fylline. Calculate the percentage of each impurity in the portion of Pentoxifylline taken by the formula:

$$286C(r_i / r_S)$$

in which C is the concentration, in mg per mL, of USP Pentoxifylline RS in the *Standard solution;* r_i is the peak area response for each impurity obtained from the *Test solution;* and r_S is the peak area response for pentoxifylline obtained from the *Standard solution:* not more than 0.2% of any individual impurity is found, and not more than 0.5% of total impurities is found.

Assay—

Perchloric acid solution—Dissolve 1.0 g of perchloric acid in 1000 mL of water, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *Perchloric acid solution*, acetonitrile, tetrahydrofuran, and methanol (80:15:2.5:2). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability solution—Dissolve suitable quantities of caffeine and USP Pentoxifylline RS in *Mobile phase* to obtain a solution containing 0.024 mg per mL and 0.048 mg per mL, respectively.

Standard preparation—Dissolve an accurately weighed quantity of USP Pentoxifylline RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.05 mg per mL.

Assay preparation—Transfer about 25 mg of Pentoxifylline, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Pipet 5.0 mL of the solution so obtained to a 25-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 273-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 0.7 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between caffeine and pentoxifylline is not less than 10.0. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major pentoxifylline peaks. Calculate the quantity, in mg, of $C_{13}H_{18}N_4O_3$ in the portion of Pentoxifylline taken by the formula:

$$500C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Pentoxifylline 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.

Pentoxifylline Extended-Release Tablets

» Pentoxifylline Extended-Release Tablets contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of pentoxifylline ($C_{13}H_{18}N_4O_3$).

Packaging and storage—Preserve in well-closed containers. Protect from light, and store between 15° and 30°.

Labeling—The labeling indicates the *Dissolution Test* with which the product complies.

USP Reference standards ⟨11⟩**—**
USP Pentoxifylline RS

Identification—

A: *Infrared Absorption* ⟨197K⟩—

Test specimen—Finely powder not fewer than 5 Tablets. (A coarse screen may be used to separate the powder from the tablet film-coating if necessary.) Transfer an accurately weighed portion of the powder, equivalent to about 200 mg of pentoxifylline, to a 15-mL centrifuge tube, add about 10 mL of methanol, cap the tube, and shake vigorously for about 5 minutes. Centrifuge for about 5 minutes to allow undissolved material to settle. Decant the supernatant into a suitable beaker, and evaporate the solution with the aid of a current of air to dryness at about 35°. Dissolve the residue in about 15 mL of methylene chloride, transfer to a separatory funnel, add about 10 mL of water, and shake. Allow the layers to separate, transfer the methylene chloride layer, and pass through a funnel partially filled with anhydrous sodium sulfate, collecting the filtrate in a small beaker. Evaporate the solution with the aid of a current of air to dryness at about 35°. Dissolve the residue so obtained in 8 to 10 mL of ether, and then chill in an ice bath, if necessary, to induce crystallization. Collect the crystals on filter paper, wash with about 2 mL of cold ether, and allow to air-dry. Prepare a mixture of about 1.5% (w/w) of the crystals in potassium bromide.

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⟩**—**

TEST 1—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1.*

Medium: water; 900 mL or 1000 mL.

Apparatus 2: 100 rpm.

Times: 1, 4, 8, and 12 hours.

Procedure—Determine the amount of $C_{13}H_{18}N_4O_3$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 274 nm on filtered portions of the solution under test, suitably diluted with *Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Pentoxifylline RS in the same *Medium.*

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to *Acceptance Table 2.*

Time (hours)	Amount dissolved
1	not more than 30%
4	between 30% and 55%
8	not less than 60%
12	not less than 80%

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

Medium: water; 900 mL.

Apparatus 2: 75 rpm.

Times: 1, 6, 10, and 20 hours.

Procedure—Proceed as directed for *Test 1.*

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to the following table.

Time (hours)	Amount dissolved
1	between 8% and 30%
6	between 35% and 60%
10	between 53% and 78%
20	not less than 80%

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

Medium: water; 900 mL.

Apparatus 1: 100 rpm.

Times: 2, 8, 12, and 20 hours.

Procedure—Proceed as directed for *Test 1.*

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to the following table.

Time (hours)	Amount dissolved
2	between 15% and 35%
8	between 55% and 75%
12	between 75% and 95%
20	not less than 85%

TEST 4—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4.*

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Times: 1, 8, and 24 hours.

Procedure—Proceed as directed for *Test 1.*

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to the following table.

Time (hours)	Amount dissolved
1	between 0% and 20%
8	between 35% and 60%
24	not less than 80%

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

Medium: water; 900 mL.

Apparatus 2: 75 rpm.

Times: 1, 2, 4, 6, and 20 hours.

Procedure—Proceed as directed for *Test 1,* except to use the wavelength of maximum absorbance at about 264 nm instead of 274 nm.

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to the following table.

Time (hours)	Amount dissolved
1	between 5% and 25%
2	between 10% and 35%
4	between 20% and 50%
6	between 30% and 60%
20	not less than 80%

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

Medium: simulated gastric fluid (without enzymes); 900 mL.

Apparatus 2: 50 rpm.

Times: 2, 8, 12, and 24 hours.

Procedure—Proceed as directed for *Test 1.*

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to the following table.

Time (hours)	Amount dissolved
2	between 10% and 30%
8	between 40% and 60%
12	between 55% and 75%
24	not less than 85%

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

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Times: 1, 3, 8, and 18 hours.

Procedure—Proceed as directed for *Test 1.*

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to the following table.

Time (hours)	Amount dissolved
1	not more than 25%
3	between 25% and 45%
8	between 55% and 75%
18	not less than 80%

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

Medium: water; 900 mL.

Apparatus 2: 75 rpm.

Times: 1, 2, 4, 10, and 16 hours.

Procedure—Proceed as directed for *Test 1.*

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to the following table.

Time (hours)	Amount dissolved
1	between 10% and 20%
2	between 15% and 35%
4	between 25% and 45%
10	between 55% and 75%
16	not less than 80%

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

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Times: 1, 3, 6, 12, and 18 hours.

Procedure—Proceed as directed for *Test 1,* except to use the wavelength of maximum absorbance at about 230 nm instead of 274 nm.

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to the following table.

Time (hours)	Amount dissolved
1	between 0% and 20%
3	between 20% and 40%
6	between 30% and 60%
12	between 50% and 80%
18	not less than 80%

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

Medium: water; 900 mL.

Apparatus 2: 75 rpm.

Times: 1, 6, 12, and 20 hours.

Procedure—Proceed as directed for *Test 1.*

Tolerances—The percentages of the labeled amount of $C_{13}H_{18}N_4O_3$ dissolved at the times specified conform to the following table.

Time (hours)	Amount dissolved
1	not more than 20%
6	between 35% and 65%

Time (hours)	Amount dissolved
12	between 60% and 90%
20	not less than 80%

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

Chromatographic purity—

Perchloric acid solution, Mobile phase, Extracting solution, and *System suitability solution*—Prepare as directed in the *Assay.*

Standard solution—Dissolve an accurately weighed quantity of USP Pentoxifylline RS in *Extracting solution* containing an amount of methanol equal to 0.8% of the total volume to be used, and dilute quantitatively, and stepwise if necessary, with *Extracting solution* to obtain a solution having a known concentration of about 0.96 µg per mL.

Test solution—Transfer 10.0 mL of the first dilution filtrate from the *Assay preparation* to a 25-mL volumetric flask, dilute with *Extracting solution* to volume, and mix. The final concentration of pentoxifylline in this solution is about 0.32 mg per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—Proceed as directed in the *Assay.* Chromatograph the *Standard solution,* and record the peak responses for pentoxifylline as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 5.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, and allow the chromatogram to run five times longer than the retention time of the pentoxifylline peak. Record the chromatograms, and measure all the peak responses from the *Test solution,* except that for pentoxifylline. Calculate the percentage of each impurity in the portion of Tablets taken by the formula:

$$312C(r_i / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Pentoxifylline RS in the *Standard solution;* r_i is the peak response for each impurity obtained from the *Test solution;* and r_S is the peak response for pentoxifylline obtained from the *Standard solution:* not more than 0.3% of any individual impurity is found; and not more than 1.0% of total impurities is found.

Assay—

Perchloric acid solution—Dissolve 1.0 g of perchloric acid in 1000 mL of water, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *Perchloric acid solution*, acetonitrile, tetrahydrofuran, and methanol (80:15:2.5:2). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Extracting solution—Prepare a mixture of water and alcohol (7:3).

System suitability solution—Transfer about 20 mg of USP Pentoxifylline RS and about 10 mg of caffeine, each accurately weighed, to a 25-mL volumetric flask. Add 0.2 mL of methanol, and swirl the flask to distribute the methanol. Dilute with *Extracting solution* to volume, and mix. Pipet 3.0 mL of the resulting solution into a 50-mL volumetric flask, dilute with *Extracting solution* to volume, and mix.

Standard preparation—Dissolve an accurately weighed quantity of USP Pentoxifylline RS in *Extracting solution* containing an amount of methanol equal to 0.8% of the total volume to be used, and dilute quantitatively, and stepwise if necessary, with *Extracting solution* to obtain a solution having a known concentration of about 0.048 mg per mL.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 40 mg of pentoxifylline, to a 50-mL volumetric flask. Pipet 0.4 mL of methanol into the flask, and swirl for at least 1 minute. Add about 30 mL of *Extracting solution,* and sonicate for 60 minutes with occasional swirling of the flask. Add an additional 15 mL of *Extracting solution,* allow to cool to room temperature, dilute with *Extracting solution* to volume, and mix. Centrifuge or pass through a suitable filter. Reserve a portion of this first dilution for preparation of the *Test solution* in the *Chromatographic purity* test. Pipet 3.0 mL of the clear solution into a 50-mL volumetric flask, dilute with *Extracting solution* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 273-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 0.7 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between caffeine and pentoxifylline is not less than 10.0. Chromatograph the *Standard preparation,* and record the peak responses for pentoxifylline as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of pentoxifylline ($C_{13}H_{18}N_4O_3$) in the portion of Tablets taken by the formula:

$$833C(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Pentoxifylline 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.

Peppermint Spirit

DEFINITION

Peppermint Spirit contains, in each 100 mL, NLT 9.0 mL and NMT 11.0 mL of peppermint oil.

Peppermint Oil	100 mL
Peppermint, in coarse powder	10 g
Alcohol, a sufficient quantity to make	1000 mL

Macerate the peppermint leaves, freed as much as possible from stems and coarsely powdered, for 1 h in 500 mL of purified water, and then strongly express them. Add the moist, macerated leaves to 900 mL of alcohol, and allow the mixture to stand for 6 h with frequent agitation. Filter, and to the filtrate add the oil, and add alcohol to make the product measure 1000 mL.

ASSAY

- **CONTENT OF PEPPERMINT OIL**

  Sample: 5.0 mL of Spirit

  Analysis: Transfer the *Sample* to a Babcock bottle, graduated to 8%. Add 1.0 mL of kerosene, and mix. Add a saturated calcium chloride solution, acidified with hydrochloric acid, almost to fill the bulb of the bottle. Rotate the bottle vigorously to ensure mixing, and then add a sufficient quantity of the calcium chloride solution to bring the separated oil into the neck of the bottle. Centrifuge at about 1500 rpm for 5 min, and read the volume of oil in the stem. Subtract five divisions for the kerosene added, and multiply the remaining number of divisions by 4.2 to obtain the volume, in mL, of peppermint oil in 100 mL of the Spirit.

  Acceptance criteria: 9.0–11.0 mL

SPECIFIC TESTS

- **ALCOHOL DETERMINATION,** *Method II* ⟨**611**⟩**:** 79.0%–85.0% of C_2H_5OH

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, protected from light.