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Clonidine Hydrochloride and Chlorthalidone Tablets

DEFINITION

Clonidine Hydrochloride and Chlorthalidone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) and NLT 90.0% and NMT 110.0% of the labeled amount of clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$).

IDENTIFICATION

• **A.**

Sample solution: Transfer an amount of powdered Tablets, equivalent to 3 mg of clonidine hydrochloride, to a beaker. Add 30 mL of water, stir for 5 min, and pass through a filter of medium pore size into a sintered-glass funnel. Transfer the filtrate to a separator, add 5 mL of 0.1 N sodium hydroxide, and extract with 20 mL of chloroform, collecting the chloroform extract in a separator. Extract the chloroform phase with 15 mL of 0.01 N hydrochloric acid, collecting the acid extract in a beaker. Remove any residual chloroform from the acid extract by heating on a steam bath.

Acceptance criteria: The UV absorption spectrum of the *Sample solution* exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Clonidine Hydrochloride RS, concomitantly measured.

• **B. Infrared Absorption**

Sample: Transfer 10 powdered Tablets to a 50-mL beaker. Add 10 mL of methanol, boil on a steam bath for 5 min, and filter. Add 20 mL of water to the filtrate, and boil on a steam bath for 5 min under a current of air. Cool, with stirring, in ice until crystals form. Filter the crystals, and dry at 105° for 1 h.

Acceptance criteria: The IR absorption spectrum of a mineral oil dispersion of the *Sample* exhibits maxima only at the same wavelengths as that of a similar preparation of USP Chlorthalidone RS.

• **C.** The retention times of the chlorthalidone and clonidine hydrochloride peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 1 g/L of monobasic ammonium phosphate in water

Mobile phase: Methanol, acetonitrile, and *Buffer* (100:100:800)

Clonidine hydrochloride standard stock solution: 1500*J* µg/mL of USP Clonidine Hydrochloride RS in *Buffer*; *J* is the ratio of the labeled amount, in mg, of clonidine hydrochloride to the labeled amount, in mg, of chlorthalidone per Tablet.

Standard solution: 150*J* µg/mL of USP Clonidine Hydrochloride RS and 150 µg/mL of USP Chlorthalidone RS prepared as follows. Transfer 15 mg of USP Chlorthalidone RS to a 100-mL volumetric flask, dissolve in 10 mL of methanol, and add 25 mL of *Buffer* and 10.0 mL of *Clonidine hydrochloride standard stock solution*. Dilute with *Buffer* to volume.

Sample solution: Transfer an amount equivalent to 15 mg of chlorthalidone from powdered Tablets (NLT 20). Add 10 mL of methanol, and sonicate for 5 min. Add 40 mL of *Buffer*, and sonicate until the solution is free from agglomerates. Allow to cool to ambient temperature, dilute with *Buffer* to volume, and centrifuge.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 10-cm; packing L7

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for clonidine hydrochloride and chlorthalidone are about 0.2 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3 between the clonidine hydrochloride and chlorthalidone peaks

Relative standard deviation: NMT 2%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$) and chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of clonidine hydrochloride or chlorthalidone from the *Sample solution*

r_S = peak response of clonidine hydrochloride or chlorthalidone from the *Standard solution*

C_S = concentration of USP Clonidine Hydrochloride RS or USP Chlorthalidone RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of clonidine hydrochloride or chlorthalidone in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL

Apparatus 2: 100 rpm

Time: 60 min

Sample solution: Pipet 20 mL of a centrifuged portion of the solution under test into a 25-mL volumetric flask, and dilute with 0.5% monobasic ammonium phosphate solution to volume. Use the resulting solution as the *Sample solution*.

Analysis: Proceed as directed in the *Assay*, making any necessary volumetric adjustments.

Tolerances: NLT 50% (*Q*) of the labeled amount of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) and NLT 80% (*Q*) of the labeled amount of clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$) are dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements for *Content Uniformity* with respect to both clonidine hydrochloride and chlorthalidone

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards** ⟨11⟩

USP Chlorthalidone RS

USP Clonidine Hydrochloride RS

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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