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

Oxycodone Capsules

General Notices

Oxycodone Hydrochloride Capsules

Action and use

Opioid receptor agonist; analgesic.

DEFINITION

Oxycodone Capsules contain Oxycodone Hydrochloride.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Content of oxycodone hydrochloride, $C_{18}H_{21}NO_4,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the capsule contents containing 50 mg of Oxycodone Hydrochloride with 10 mL of *water*, filter and make the filtrate alkaline with *dilute ammonia R1*. Allow the solution to stand until a precipitate is formed. Filter and wash the precipitate with 10 mL of cold *water*. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of oxycodone hydrochloride *(RS 457)*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.
(b) Use 900 mL of *0.1M hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 45 minutes withdraw a sample of the medium and filter. Use the filtered medium, diluted with *0.1M hydrochloric acid* if necessary, expected to contain 0.0005% w/v of Oxycodone Hydrochloride.
(2) 0.0005% w/v of *oxycodone hydrochloride BPCRS* in *0.1M hydrochloric acid*.
(3) 0.0002% w/v of *oxycodone impurity standard BPCRS* in 0.02M *acetic acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm x 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil 100-5C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 230 nm.
(f) Inject 100 µL of each solution.
(g) For solution (3) allow the chromatography to proceed for 4 times the retention time of the peak due to oxycodone.

MOBILE PHASE

100 volumes of *acetonitrile*, 200 volumes of *methanol* and 700 volumes of a solution containing 0.11% w/v of *sodium heptanesulfonate monohydrate* previously adjusted to pH 2.0 with 8M *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to oxycodone and 14-hydroxycodeinone is at least 2.0.

DETERMINATION OF CONTENT

Calculate the total content of oxycodone hydrochloride, $C_{18}H_{21}NO_4$, HCl, in the medium from the chromatograms obtained and using the declared content of $C_{18}H_{21}NO_4$,HCl in *oxycodone hydrochloride BPCRS*.

LIMITS

The amount of oxycodone hydrochloride released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in 0.02M *acetic acid*.

(1) Shake, with the aid of ultrasound, a quantity of the capsule contents containing 20 mg of Oxycodone Hydrochloride with 40 mL of 0.02M *acetic acid*, add sufficient 0.02M *acetic acid* to produce 50 mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) Dilute 2 volumes of solution (2) to 10 volumes.
(4) 0.0002% w/v of *oxycodone impurity standard BPCRS*.
(5) Dilute 1 volume of solution (3) to 4 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm x 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Kromasil C18 is suitable).
(b) Use gradient elution and the mobile phases described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 230 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

Mobile phase A 70 volumes of *acetonitrile*, 100 volumes of *methanol* and 830 volumes of a 0.11% w/v solution of *sodium heptanesulfonate monohydrate* previously adjusted to pH 2.0 with 8M *orthophosphoric acid*.

Mobile phase B 150 volumes of *acetonitrile*, 250 volumes of *methanol* and 600 volumes of a 0.11% w/v solution of *sodium heptanesulfonate monohydrate* previously adjusted to pH 2.0 with 8M *orthophosphoric acid*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-60	100→50	0→50	linear gradient
60-62	50→100	50→0	linear gradient
62-70	100	0	isocratic

When the chromatograms are recorded using the prescribed conditions the retention time of oxycodone is about 24 minutes. The retention times relative to oxycodone are: impurity D, about 1.18; impurity E, about 1.18 and impurity F, about 2.4.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to oxycodone and 14-hydroxycodeinone is at least 3.0.

LIMITS

Identify any peaks in the chromatogram obtained with solution (1) corresponding to thebaine and multiply the area of this peak by 0.5.

In the chromatogram obtained with solution (1):

the sum of the areas of any peaks corresponding to 14-hydroxycodeinone and hydrocodone is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.05%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in 0.02M *acetic acid*.

(1) Shake, with the aid of ultrasound, a quantity of the capsule contents containing 25 mg of Oxycodone Hydrochloride with 40 mL of 0.02M *acetic acid*, add sufficient 0.02M *acetic acid* to produce 50 mL and filter. Dilute 1 volume of the filtrate to 100 volumes with 0.02M *acetic acid*.
(2) 0.0005% w/v of *oxycodone hydrochloride BPCRS*.
(3) 0.0002% w/v of *oxycodone impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to oxycodone and 14-hydroxycodeinone is at least 2.0.

DETERMINATION OF CONTENT

Calculate the total content of oxycodone hydrochloride, $C_{18}H_{21}NO_4$,HCl, in the capsules using the declared content of $C_{18}H_{21}NO_4$,HCl in *oxycodone hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of the monograph include:

D. 7,8-didehydro-4,5α-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one (14-hydroxycodeinone);
E. 4,5α-epoxy-3-methoxy-17-methylmorphinan-6-one (hydrocodone);
F. 6,7,8,14-tetradehydro-4,5α-epoxy-3-6-dimethoxy-17-methylmorphinan (thebaine).