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Oxytetracycline Capsules

General Notices

Action and use

Tetracycline antibacterial.

DEFINITION

Oxytetracycline Capsules contain Oxytetracycline Hydrochloride.

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

Content of oxytetracycline hydrochloride, $C_{22}H_{24}N_2O_9$,HCl

95.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Extract a quantity of the contents of the capsules containing 10 mg of Oxytetracycline Hydrochloride with 20 mL of *methanol*, centrifuge and use the supernatant liquid.
(2) Dissolve 5 mg of *oxytetracycline hydrochloride BPCRS* in sufficient *methanol* to produce 10 mL.
(3) Dissolve 5 mg of *oxytetracycline hydrochloride BPCRS* and 5 mg of *demeclocycline hydrochloride BPCRS* in sufficient *methanol* to produce 10 mL.

CHROMATOGRAPHIC CONDITIONS

(a) Use a silica gel precoated plate (Merck silica gel 60 plates are suitable). Adjust the pH of a 10% w/v solution of *disodium edetate* to 7.0 with 10M *sodium hydroxide* and spray the solution evenly onto the plate (about 10 mL for a plate 100 mm × 200 mm). Allow the plate to dry in a horizontal position for at least 1 hour. Before use, dry the plate at 110° for 1 hour.
(b) Use the mobile phase as described below.
(c) Apply 1 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry it in a current of air and examine under *ultraviolet light (365 nm)*.

MOBILE PHASE

6 volumes of *water*, 35 volumes of *methanol* and 59 volumes of *dichloromethane*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows two clearly separated spots.

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The principal spot in the chromatogram obtained with solution (1) corresponds in position, colour and size to that in the chromatogram obtained with solution (2).

B. To 0.5 mg of the contents of the capsules add 2 mL of *sulfuric acid*; a deep crimson colour is produced. Add 1 mL of *water*; the colour changes to yellow.
C. The contents of the capsules yield the reactions characteristic *of chlorides*, Appendix VI.

TESTS

Dissolution

Comply with the requirements in 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

After 45 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium if necessary, at the maximum at 353 nm, Appendix II B, using 0.1M *hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of oxytetracycline hydrochloride, $C_{22}H_{24}N_2O_9$,HCl, in the medium taking 282 as the value of A(1%, 1 cm) at the maximum at 353 nm.

LIMITS

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

Light-absorbing impurities

Dissolve a portion of the mixed contents of five capsules as completely as possible in sufficient of a mixture of 1 volume of 1M *hydrochloric acid* and 99 volumes of *methanol* to produce two solutions of Oxytetracycline Hydrochloride containing (1) 0.20% w/v and (2) 1.0% w/v, and filter each solution.

The *absorbance* of the filtrate obtained from solution (1) at 430 nm is not more than 0.75, Appendix II B, calculated with reference to the dried capsule contents. The *absorbance* of the filtrate obtained from solution (2) at 490 nm is not more than 0.40, calculated with reference to the dried capsule contents.

Loss on drying

When dried at 60° at a pressure not exceeding 0.7 kPa for 3 hours, the contents of the capsules lose not more than 5.0% of their weight. Use 1 g.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 20 volumes of *acetonitrile* and 80 volumes of 0.01M *oxalic acid* (solvent A). Prepare the solutions immediately before use.

(1) Shake a quantity of the mixed contents of the capsules containing 0.16 g of Oxytetracycline Hydrochloride in 150 mL of solvent A and dilute to 200 mL. Filter the resulting solution (Whatman GF/C filter is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.08% w/v of *oxytetracycline for system suitability A EPCRS*.
(4) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

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(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octylsilyl silica gel for chromatography* (5 µm) (Intertsil C8 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.3 mL per minute.
(d) Use a column temperature of 50°.
(e) Use a detection wavelength of 254 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 0.05% v/v *trifluoroacetic acid*.

Mobile phase B 5 volumes of *tetrahydrofuran*, 15 volumes of *methanol* and 80 volumes of *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	90	10	isocratic
5-20	90→65	10→35	linear gradient
20-21	65→90	35→10	linear gradient
21-27	90	10	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to oxytetracycline (retention time about 6.5 minutes) are: impurity A, about 0.9; impurity B, about 1.2; impurity C, about 1.3; impurity D, about 1.4; impurity E, about 2.2; impurity F, about 2.3.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 3.0, where *Hp* is the height above the baseline of the peak due to impurity A and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to oxytetracycline.

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 3.0, where *Hp* is the height above the baseline of the peak due to impurity B and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to oxytetracycline.

LIMITS

Identify any peak corresponding to impurities A, B, C, D, E and F in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3). Multiply the areas of any peaks due to impurity D and E by a correction factor of 0.4.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than half the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any peak corresponding to impurity B is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the area of any peak corresponding to impurity C is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (2.0%);

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

the sum of the areas of all the *secondary peaks* is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (2) (4.0%).

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

ASSAY

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Weigh the contents of 20 capsules. Mix and powder if necessary. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 20 volumes of *acetonitrile* and 80 volumes of 0.01M *oxalic acid* (solvent A). Prepare the solutions immediately before use.

(1) Shake, with the aid of ultrasound, a quantity of the mixed capsule contents containing 0.16 mg of Oxytetracycline Hydrochloride with 150 mL of solvent A. Dilute to 200 mL and filter (Whatman GF/C filter is suitable). Dilute 1 volume of the filtrate to 10 volumes.
(2) 0.0074% w/v of *oxytetracycline BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions stated under Related substances may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{22}H_{24}N_2O_9$,HCl in the capsules using the declared content of $C_{22}H_{24}N_2O_9$ in *oxytetracycline BPCRS*. Each mg of $C_{22}H_{24}N_2O_9$ is equivalent to 1.079 mg of $C_{22}H_{24}N_2O_9$,HCl.

STORAGE

Oxytetracycline Capsules should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Oxytetracycline Hydrochloride.

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