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

Hydrochlorothiazide Tablets

General Notices

Action and use

Thiazide diuretic.

DEFINITION

Hydrochlorothiazide Tablets contain Hydrochlorothiazide.

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

Content of hydrochlorothiazide, $C_7H_8ClN_3O_4S_2$

92.5 to 107.5% of the stated amount.

IDENTIFICATION

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.

(1) Triturate a quantity of the powdered tablets containing 10 mg of Hydrochlorothiazide with 10 mL of *acetone* and filter.
(2) 0.1% w/v of *hydrochlorothiazide BPCRS* in *acetone*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel GF_{254}*.
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in a current of air, examine under *ultraviolet light (254 nm)* and then treat the plate by *Method I* and examine again.

MOBILE PHASE

ethyl acetate.

CONFIRMATION

By each method of visualisation the principal spot in the chromatogram obtained with solution (1) corresponds in colour and intensity to that in the chromatogram obtained with solution (2).

TESTS

Related substances

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

(1) Shake a quantity of the powdered tablets containing 50 mg of Hydrochlorothiazide with 25 mL of a mixture of equal volumes of *acetonitrile* and *methanol* and dilute to 100 mL with *phosphate buffer solution pH 3.2 R1*. Filter through a glass-fibre filter (Whatman 0.45µ GD/X is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with a mixture containing 1 volume of *methanol*, 1 volume of *acetonitrile* and 2 volumes of *phosphate buffer solution pH 3.2 R1*.
(3) Dissolve, with the aid of ultrasound, 15 mg each of *hydrochlorothiazide BPCRS* and *chlorothiazide BPCRS* in 25 mL of a mixture of equal volumes of *acetonitrile* and *methanol* and dilute to 100 mL with *phosphate buffer solution pH 3.2 R1*. Dilute 5 volumes of this solution to 100 volumes with the same solvent mixture.
(4) Dilute 1 volume of solution (2) to 10 volumes with a mixture containing 1 volume of *methanol*, 1 volume of *acetonitrile* and 2 volumes of *phosphate buffer solution pH 3.2 R1*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (3 µm) (Phenosphere ODS 3µ or Microsorb ODS 3µ is suitable).
(b) Use gradient elution and the mobile phases described below.
(c) Use a flow rate of 0.8 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 224 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE A

10 volumes of *tetrahydrofuran*, 60 volumes of *methanol* and 940 volumes of *phosphate buffer solution pH 3.2 R1*.

MOBILE PHASE B

50 volumes of *tetrahydrofuran*, 500 volumes of *methanol* and 500 volumes of *phosphate buffer solution pH 3.2 R1*.

Equilibrate the column for at least 20 minutes with mobile phase A.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-17	100→55	0→45	linear gradient
17-30	55	45	isocratic
30-35	55→100	45→0	linear gradient
35-50	100	0	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks corresponding to chlorothiazide and hydrochlorothiazide is at least 2.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the sum of the areas of any *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (2.5%).

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

ASSAY

Weigh and powder 20 tablets. To a quantity of the powder containing 30 mg of Hydrochlorothiazide add 50 mL of 0.1M *sodium hydroxide*, shake for 20 minutes and dilute to 100 mL with 0.1M *sodium hydroxide*. Mix, filter, dilute 5 mL of the filtrate to 100 mL with *water* and measure the *absorbance* of the resulting solution at the maximum at 273 nm, Appendix II B. Calculate the content of $C_7H_8ClN_3O_4S_2$ taking 520 as the value of A(1%, 1 cm) at the maximum at 273 nm.