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Acetaminophen and Pseudoephedrine Hydrochloride Tablets

DEFINITION

Acetaminophen and Pseudoephedrine Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$).

IDENTIFICATION

• **A.** The retention times of the acetaminophen and pseudoephedrine peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Diluent: Acetonitrile and water (10:90)

Solution A: 0.005 M ethanesulfonic acid and 0.05 M monobasic potassium phosphate

Mobile phase: Acetonitrile and *Solution A* (100:900). Adjust with 5 N sodium hydroxide or 1 N hydrochloric acid to a pH of 4.6.

Pseudoephedrine hydrochloride standard stock solution: 0.6 mg/mL of USP Pseudoephedrine Hydrochloride RS in *Diluent*

Standard solution: Transfer 6*J* mg of USP Acetaminophen RS to a 100-mL volumetric flask, *J* being the ratio of the labeled quantity (mg) of acetaminophen to the labeled quantity (mg) of pseudoephedrine hydrochloride in each Tablet. Add 2.0 mL of 1 N hydrochloric acid and 20 mL of *Diluent*, and mix to dissolve. Add 10.0 mL of *Pseudoephedrine hydrochloride standard stock solution* and dilute with *Diluent* to volume. This solution contains 0.06*J* mg/mL of USP Acetaminophen RS and 0.06 mg/mL of USP Pseudoephedrine Hydrochloride RS.

Sample solution: Nominally 0.06 mg/mL of pseudoephedrine hydrochloride prepared as follows. Transfer a portion of finely powdered Tablets (NLT 20), equivalent to 30 mg of pseudoephedrine hydrochloride, to a 500-mL volumetric flask, add 10.0 mL of 1 N hydrochloric acid and 100 mL of *Diluent*, and sonicate for 30 min, with occasional shaking. Allow to cool, and dilute with *Diluent* to volume. Pass a portion of this solution through a glass fiber filter, and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 25-cm; base-deactivated or end-capped packing L1

Flow rate: 3 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for acetaminophen and pseudoephedrine are about 0.55 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.5 between acetaminophen and pseudoephedrine

Tailing factor: NMT 2 for the pseudoephedrine peak

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response of the corresponding analyte from the *Sample solution*

r_S = peak response of the corresponding analyte from the *Standard solution*

C_S = concentration of the appropriate USP Reference Standard in the *Standard solution* (mg/mL)

C_U = nominal concentration of the appropriate analyte in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$)

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩, *Procedure, Apparatus 1 and Apparatus 2, Immediate-Release Dosage Forms, Procedure for a pooled sample for immediate-release dosage forms*

Medium: pH 5.8 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Determine the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved by using the following method.

Mobile phase: Proceed as directed in the *Assay*.

Standard solution: (*L*/900) mg/mL of USP Pseudoephedrine Hydrochloride RS and (*LJ*/900) mg/mL of USP Acetaminophen RS in *Medium*. [Note—*L* is the labeled quantity, in mg, of pseudoephedrine hydrochloride in each Tablet; and *J* is the ratio of the labeled quantity, in mg, of acetaminophen to the labeled quantity, in mg, of pseudoephedrine hydrochloride in each Tablet.]

Sample solution: Filtered portion of the solution under test, suitably diluted with *Medium*, if necessary

Chromatographic system and **System suitability:** Proceed as directed in the *Assay*, except to inject the *Standard solution*.

Analysis

Samples: *Standard solution* and *Sample solution*

[Note—Inject 20 µL of the *Samples*, and measure the responses for the acetaminophen and pseudoephedrine peaks.]

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved:

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

r_U = peak response of the corresponding analyte from the *Sample solution*

r_S = peak response of the corresponding analyte from the *Standard solution*

V = volume of *Medium*, 900 mL

C_S = concentration of the appropriate USP Reference Standard in the *Standard solution* (mg/mL)

L = label amount of the corresponding analyte in a Tablet (mg)

Tolerances: NLT 75% (*Q*) of the labeled amount of acetaminophen ($C_8H_9NO_2$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) is dissolved.

For Tablets labeled as chewable

Medium: pH 5.8 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 900 mL

Apparatus 2: 75 rpm

Time: 45 min

Standard solution, Sample solution, Chromatographic system, System suitability, and **Analysis:** Proceed as directed above in *Procedure for a pooled sample for immediate-release dosage forms*.

Tolerances: NLT 75% (*Q*) of the labeled amount of acetaminophen ($C_8H_9NO_2$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

• **4-Aminophenol in Acetaminophen-Containing Drug Products** ⟨227⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Acetaminophen RS

USP Pseudoephedrine Hydrochloride RS

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

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

Topic/Question	Contact	Expert Committee
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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