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Acetaminophen, Chlorpheniramine Maleate, and Dextromethorphan Hydrobromide Tablets

DEFINITION

Acetaminophen, Chlorpheniramine Maleate, and Dextromethorphan Hydrobromide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$), chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$), and dextromethorphan hydrobromide monohydrate ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$).

IDENTIFICATION

• **A.** The retention time of the major peak for acetaminophen of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Acetaminophen*.

• **B.** The retention time of the major peak for chlorpheniramine of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Chlorpheniramine Maleate*.

• **C.** The retention time of the major peak for dextromethorphan of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Dextromethorphan Hydrobromide*.

ASSAY

• **Acetaminophen**

Mobile phase: Methanol, glacial acetic acid, and water (20:1:79)

Standard solution: 0.5 mg/mL of USP Acetaminophen RS prepared as follows. Transfer an appropriate amount of USP Acetaminophen RS to a suitable volumetric flask and add methanol using 4% of the final volume. Mix until solution is complete and dilute with 0.1% phosphoric acid to volume.

Sample stock solution: Nominally 2 mg/mL of acetaminophen prepared as follows. Transfer a portion of powdered Tablets (NLT 20), equivalent to 100 mg of acetaminophen, to a 50-mL volumetric flask. Add 7.5 mL of methanol, and sonicate to disperse the powder. Add 0.5 mL of phosphoric acid, dilute with water to volume, and filter.

Sample solution: Nominally 0.5 mg/mL of acetaminophen from *Sample stock solution* in water

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) in the portion of Tablets taken:

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

r_U = peak response of acetaminophen from the *Sample solution*

r_S = peak response of acetaminophen from the *Standard solution*

C_S = concentration of USP Acetaminophen RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$)

- **Chlorpheniramine Maleate**

Mobile phase: Methanol and water (60:40) containing 0.34 g of monobasic potassium phosphate, 0.3 g of triethylamine hydrochloride, 0.15 g of sodium lauryl sulfate, and 0.1 mL of phosphoric acid in each 100 mL of solution

Standard stock solution: 0.8 mg/mL of USP Chlorpheniramine Maleate RS in water

Standard solution: 8 µg/mL of USP Chlorpheniramine Maleate RS in 0.1% phosphoric acid from *Standard stock solution*

Sample solution: Nominally 8 µg/mL of chlorpheniramine maleate prepared as follows. Transfer a portion of powdered Tablets (NLT 20), equivalent to 2 mg of chlorpheniramine maleate, to a 250-mL volumetric flask. Add 25 mL of methanol, and sonicate to disperse the powder. Add 1 mL of phosphoric acid, dilute with water to volume, and filter.

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 15-cm; 5-µm packing L11

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Samples: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$) in the portion of Tablets taken:

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

r_U = peak response of chlorpheniramine from the *Sample solution*

r_S = peak response of chlorpheniramine from the *Standard solution*

C_S = concentration of USP Chlorpheniramine Maleate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of chlorpheniramine maleate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0% of the labeled amount of chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$)

- **Dextromethorphan Hydrobromide**

Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay* for *Chlorpheniramine Maleate*.

Standard stock solution: 0.6 mg/mL of USP Dextromethorphan Hydrobromide RS in water

Standard solution: 0.06 mg/mL of USP Dextromethorphan Hydrobromide RS in 0.1% phosphoric acid, from *Standard stock solution*

Sample solution: Nominally 0.06 mg/mL of dextromethorphan hydrobromide prepared as follows. Transfer a portion of powdered Tablets (NLT 20), equivalent to 6 mg of dextromethorphan hydrobromide, to a 100-mL volumetric flask. Add 10 mL of methanol, and sonicate to disperse the powder. Add 0.4 mL of phosphoric acid, dilute with water to volume, and filter.

System suitability

Samples: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dextromethorphan hydrobromide monohydrate ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of dextromethorphan from the *Sample solution*

r_S = peak response of dextromethorphan from the *Standard solution*

C_S = concentration of USP Dextromethorphan Hydrobromide RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of dextromethorphan hydrobromide in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of dextromethorphan hydrobromide monohydrate, 370.32

M_{r2} = molecular weight of anhydrous dextromethorphan hydrobromide, 352.32

Acceptance criteria: 90.0%–110.0% of the labeled amount of dextromethorphan hydrobromide monohydrate ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$)

PERFORMANCE TESTS

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

Test 1

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Sample solution: Mix 9.0 mL of a filtered portion of the solution with 1.0 mL of 1% phosphoric acid solution.

Analysis: Determine the percentage of the labeled amount of acetaminophen, chlorpheniramine maleate, and dextromethorphan hydrobromide dissolved, using the *Analysis* set forth in the *Assay* for *Acetaminophen*, the *Assay* for *Chlorpheniramine Maleate*, and the *Assay* for *Dextromethorphan Hydrobromide*, respectively, making any necessary volumetric adjustments.

Tolerances: NLT 75% (*Q*) of the labeled amount of acetaminophen ($C_8H_9NO_2$), chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$), and dextromethorphan hydrobromide monohydrate ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.1 M hydrochloric acid; 900 mL

Apparatus 2, Time, Sample solution, Analysis, and **Tolerances:** Proceed as directed in *Test 1*.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

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

Apparatus 2, Time, Sample solution, Analysis, and **Tolerances:** Proceed as directed in *Test 1*.

• **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.

• **Labeling:** The label states the name and quantity of each active ingredient and indicates its function (or purpose) in the article. When more than one *Dissolution Test* is given, the labeling states the *Dissolution Test* used only if *Test 1* is not used.

• **USP Reference Standards** ⟨11⟩

USP Acetaminophen RS

USP Chlorpheniramine Maleate RS

USP Dextromethorphan Hydrobromide RS

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

Topic/Question	Contact	Expert Committee
ACETAMINOPHEN, CHLORPHENIRAMINE MALEATE, AND DEXTROMETHORPHAN HYDROBROMIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

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