Triamterene and Hydrochlorothiazide Tablets

Triamterene and Hydrochlorothiazide Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amounts of triamterene, $C_{12}H_{11}N_7$ and hydrochlorothiazide, $C_7H_8ClN_3O_4S_2$.

Usual strength. Triamterene, 50 mg and Hydrochlorothiazide, 25 mg.

Identification

In the Assay, the principal peaks in the chromatogram obtained with the test solution correspond to the peaks in the chromatogram obtained with reference solution (a).

Tests

Dissolution (2.5.2).
Apparatus No. 2 (Paddle),
Medium. 900 ml of *0.1M hydrochloric acid*,
Speed and time. 75 rpm and 30 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Use the filtrate, dilute if necessary, with the dissolution medium.

Reference solution. Dissolve a suitable quantity of *triamterene IPRS* and *hydrochlorothiazide IPRS* in the dissolution medium to obtain a solution of known concentration similar to the expected concentration of the test solution.

Chromatographic system
- a stainless steel column 25cm x 4.0 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 80 volumes of a buffer solution prepared by dissolving 6.9 g of *sodium dihydrogen phosphate* and 1.43 g of *propylamine hydrochloride* in 1000 ml of *water*, adjusted to pH 5.5 with *1M sodium hydroxide* and 20 volumes of *acetonitrile*,
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 280 nm,
- injection volume: 10 µl.

The relative retention times with reference to triamterene for hydrochlorothiazide is about 0.65.

Inject the reference solution. The test is not valid unless the resolution between the hydrochlorothiazide and triamterene peaks is not less than 3.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent for both the peaks.

Inject the reference solution and the test solution.

Calculate the contents of $C_{12}H_{11}N_7$ and $C_7H_8ClN_3O_4S_2$ in the medium.

Q. Not less than 80 per cent of the stated amount of $C_{12}H_{11}N_7$ and $C_7H_8ClN_3O_4S_2$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture A. A buffer solution prepared by dissolving 6.8 g of *sodium acetate trihydrate* in 1000 ml of *water,* adjusted to pH 5.0 with *glacial acetic acid.*

Solvent mixture B. 75 volumes of *acetonitrile* and 25 volumes of *methanol.*

Test solution. Disperse a quantity of the powdered tablets containing 150 mg of Hydrochlorothiazide in 60 ml of *acetonitrile* and 6 ml of *glacial acetic acid*, with the aid of ultrasound for 10 minutes. Cool and dilute to 100.0 ml with *water.*

Reference solution. A 0.015 per cent w/v solution of *benzothiadiazine related compound A (4-Amino-6-chloro-1,3-benzenedisulphonamide) IPRS* in *acetonitrile*. Transfer 10.0 ml of the solution to 100-ml volumetric flask, add 50 ml of *acetonitrile* and 6 ml of *glacial acetic acid* and dilute with *water* to volume.

Chromatographic system
- a stainless steel column 30 cm x 3.9 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 10 volumes of solvent mixture B and 90 volumes of solvent mixture A,
- flow rate: 2 ml per minute,
- spectrophotometer set 273 nm,
- injection volume: 10 µl.

The relative retention times with reference to benzothiadiazine related compound A for hydrochlorothiazide and triamterene are 1.5 and 10, respectively.

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area any peak corresponding to benzothiadiazine related compound A is not more than the area of the principal peak in the chromatogram obtained with the reference solution (1.0 per cent).

Other tests. Comply with the tests stated under tablets.

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. 35 volumes of *acetonitrile,* 3.5 volumes of *glacial acetic acid* and 65 volumes of *water*.

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 250 mg of hydrochlorothiazide in the solvent mixture, with the aid of ultrasound for 30 minutes and dilute to 500.0 ml with the solvent mixture, filter. Dilute 3.0 ml of the solution to 100.0 ml with the mobile phase.

Reference solution (a). A solution containing 0.3 per cent w/v of *triamterene IPRS* and 0.15 per cent w/v of *hydrochlorothiazide IPRS* in the solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with the mobile phase.

Reference solution (b). A solution containing 0.225 per cent w/v of *triamterene IPRS*, 0.15 per cent w/v of *hydrochlorothiazide IPRS* and 0.00075 per cent w/v of *benzothiadiazine related Compound A IPRS* in the solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with the mobile phase.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 65 volumes of a buffer solution prepared by dissolving 0.82 g of *sodium acetate anhydrous* in 1000 ml of *water*, adjusted to pH 4.5 with *glacial acetic acid* and 35 volumes of *acetonitrile*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 272 nm,
- injection volume: 20 µl,

The relative retention time with reference to hydrochlorothiazide for benzothiadiazine related compound A, is about 0.93.

Inject reference solution (a) and reference solution (b). The test is not valid unless the resolution between the peaks due to hydrochlorothiazide and benzothiadiazine related compound A is not less than 1.5 in the chromatogram obtained with reference solution (b) and the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution. Run the chromatogram twice the retention time of hydrochlorothiazide peak.

Calculate the content of $C_{12}H_{11}N_7$ and $C_7H_8ClN_3O_4S_2$ in the tablets.

Storage. Store protected from light and moisture, at a temperature not exceeding 30˚