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

Oxybutynin Prolonged-release Tablets

General Notices

Prolonged-release Oxybutynin Tablets

Oxybutynin Prolonged-release Tablets from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

Anticholinergic.

DEFINITION

Oxybutynin Prolonged-release Tablets contain Oxybutynin Hydrochloride. They are formulated so that the medicament is released over a period of several hours.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Oxybutynin Hydrochloride. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of oxybutynin hydrochloride, $C_{22}H_{31}NO_3$,HCl

92.5 to 107.0% of the stated amount.

IDENTIFICATION

To a quantity of the powdered tablets containing 25 mg of Oxybutynin Hydrochloride add sufficient 2M *sodium hydroxide* to adjust to pH 12.0 and extract with 4 20-mL quantities of *hexane*. Filter the collected hexane layers through *anhydrous sodium sulfate* (Whatman GF/C is suitable). Evaporate the filtrate to dryness under a current of nitrogen, to yield a clear, sticky liquid residue. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of oxybutynin *(RS 442)*.

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Mix a quantity of the powdered tablets containing 50 mg of Oxybutynin Hydrochloride with 40 mL of 0.01M *hydrochloric acid* with the aid of ultrasound for 15 minutes, add sufficient 0.01M *hydrochloric acid* to produce 50 mL, mix and filter (Whatman GF/A filters are suitable).
(2) 0.0015% w/v of *oxybutynin impurity A EPCRS* in 0.01M *hydrochloric acid*.

(3) 0.0014% w/v of *phenylcyclohexylglycolic acid BPCRS* in 0.01M *hydrochloric acid*.
(4) Dilute 1 volume of solution (1) to 200 volumes with 0.01M *hydrochloric acid*.
(5) 0.001% w/v of *oxybutynin impurity A EPCRS* in solution (4).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography R1* (5 µm) (Symmetry C18 is suitable).
(b) Use gradient elution and the mobile phases described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 210 nm.
(f) Inject 50 µL of each solution.
(g) When the chromatograms are recorded under the prescribed conditions the retention times are about 31 minutes for oxybutynin hydrochloride and about 47 minutes for oxybutynin impurity A.

MOBILE PHASE

Mobile phase A 0.34% w/v of *potassium dihydrogen orthophosphate* and 0.436% w/v of *dipotassium hydrogen orthophosphate*.

Mobile phase B *acetonitrile R1*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	70	30	isocratic
5-6	70→45	30→55	linear gradient
6-50	45	55	isocratic
50-51	45→70	55→30	linear gradient
51-60	70	30	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (5), the *resolution factor* between the peaks due to oxybutynin hydrochloride and oxybutynin impurity A is at least 10.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to oxybutynin impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.5%);

the area of any peak corresponding to phenylcyclohexylglycolic acid is not greater than half the area of the principal peak in the chromatogram obtained with solution (3) (0.7%);

the area of any other *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

the sum of the areas of any s*econdary peaks* is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (4) (1.5%).

Disregard any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with solution (4) (0.05%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Mix 10 whole tablets with 400 mL of 0.01M *hydrochloric acid* for 20 minutes with the aid of ultrasound, cool, add sufficient 0.01M *hydrochloric acid* to produce 500 mL, mix and filter (Whatman GF/A filters are suitable). Dilute a volume of

this solution with sufficient 0.01M *hydrochloric acid* to produce a solution containing 0.005% w/v of Oxybutynin Hydrochloride.
(2) 0.005% w/v of *oxybutynin hydrochloride BPCRS* in 0.01M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *nitrile silica gel for chromatography R1* (5 µm) (Spherisorb CN is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 200 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

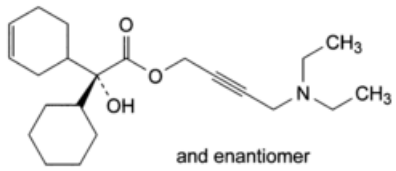
300 volumes of *acetonitrile R1* and 700 volumes of a 0.48% w/v solution of *anhydrous potassium dihydrogen orthophosphate* previously adjusted to pH 3.0 to 3.5 with *orthophosphoric acid*.

DETERMINATION OF CONTENT

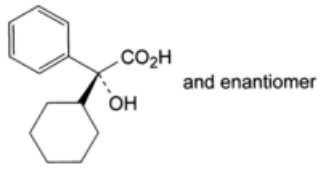
Calculate the content of $C_{22}H_{31}NO_3$,HCl in the tablets using the declared content of $C_{22}H_{31}NO_3$,HCl in *oxybutynin hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include:



1. 4-(diethylamino)but-2-ynyl (*RS*)-2-(cyclohex-3-enyl)-2-cyclohexyl-2-hydroxyacetate (European Pharmacopoeia impurity A),



2. (*RS*)-2-cyclohexyl-2-hydroxy-2-phenylacetic acid (phenylcyclohexylglycolic acid) (European Pharmacopoeia impurity D).