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Amphetamine Sulfate Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-amphetamine-sulfate-tabs-20250131.

DEFINITION
Amphetamine Sulfate Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$.

IDENTIFICATION
• **A. Melting Range or Temperature ⟨741⟩, *Procedures*:** Class I
Sample: Nominally 50 mg of amphetamine sulfate from a suitable quantity of powdered Tablets
Analysis: Macerate the *Sample* with 10 mL of water for 30 min and filter into a small flask. To the filtrate add 3 mL of 1 N sodium hydroxide. Cool to 10°–15°, add 1 mL of a mixture of absolute ether and benzoyl chloride (2:1), insert the stopper, and shake well for 3 min. Filter the precipitate, wash with 15 mL of cold water, and recrystallize twice from diluted alcohol. Dry the residue at 80° for 2 h.
Acceptance criteria: The crystals of the benzoyl derivative of amphetamine melt between 131° and 135°.
• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **Procedure**
Solution A: 14 mL of glacial acetic acid in 100 mL of water
Mobile phase: Dissolve 1.1 g of sodium 1-heptanesulfonate in 525 mL of water. Add 25 mL of *Solution A* and 450 mL of methanol. Adjust with glacial acetic acid to a pH of 3.3 ± 0.1.
Standard solution: 0.3 mg/mL of USP Dextroamphetamine Sulfate RS in 0.12 N phosphoric acid
Sample solution: Nominally 0.3 mg/mL of amphetamine sulfate from Tablets prepared as follows. Finely powder Tablets (NLT 20). Transfer a suitable amount of the powdered Tablets to a suitable volumetric flask. Add 80% of the flask volume of 0.12 N phosphoric acid, and sonicate for 15 min. Dilute with 0.12 N phosphoric acid to volume. Pass through a membrane filter of 0.5-µm pore size, discarding the first 20 mL of the filtrate.
Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: 3.9-mm × 30-cm; 10-µm packing L1
Flow rate: 2 mL/min. [Note—Alternatively, a 4.6-mm × 25-cm column with 5-µm packing L1 may be used with a flow rate of 1 mL/min.]
Injection volume: 50 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 3
Relative standard deviation: NMT 1.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$ in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

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

Medium: Water; 500 mL

Apparatus 1: 100 rpm

Time: 45 min

Solution A: 14 mL of glacial acetic acid in 100 mL of water

Mobile phase: 1.1 g of sodium 1-heptanesulfonate in 575 mL of water. Add 25 mL of *Solution A*, and 400 mL of methanol. Adjust with glacial acetic acid to a pH of 3.3 ± 0.1.

Standard solution: USP Dextroamphetamine Sulfate RS in *Medium* having a known concentration of USP Dextroamphetamine Sulfate RS similar to the concentration expected in the sample.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 1 mL/min

Injection volume: 500 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$ dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

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

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

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

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$ is dissolved.

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

Medium: Water; 500 mL, deaerated if necessary

Apparatus 1: 100 rpm

Time: 15 min

Solution A: 5 mL of trifluoroacetic acid in 950 mL of water. Adjust with ammonium hydroxide to a pH of 2.2. Add 50 mL of acetonitrile.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
8.0	79	21
8.1	0	100
12.0	0	100
12.1	95	5

Time (min)	Solution A (%)	Solution B (%)
15.0	95	5

Standard solution: (*L*/500) mg/mL of USP Dextroamphetamine Sulfate RS in *Solution A*, where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 257 nm

Column: 4.6-mm × 15-cm; 2.6-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$ dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

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

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

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

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$ is dissolved.

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

Medium: Water; 500 mL

Apparatus 1: 100 rpm

Time: 20 min

Solution A: 14 mL of glacial acetic acid in 100 mL of water

Mobile phase: Dissolve 1.1 g of sodium 1-heptanesulfonate in 525 mL of water. Add 25 mL of *Solution A* and 450 mL of methanol. Adjust with glacial acetic acid to a pH of 3.3.

Diluent: 0.12 N phosphoric acid in water

Standard stock solution: 0.10 mg/mL of USP Dextroamphetamine Sulfate RS in *Diluent*. Sonicate to dissolve, if necessary.

Standard solution: (*L*/500) mg/mL of USP Dextroamphetamine Sulfate RS from the *Standard stock solution* in water, where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 200 µL

Run time: NLT 2 times the retention time of amphetamine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing Factor: NMT 3.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$ dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

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

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

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

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$ is dissolved.▲ (RB 1-Feb-2025)

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

• **Labeling:** 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 Dextroamphetamine Sulfate RS

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

Topic/Question	Contact	Expert Committee
AMPHETAMINE SULFATE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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