

let light (main wavelength: 365 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 4 hours).

**Residue on ignition** Not more than 0.10% (1 g).

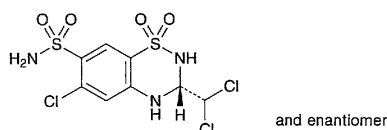
**Assay** Weigh accurately about 0.15 g of Triamterene, previously dried, and dissolve in 100 mL of acetic acid (100) by warming. Titrate with 0.05 mol/L perchloric acid VS (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

$$\begin{aligned} \text{Each mL of 0.05 mol/L perchloric acid VS} \\ = 12.663 \text{ mg of } C_{12}H_{11}N_7 \end{aligned}$$

**Containers and storage** Containers—Well-closed containers.

## Trichlormethiazide

トリクロルメチアジド



$C_8H_8Cl_3N_3O_4S_2$ : 380.66

(*RS*)-6-Chloro-3-dichloromethyl-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide [133-67-5]

Trichlormethiazide, when dried, contains not less than 98.0% of  $C_8H_8Cl_3N_3O_4S_2$ .

**Description** Trichlormethiazide occurs as a white powder. It is odorless or has a slight, characteristic odor.

It is very soluble in *N,N*-dimethylformamide, freely soluble in acetone, in dimethylsulfoxide and in *n*-butylamine, slightly soluble in ethanol (95), and practically insoluble in water and in diethyl ether.

It dissolves in sodium hydroxide TS.

Melting point: about 270°C (with decomposition).

**Identification (1)** Dissolve 0.02 g of Trichlormethiazide in 5 mL of water and 1 mL of *n*-butylamine, add 2 to 3 drops of copper (II) sulfate TS, and mix well. To this solution add 5 mL of chloroform, shake, and allow to stand: a green color develops in the chloroform layer.

**(2)** Dissolve 0.01 g of Trichlormethiazide in 2 mL of sodium hydroxide TS, and heat over a flame for 2 minutes. After cooling, and add 3 mL of dilute nitric acid and 1 drop of silver nitrate TS: a white precipitate is produced. To 5 mg of Trichlormethiazide add 5 mL of disodium chlomotropate TS, and allow to stand for 5 minutes: no purple color develops.

**(3)** Dissolve 0.015 g of Trichlormethiazide in 100 mL of sodium hydroxide TS, and to 10 mL of the solution add water to make 100 mL. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

**(4)** Proceed with 0.01 g of Trichlormethiazide as directed under Oxgen Flask Combustion Method, using 10 mL of diluted hydrogen peroxide (30) (1 in 5) as the absorbing liquid, and prepare the test solution. Apply a small amount of water to the upper part of the apparatus A, pull out C carefully, wash C, B and the inner side of A with 15 mL of methanol, and use the obtained solution as the test solution. The solution prepared by adding 0.5 mL of dilute nitric acid to 15 mL of the test solution responds to the Qualitative Test (2) for chloride. The remainder of the test solution responds to the Qualitative Tests (1) for sulfate.

**Purity (1) Chloride**—Dissolve 1.0 g of Trichlormethiazide in 30 mL of acetone, add 6 mL of dilute nitric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution as follows: to 1.0 mL of 0.01 mol/L hydrochloric acid VS add 30 mL of acetone, 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.036%).

**(2) Sulfate**—Dissolve 1.0 g of Trichlormethiazide in 30 mL of acetone, add 1 mL of dilute hydrochloric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution as follows: to 1.0 mL of 0.005 mol/L sulfuric acid VS add 30 mL of acetone, 1 mL of dilute hydrochloric acid and water to make 50 mL (not more than 0.048%).

**(3) Heavy metals**—Proceed with 1.0 g of Trichlormethiazide according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

**(4) Arsenic**—Prepare the test solution with 0.6 g of Trichlormethiazide according to Method 3, and perform the test using Apparatus B (not more than 3.3 ppm).

**(5) Primary aromatic amines**—Dissolve 0.025 g of Trichlormethiazide in acetone to make exactly 100 mL. Pipet 1 mL of this solution, add 3.0 mL of dilute hydrochloric acid, 3.0 mL of water and 0.15 mL of a solution of sodium nitrite (1 in 30), mix well, and allow to stand for 1 minute. To this solution add 1.0 mL of ammonium amidosulfate TS, mix well, allow to stand for 3 minutes, add 1.0 mL of *N,N*-diethyl-*N'*-1-naphthylethylenediamine oxalate TS, mix well, and then allow to stand for 5 minutes. Determine the absorbance of this solution at 525 nm as directed under the Ultraviolet-visible Spectrophotometry, using a solution prepared with 1.0 mL of acetone in the same manner as the blank: the absorbance is not more than 0.08.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 3 hours).

**Residue on ignition** Not more than 0.10% (1 g).

**Assay** Weigh accurately about 0.3 g of Trichlormethiazide, previously dried, dissolve in 50 mL of a mixture of water and dimethylsulfoxide (1:1), and titrate with 0.1 mol/L sodium hydroxide VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

$$\begin{aligned} \text{Each mL of 0.1 mol/L sodium hydroxide VS} \\ = 38.066 \text{ mg of } C_8H_8Cl_3N_3O_4S_2 \end{aligned}$$

**Containers and storage** Containers—Well-closed containers.