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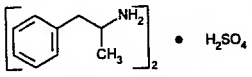
tained from the *Assay preparation* and the *Standard preparation*, respectively.

Amphetamine Sulfate



$(C_9H_{13}N)_2 \cdot H_2SO_4$ 368.49
Benzeneethanamine, α-methyl-, sulfate (2:1), (±)-.
(±)-α-Methylphenethylamine sulfate (2:1) [*60-13-9*].

» Amphetamine Sulfate, dried at 105° for 2 hours, contains not less than 98.0 percent and not more than 100.5 percent of $(C_9H_{13}N)_2 \cdot H_2SO_4$.

Packaging and storage—Preserve in well-closed containers.
USP Reference standards ⟨11⟩—*USP Dextroamphetamine Sulfate RS.*

Identification—
A: Dissolve about 100 mg in 5 mL of water, add 5 mL of 1 *N* sodium hydroxide, cool to about 10°, add 1 mL of a mixture of 1 volume of benzoyl chloride and 2 volumes of absolute ether, insert the stopper, and shake for 3 minutes. Filter the precipitate, wash with about 10 mL of cold water, and recrystallize from diluted alcohol: the crystals of the benzoyl derivative of amphetamine so obtained, after drying at 80° for 2 hours, melt between 131° and 135°, the procedure for *Class I* being used (see *Melting Range or Temperature* ⟨741⟩).
B: A solution (1 in 10) responds to the tests for *Sulfate* ⟨191⟩.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.2%.

Dextroamphetamine—A solution (1 in 50) is optically inactive.

Ordinary impurities ⟨466⟩—
Test solution: methanol.
Standard solution: methanol.
Eluant: a mixture of methanol and ammonium hydroxide (50:1).
Visualization: 1.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—
Standard preparation—Prepare as directed under *Amphetamine Assay* ⟨331⟩.
Assay preparation—Dissolve about 125 mg of Amphetamine Sulfate, previously dried and accurately weighed, in 25 mL of hydrochloric acid solution (1 in 100) in a 50-mL volumetric flask, dilute with the solvent to volume, and mix. Pipet 2.0 mL of the solution into a 100-mL beaker containing 3 g of purified siliceous earth, and mix until a fluffy mixture is obtained.
Procedure—Proceed as directed under *Amphetamine Assay* ⟨331⟩. Calculate the quantity, in mg, of $(C_9H_{13}N)_2 \cdot H_2SO_4$ in the portion of Amphetamine Sulfate taken by the formula:

$$0.25C[(A_{U257} - A_{U280})/(A_{S257} - A_{S280})],$$

in which C is the concentration, in µg per mL, of USP Dextroamphetamine Sulfate RS in the *Standard preparation*, and the other terms are as defined therein.

Amphetamine Sulfate Tablets

» Amphetamine Sulfate Tablets contain not less than [illegible] than 107.0 percent of the

Packaging and storage—Preserve in well-closed containers.
USP Reference standards ⟨11⟩—*USP Dextroamphetamine Sulfate RS.*

Identification—Macerate a quantity of powdered Tablets, equivalent to about 50 mg of amphetamine sulfate, with 10 mL of water for 30 minutes, and filter into a small flask. To the filtrate add 3 mL of 1 *N* sodium hydroxide. Cool to about 10° to 15°, add 1 mL of a mixture of 1 volume of benzoyl chloride and 2 volumes of absolute ether, insert the stopper, and shake well for 3 minutes. Filter the precipitate, wash with about 15 mL of cold water, and recrystallize twice from diluted alcohol: the crystals of the benzoyl derivative of amphetamine so obtained, after drying at 80° for 2 hours, melt between 131° and 135°, the procedure for *Class I* being used (see *Melting Range or Temperature* ⟨741⟩).

Dissolution, *Procedure for a Pooled Sample* ⟨711⟩—
Medium: water; 500 mL.
Apparatus 1: 100 rpm.
Time: 45 minutes.
Mobile phase—Dissolve 1.1 g of sodium 1-heptanesulfonate in 575 mL of water. Add 25 mL of dilute glacial acetic acid (14 in 100) and 400 mL of methanol. Adjust by the dropwise addition of glacial acetic acid to a pH of 3.3 ± 0.1, if necessary, filter, and degas the solution. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph replicate injections of the Standard solution, and record the peak responses as directed for *Procedure:* the relative standard deviation is not more than 2.0%.
Procedure—Inject a volume (about 500 µL) of a filtered portion of the solution under test into the chromatograph, record the chromatogram, and measure the response for the major peak. Calculate the quantity of $(C_9H_{13}N)_2 \cdot H_2SO_4$ dissolved in comparison with a Standard solution having a known concentration of USP Dextroamphetamine Sulfate RS in the same medium and similarly chromatographed.
Tolerances—Not less than 75% (Q) of the labeled amount of $(C_9H_{13}N)_2 \cdot H_2SO_4$ is dissolved in 45 minutes.

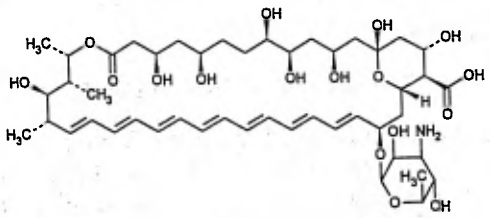
Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—
Standard preparation—Prepare as directed under *Amphetamine Assay* ⟨331⟩.
Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 5 mg of amphetamine sulfate, to a 100-mL beaker, add 2 mL of hydrochloric acid solution (1 in 100), swirl gently to wet the powder thoroughly, warm on a steam bath for about 1 minute, with occasional gentle swirling, and cool. Add 3 g of purified siliceous earth, and mix until a fluffy mixture is obtained.
Procedure—Proceed as directed under *Amphetamine Assay* ⟨331⟩. Calculate the quantity, in mg, of $(C_9H_{13}N)_2 \cdot H_2SO_4$ in the portion of Tablets taken by the formula:

$$0.01C[(A_{U257} - A_{U280})/(A_{S257} - A_{S280})],$$

in which C is the concentration, in µg per mL, of USP Dextroamphetamine Sulfate RS in the *Standard preparation*.

Amphotericin B



$C_{47}H_{73}NO_{17}$ 924.08
Amphotericin B

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Mobile phase—Prepare a solution containing a mixture of water, methanol, and glacial acetic acid (64:35:1).

Standard preparation—Dissolve an accurately weighed quantity of USP Theophylline RS in methanol to obtain a solution having a known concentration of about 400 µg per mL.

Assay preparation for hard Capsules—Remove, as completely as possible, the contents of not less than 20 Capsules, weigh, and mix. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of anhydrous theophylline, to a 250-mL volumetric flask, add about 150 mL of methanol, and shake to dissolve. Dilute with methanol to volume, mix, and filter, using a membrane filter.

Assay preparation for soft Capsules—Cut open 20 Capsules, and place them in a 200-mL volumetric flask. Add 50 mL of 6 N ammonium hydroxide, shake to dissolve the contents, add water to volume, mix, and filter, discarding the first 20 mL of the filtrate. Transfer an accurately measured portion of the filtrate, equivalent to about 100 mg of anhydrous theophylline, to a 250-mL volumetric flask, add methanol to volume, mix, and filter through a membrane filter.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph three replicate injections of the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation is not more than 2%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses. Calculate the quantity, in mg, of anhydrous theophylline in the portion of Capsule contents taken by the formula:

$$0.25C(r_U / r_S)$$

in which C is the concentration, in µg per mL, of USP Theophylline RS in the *Standard preparation*, and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Theophylline Extended-Release Capsules

» Theophylline Extended-Release Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of anhydrous theophylline ($C_7H_8N_4O_2$).

Packaging and storage—Preserve in well-closed containers.

Labeling—The labeling indicates whether the product is intended for dosing every 12 or 24 hours, and states with which in vitro *Dissolution Test* the product complies.

USP Reference standards ⟨11⟩—
USP Theophylline RS

Identification—

A: Transfer a quantity of Capsule contents, equivalent to about 100 mg of anhydrous theophylline, to a suitable conical flask. Add 150 mL of methanol, and sonicate until the insoluble material is dispersed into fine particles. Shake by mechanical means for 15 minutes, and filter into a 250-mL volumetric flask. Dilute with water to volume, and mix. Pipet 5 mL of this solution into a 200-mL volumetric flask, dilute with 0.1 N hydrochloric acid to volume, and mix: the UV absorption spectrum of the solution so obtained exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Theophylline RS, concomitantly measured.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Dissolution ⟨711⟩—[NOTE—The following tests, which were assigned numbers chronologically, are placed in groups corresponding to product dosing intervals. Thus, individual tests do not necessarily appear in numerical order.]

FOR PRODUCTS LABELED FOR DOSING EVERY 12 HOURS—

TEST 1—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1*. Proceed as directed for *Method B* under *Apparatus 1 and 2, Delayed-Release Dosage Forms*, except to use *Acceptance Table 2*.

Medium: pH 1.2 simulated gastric fluid (without pepsin) for the first hour; pH 6.0 phosphate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*); 900 mL.

Apparatus 2: 50 rpm.

Procedure—Determine the amount of $C_7H_8N_4O_2$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 271 nm on filtered portions of the solution under test, diluted with *Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Theophylline RS in the same *Medium*.

Times and *Tolerances*—The percentage of the labeled amount of $C_7H_8N_4O_2$ dissolved at the times given conforms to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 3% and 15%
2	between 20% and 40%
4	between 50% and 75%
6	between 65% and 100%
8	not less than 80%

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

pH 4.5 Phosphate buffer—Dissolve 6.8 g of monobasic potassium phosphate in 750 mL of water, mix, and dilute with water to 1000 mL. Adjust with either 1 N hydrochloric acid or 1 N sodium hydroxide to a pH of 4.5 ± 0.05.

Medium: pH 4.5 Phosphate buffer; 900 mL.

Apparatus 2: 75 rpm.

Procedure—Proceed as directed under *Test 1*.

Times and *Tolerances*—The percentages of the labeled amount of $C_7H_8N_4O_2$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 10% and 30%
2	between 30% and 55%
4	between 55% and 80%
8	not less than 80%

TEST 3—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*. Proceed as directed for *Method B* under *Apparatus 1 and 2, Delayed-Release Dosage Forms*, except to use *Acceptance Table 2*.

Medium: pH 1.2 simulated gastric fluid (without pepsin) for 1 hour; pH 7.5 simulated intestinal fluid (without enzyme); 900 mL.

Apparatus 2: 50 rpm.

Procedure—Proceed as directed under *Test 1*.

Times and *Tolerances*—The percentage of the labeled amount of $C_7H_8N_4O_2$ dissolved at the times given conforms to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 1% and 17%
2	between 30% and 60%
3	between 50% and 90%
4	not less than 65%
7	not less than 85%

TEST 4—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*. Proceed as directed for *Method A* under *Apparatus 1 and 2, Delayed-Release Dosage Forms*, except to use *Acceptance Table 2*.

Medium: pH 3.0 phosphate buffer prepared by adjusting 0.05 M potassium phosphate buffer with phosphoric acid to a pH of 3.0 ± 0.05, for the first 3½ hours, followed by the addition of 5.3 M sodium hydroxide to adjust to a pH of 7.4 ± 0.05; 900 mL.

Apparatus 2: 50 rpm.

Procedure—Proceed as directed under *Test 1*.

Times and *Tolerances*—The percentage of the labeled amount of $C_7H_8N_4O_2$ dissolved at the times given conforms to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 13% and 38%
2	between 25% and 50%
3.5	between 37% and 65%
5	between 85% and 115%

TEST 5—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

Medium, Apparatus, and *Procedure*—Proceed as directed under *Test 4*.

Times and *Tolerances*—The percentage of the labeled amount of $C_7H_8N_4O_2$ dissolved at the times given conforms to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 10% and 30%
3.5	between 30% and 60%
5	between 50% and 80%
7	not less than 65%
10	not less than 80%

TEST 7—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 7*.

Phosphate buffer—Dissolve 40.8 g of monobasic potassium phosphate in 6 L of water, add 667 mg of octoxynol 9, mix, and adjust with dilute hydrochloric acid or sodium hydroxide to a pH of 4.5.

Medium: Phosphate buffer; 900 mL.

Apparatus 2: 50 rpm.

Procedure—Proceed as directed under *Test 1*.

Times and *Tolerances*—The percentages of the labeled amount of $C_7H_8N_4O_2$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 10% and 40%
2	between 35% and 70%
4	between 60% and 90%
8	not less than 85%

TEST 8—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 8*.

Medium: pH 7.5 simulated intestinal fluid (without enzyme); 900 mL.

Apparatus 1: 100 rpm.

Procedure—Proceed as directed under *Test 1*.

Times and *Tolerances*—The percentages of labeled amount of $C_7H_8N_4O_2$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 3% and 30%
2	between 15% and 50%
4	between 45% and 80%
6	not less than 70%
8	not less than 85%

TEST 9—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 9*.

Medium 1: 0.1 N hydrochloric acid; 900 mL.

Medium 2: simulated intestinal fluid (without enzyme); 900 mL.

Apparatus 1: 50 rpm.

Determine the amount of theophylline dissolved at the times specified, using *Medium 1* for the first hour and *Medium 2* for the next five hours.

Procedure—Proceed as directed under *Test 1*.

Times and *Tolerances*—The percentage of the labeled amount of $C_7H_8N_4O_2$ dissolved at the times given conforms to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 5% and 15%
2	between 25% and 45%
3	between 50% and 65%
4	not less than 70%
6	not less than 85%

TEST 10—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 10*. Proceed as directed for *Test 3*.

Times and *Tolerances*—The percentage of the labeled amount of $C_7H_8N_4O_2$ dissolved at the times given conforms to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 6% and 27%
2	between 25% and 50%
4	between 65% and 85%
8	not less than 80%

FOR PRODUCTS LABELED FOR DOSING EVERY 24 HOURS—

TEST 6—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Medium: 0.05 M pH 6.6 phosphate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*); 1000 mL.

Apparatus 1: 100 rpm.

Procedure—Proceed as directed under *Test 1*.

Times and *Tolerances*—The percentages of the labeled amount of $C_7H_8N_4O_2$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1	between 5% and 15%
2	between 12% and 30%
4	between 25% and 50%
5	between 30% and 60%
8	between 55% and 75%

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