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Status: Currently Official on 13-Feb-2025
Official Date: Official as of 01-May-2017
Document Type: USP Monographs
DocId: GUID-36376BA5-52C8-469D-AC2E-E17BD8223113_1_en-US
DOI: https://doi.org/10.31003/USPNF_M275_01_01
DOI Ref: 4p5s5

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Acetaminophen, Dextromethorphan Hydrobromide, Doxylamine Succinate, and Pseudoephedrine Hydrochloride Oral Solution

DEFINITION

Acetaminophen, Dextromethorphan Hydrobromide, Doxylamine Succinate, and Pseudoephedrine Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$), dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$), doxylamine succinate ($C_{17}H_{22}N_2O \cdot C_4H_6O_4$), and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$).

IDENTIFICATION

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

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

• **C.** The retention time of the doxylamine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Doxylamine Succinate*.

• **D.** The retention time of the pseudoephedrine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Pseudoephedrine Hydrochloride*.

ASSAY

• **Acetaminophen**

Mobile phase: Methanol and water (45:55)

Standard solution: 0.2 mg/mL of USP Acetaminophen RS in *Mobile phase*

Sample solution: Nominally 0.2 mg/mL of acetaminophen from a volume of Oral Solution in *Mobile phase* prepared as follows. Dilute a volume of Oral Solution, equivalent to about 200 mg of acetaminophen, in *Mobile phase*.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for the acetaminophen peak

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 Oral Solution 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 ($C_8H_9NO_2$)

• **Dextromethorphan Hydrobromide**

Solution A: 6.8 g/L of monobasic potassium phosphate in water

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Mobile phase: Acetonitrile and *Solution A* (45:55)

Standard solution: 0.1 mg/mL of USP Dextromethorphan Hydrobromide RS, 0.04 mg/mL of USP Doxylamine Succinate RS, and 0.2 mg/mL of USP Pseudoephedrine Hydrochloride RS in *Mobile phase*

Sample solution: Nominally 0.1 mg/mL of dextromethorphan hydrobromide from a volume of Oral Solution in *Mobile phase* prepared as follows. Dilute a volume of Oral Solution, equivalent to about 5 mg of dextromethorphan hydrobromide, in *Mobile phase*.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; packing L9

Flow rate: 2.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for pseudoephedrine, dextromethorphan, and doxylamine are 0.38, 0.65, and 1.0, respectively.]

Suitability requirements

Tailing factor: NMT 2.5 for the dextromethorphan, doxylamine, and pseudoephedrine peaks

Relative standard deviation: NMT 2.0% for dextromethorphan, doxylamine, and pseudoephedrine

Analysis

Samples: *Standard solution* and *Sample solution*

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

- **DOXYLAMINE SUCCINATE**

Solution A, Mobile phase, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay* for *Dextromethorphan Hydrobromide*.

Sample solution: Nominally 0.04 mg/mL of doxylamine succinate from a volume of Oral Solution in *Mobile phase* prepared as follows. Dilute a volume of Oral Solution, equivalent to about 2 mg of doxylamine succinate, in *Mobile phase*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of doxylamine succinate ($C_{17}H_{22}N_2O \cdot C_4H_6O_4$) in the portion of Oral Solution taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0% of the labeled amount of doxylamine succinate ($C_{17}H_{22}N_2O \cdot C_4H_6O_4$)

- **PSEUDOEPHEDRINE HYDROCHLORIDE**

Solution A, Mobile phase, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay* for *Dextromethorphan Hydrobromide*.

Sample solution: Nominally 0.2 mg/mL of pseudoephedrine hydrochloride from a volume of Oral Solution in *Mobile phase* prepared as follows. Dilute a volume of Oral Solution, equivalent to about 10 mg of pseudoephedrine hydrochloride, in *Mobile phase*.

Analysis

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Samples: *Standard solution* and *Sample solution*

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

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

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

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

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

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

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

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩**

For single-unit containers

Acceptance criteria: Meets the requirements

• **Deliverable Volume ⟨698⟩**

For multiple-unit containers

Acceptance criteria: Meets the requirements

IMPURITIES

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

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total bacterial count does not exceed 100 cfu/g, the total combined molds and yeasts count does not exceed 10 cfu/g, and it meets the requirements of the tests for absence of *Salmonella* species and *Escherichia coli*.

• **pH ⟨791⟩:** 4.5–6.3

• **Alcohol Determination ⟨611⟩, *Method II*** (if present)**:** 90.0%–110.0% of the labeled amount of alcohol (C_2H_5OH)

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Acetaminophen RS
USP Dextromethorphan Hydrobromide RS
USP Doxylamine Succinate RS
USP Pseudoephedrine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
ACETAMINOPHEN, DEXTROMETHORPHAN HYDROBROMIDE, DOXYLAMINE SUCCINATE, AND PSEUDOEPHEDRINE HYDROCHLORIDE ORAL SOLUTION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(1)

Current DocID: GUID-36376BA5-52C8-469D-AC2E-E17BD8223113_1_en-US

DOI: https://doi.org/10.31003/USPNF_M275_01_01

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