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

Tetracycline Tablets

General Notices

Action and use

Tetracycline antibacterial.

DEFINITION

Tetracycline Tablets contain Tetracycline Hydrochloride.

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

Content of tetracycline hydrochloride, $C_{22}H_{24}N_2O_8,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

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

After 45 minutes withdraw a sample of the medium. Measure the *absorbance* of the filtered sample, suitably diluted if necessary, at the maximum at 353 nm, Appendix II B.

DETERMINATION OF CONTENT

Calculate the total content of tetracycline hydrochloride, $C_{22}H_{24}N_2O_8$,HCl, in the medium taking 310 as the value of A(1%, 1 cm) at the maximum at 353 nm.

LIMITS

The amount of tetracycline hydrochloride released is not less than 70% (Q) of the stated amount.

Related substances

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

(1) Dissolve, with the aid of ultrasound, a quantity of the powdered tablets containing 25 mg of Tetracycline Hydrochloride in sufficient mobile phase A, dilute to produce 250 mL and filter.
(2) Dilute 3 volumes of solution (1) to 200 volumes.
(3) 0.0003% w/v of *4-epitetracycline hydrochloride EPCRS* (impurity A), 0.0001% w/v each of *anhydrotetracycline hydrochloride EPCRS* (impurity C) and *4-epianhydrotetracycline hydrochloride EPCRS* (impurity D) and 0.00001% w/v of *tetracycline hydrochloride BPCRS*.
(4) 0.0025% w/v each of *4-epitetracycline hydrochloride EPCRS* (impurity A), *anhydrotetracycline hydrochloride EPCRS* (impurity C), *4-epianhydrotetracycline hydrochloride EPCRS* (impurity D) and *tetracycline hydrochloride BPCRS*.
(5) Dilute 1 volume of solution (2) to 15 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Phenomenex Prodigy ODS 3 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an autosampler temperature of 4°.
(e) Use a column temperature of 50°.
(f) Use a detection wavelength of 280 nm.
(g) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 0.1% v/v of *orthophosphoric acid*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-7.5	85→60	15→40	linear gradient
7.5-7.6	60→85	40→15	linear gradient
7.6-10	85	15	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4):

the *resolution* between the peaks due to impurity A and tetracycline is at least 2.5;

the *resolution* between the peaks due to impurities C and D is at least 2.5.

CALCULATION OF IMPURITIES

For impurities A, C and D, use the concentration of each impurity in solution (3).

For impurity B, use the concentration of tetracycline in solution (2).

For any other impurity, use the concentration of tetracycline in solution (5).

For the reporting threshold, use the concentration of tetracycline in solution (5).

For peak identification, use solution (3).

Tetracycline retention time: about 4 minutes.

Relative retention: impurity A, about 0.9; impurity B, about 1.3; impurity D, about 1.7 and impurity C, about 1.8.

LIMITS

— impurity A: not more than 4.0%;

— impurity B: not more than 1.5%;

— impurity C: not more than 3.0%;

— impurity D: not more than 2.0%;

— unspecified impurities: for each impurity, not more than 0.1%;

— total impurities: not more than 4.0%;

— reporting threshold: 0.05%.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in mobile phase A.

(1) Dissolve, with the aid of ultrasound, a quantity of the powdered tablets containing 25 mg of Tetracycline Hydrochloride in sufficient mobile phase A, dilute to produce 250 mL and filter.
(2) 0.01% w/v of *tetracycline hydrochloride BPCRS*.
(3) 0.0025% w/v each of *4-epitetracycline hydrochloride EPCRS* (impurity A), *anhydrotetracycline hydrochloride EPCRS* (impurity C), *4-epianhydrotetracycline hydrochloride EPCRS* (impurity D) and *tetracycline hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances 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 impurity A and tetracycline is at least 2.5;

the *resolution* between the peaks due to impurities C and D is at least 2.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{22}H_{24}N_2O_8$,HCl in the tablets from the chromatograms obtained and using the declared content of $C_{22}H_{24}N_2O_8$,HCl in *tetracycline hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B, C and D listed under Tetracycline Hydrochloride.