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

Chlortetracycline Tablets

General Notices

Action and use

Tetracycline antibacterial.

DEFINITION

Chlortetracycline Tablets contain Chlortetracycline Hydrochloride.

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

Content of chlortetracycline hydrochloride, $C_{22}H_{23}ClN_2O_8,HCl$

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 powdered tablets containing 10 mg of Chlortetracycline Hydrochloride with 20 mL of *methanol* and centrifuge.
(2) 0.05% w/v of *chlortetracycline hydrochloride BPCRS* in *methanol*.
(3) 0.05% w/v of each of *chlortetracycline hydrochloride BPCRS*, *tetracycline hydrochloride BPCRS* and *metacycline hydrochloride BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use *silica gel H* as the coating. Adjust the pH of a 10% w/v solution of *disodium edetate* to 8.0 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. At the time of use, dry the plate in an oven 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, allow it to dry 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 three clearly separated spots.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

B. To a quantity of the powdered tablets containing 10 mg of Chlortetracycline Hydrochloride add 20 mL of warm *ethanol (96%)*, allow to stand for 20 minutes, filter and evaporate to dryness on a water bath. A 0.1% w/v solution of the residue in *phosphate buffer pH 7.6*, when heated at 100° for 1 minute, exhibits a strong blue fluorescence in ultraviolet light.

TESTS

Tetracycline hydrochloride and 4-epichlortetracycline hydrochloride

Not more than 8.0% and 6.0% respectively, determined as described under Assay. Inject separately solutions (1) and (4).

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 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 10 mL sample of the medium and filter. Measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium if necessary, at the maximum at 266 nm, Appendix II B, using 0.1M *hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of chlortetracycline hydrochloride, $C_{22}H_{23}ClN_2O_8$,HCl, in the medium taking 346 as the value of A(1%, 1 cm) at the maximum at 266 nm.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions *prepared immediately before use*.

(1) Mix a quantity of the powdered tablets containing 25 mg of Chlortetracycline Hydrochloride with 50 mL of 0.01M *hydrochloric acid*, shake for 10 minutes, dilute to 100 mL with 0.01M *hydrochloric acid* and filter (GF/C paper is suitable).
(2) 0.025% w/v of *chlortetracycline hydrochloride BPCRS* in 0.01M *hydrochloric acid*.
(3) 0.025% w/v of each of *chlortetracycline hydrochloride BPCRS* and *4-epichlortetracycline hydrochloride* in 0.01M *hydrochloric acid*.
(4) 0.002% w/v of *tetracycline hydrochloride BPCRS* and 0.0015% w/v of *4-epichlortetracycline hydrochloride* in 0.01M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (10 µm) (Nucleosil C18 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 355 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

20 volumes of *dimethylformamide* and 80 volumes of 0.1M *oxalic acid* the pH of which has been adjusted to 2.2 with *triethylamine*.

SYSTEM SUITABILITY

The assay is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the two principal peaks is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{22}H_{23}ClN_2O_8$,HCl in the tablets using the declared content of $C_{22}H_{23}ClN_2O_8$,HCl in *chlortetracycline hydrochloride BPCRS*.