyl)hydroxyacetate,

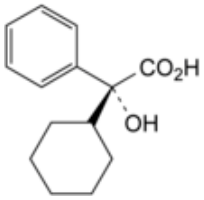


B. 4-(diethylamino)but-2-yn-1-yl hydroxy(diphenyl)acetate (diphenyl analogue of oxybutynin),



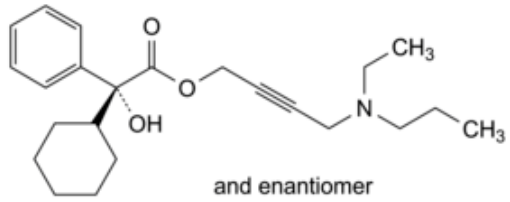
and enantiomer

C. 4-[ethyl(methyl)amino]but-2-yn-1-yl (*RS*)-cyclohexyl(hydroxy)phenylacetate (methylethyl analogue of oxybutynin),



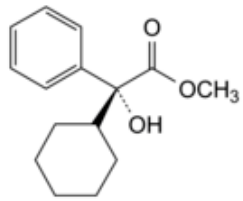
and enantiomer

D. (*RS*)-cyclohexyl(hydroxy)phenylacetic acid (cyclohexylphenylglycolic acid),



and enantiomer

E. 4-[ethyl(propyl)amino]but-2-yn-1-yl (*RS*)-cyclohexyl(hydroxy)phenylacetate (ethylpropyl analogue of oxybutynin),



and enantiomer

F. methyl (*RS*)-cyclohexyl(hydroxy)phenylacetate.

Ph Eur