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Atenolol and Chlorthalidone Tablets

» Atenolol and Chlorthalidone Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of atenolol ($C_{14}H_{22}N_2O_3$) and chlorthalidone ($C_{14}H_{11}ClN_2O_4S$).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—

USP Atenolol RS
USP Chlorthalidone RS

Identification—

A: Shake a quantity of powdered Tablets, equivalent to about 50 mg of chlorthalidone, with 5 mL of methanol for 15 minutes, and filter. Apply 10 µL of this test solution, 10 µL of a Standard solution of USP Chlorthalidone RS in methanol containing 10 mg per mL, and 10 µL of a second Standard solution of USP Atenolol RS in methanol containing 10*J* mg per mL, *J* being the ratio of the labeled amount, in mg, of atenolol to the labeled amount, in mg, of chlorthalidone per Tablet to a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of *n*-butyl alcohol and 1 N ammonium hydroxide (5:1) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, and air-dry. Locate the spots on the plate by viewing under short-wavelength UV light: the principal spots obtained from the test solution correspond in R_F value, size, and intensity to those obtained from the respective Standard solutions.

B: The retention times of the major peaks in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Dissolution ⟨711⟩—

Medium: 0.01 N hydrochloric acid; 900 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Determine the amounts of atenolol ($C_{14}H_{22}N_2O_3$) and chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) dissolved by employing the following method.

Mobile phase and *Chromatographic system*—Prepare as directed in the *Assay.*

Diluent—Prepare a mixture of 1000 mL of acetonitrile and 32 mL of 3.6 N sulfuric acid.

Standard solvent—Prepare a mixture of water and *Diluent* (750: 225).

Standard solution—Dissolve accurately weighed quantities of USP Atenolol RS and USP Chlorthalidone RS in *Standard solvent* to obtain a solution having known concentrations of about 0.00085*L* mg of USP Atenolol RS and 0.00085*L*' mg of USP Chlorthalidone RS per mL, *L* and *L*' being the labeled amounts, in mg, of atenolol and chlorthalidone, respectively, per Tablet.

Test solution—Mix 10.0 mL of the filtered solution under test and 3.0 mL of *Diluent.*

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantities, in mg, of atenolol ($C_{14}H_{22}N_2O_3$) and chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) dissolved by the same formula:

$$1170C(r_U/r_S)$$

in which *C* is the concentration, in mg per mL, of the appropriate Reference Standard in the *Standard solution;* and r_U and r_S are the responses of the corresponding analyte obtained from the *Test solution* and the *Standard solution,* respectively.

Tolerances—Not less than 80% *(Q)* of the labeled amount of atenolol ($C_{14}H_{22}N_2O_3$) is dissolved in 45 minutes, and not less than 70% *(Q)* of the labeled amount of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩**:** meet the requirements.

Procedure for content uniformity—Proceed as directed in the *Assay,* except to prepare the *Assay preparation* as follows. Transfer 1 Tablet to a volumetric flask of such capacity that when filled to volume, a concentration of about 0.25 mg of chlorthalidone per mL is obtained. Add a mixture of water and acetonitrile (1:1) to about half the capacity of the flask, and shake by mechanical means for not less than 15 minutes to disintegrate the Tablet. Dilute with water to volume, and mix. Pass a portion of this solution through a filter having a 0.5-µm or finer porosity, and use the filtrate as the *Assay preparation.* Calculate the quantities, in mg, of atenolol ($C_{14}H_{22}N_2O_3$) and chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) in the Tablet taken by the formula:

$$CV(r_U/r_S)$$

in which V is the volume, in mL, of the volumetric flask used to prepare the *Assay preparation;* and the other terms are as defined in the *Assay.*

Assay—

Mobile phase—Prepare a mixture of 740 mL of water, 250 mL of acetonitrile, 8 mL of 3.6 N sulfuric acid, and 930 mg of sodium octyl sulfate. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve accurately weighed quantities of USP Atenolol RS and USP Chlorthalidone RS in a mixture of water and acetonitrile (3:1) to obtain a solution having known concentrations of about 0.25 mg of USP Chlorthalidone RS and 0.25J mg of USP Atenolol RS per mL, J being the ratio of the labeled amount, in mg, of atenolol to the labeled amount, in mg, of chlorthalidone per Tablet.

Assay preparation—Transfer 10 Tablets to a volumetric flask of such capacity that when filled to volume, a concentration of about 0.5 mg of chlorthalidone per mL is obtained. Add a mixture of water and acetonitrile (1:1) to about half the capacity of the flask, and shake by mechanical means for not less than 15 minutes to disintegrate the Tablets. Dilute with a mixture of water and acetonitrile (1:1) to volume, and mix. Pass a portion of this stock solution through a filter having a 0.5-µm or finer porosity. Transfer 25.0 mL of the clear filtrate to a 50-mL volumetric flask, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 275-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1.7 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.8 for atenolol and 1.0 for chlorthalidone; the resolution, R, between the atenolol and chlorthalidone peaks is not less than 3.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Assay preparation* and the *Standard preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantities, in mg, of atenolol ($C_{14}H_{22}N_2O_3$) and chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) in each Tablet taken by the formula:

$$2C(V/10)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of the appropriate USP Reference Standard in the *Standard preparation; V* is the volume, in mL, of the volumetric flask used to prepare the stock solution for the *Assay preparation;* and r_U and r_S are the responses for the corresponding analyte obtained from the *Assay preparation* and the *Standard preparation,* respectively.

[Note—If a trailing peak or shoulder is observed on the chlorthalidone peak with a relative retention time of not more than 1.1 in the chromatograms of both the *Standard preparation* and the *Assay preparation,* sum the areas for the chlorthalidone peak with the trailing peak or shoulder to report the peak responses for chlorthalidone.]

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ATENOLOL AND CHLORTHALIDONE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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