Dissolution, *Procedure for a Pooled Sample* ⟨711⟩**—**

Medium: water; 900 mL. Use 500 mL for Tablets containing 15 mg of phentermine hydrochloride or less.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Determine the amount of $C_{10}H_{15}N \cdot HCl$ dissolved by employing the following method.

Ion-pair solution—Dissolve 1.1 g of sodium 1-heptanesulfonate in 1 L of water. Add 3.5 mL of glacial acetic acid, and mix.

Mobile phase—Prepare a filtered and degassed mixture of methanol and *Ion-pair solution* (21:19). Adjust with phosphoric acid to a pH of 2.5. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard solution—Dissolve an accurately weighed quantity of USP Phentermine Hydrochloride RS in water, and dilute quantitatively, and stepwise if necessary, with water to obtain a solution having a known concentration approximately equivalent to the *Test solution*.

Test solution—Use a filtered portion of the pooled sample under test.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 208-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure:* the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 25 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Determine the amount, in mg, of phentermine hydrochloride ($C_{10}H_{15}N \cdot HCl$) dissolved by the formula:

$$VC(r_U / r_S)$$

in which V is the volume of dissolution media used per vessel; C is the concentration, in mg per mL, of USP Phentermine Hydrochloride RS in the *Standard solution;* and r_U and r_S are the peak responses obtained from the *Test solution* and the *Standard solution*, respectively.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{10}H_{15}N \cdot HCl$ is dissolved in 45 minutes.

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

Procedure for content uniformity—Proceed as directed in the *Assay*, except to prepare the *Test preparations* as follows. Transfer 1 Tablet to each of 10 suitable containers, add 1 mL of water and 10 mL of *Internal standard solution* to each, mix, sonicate for about 10 minutes after each Tablet has disintegrated, and filter.

Assay—

Mobile phase—Prepare a suitably degassed solution containing 0.03% diethylamine in methanol. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Prepare a solution of caffeine in *Mobile phase* having a final concentration of about 0.02 mg per mL.

Standard preparation—Transfer an accurately weighed amount of USP Phentermine Hydrochloride RS, equivalent to about 7.5 mg of phentermine hydrochloride, to a 10-mL volumetric flask. Add *Internal standard solution* to volume, and mix.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 7.5 mg, to a suitable flask. Pipet 10.0 mL of *Internal standard solution* into the flask. Insert the stopper, mix, and sonicate for about 10 minutes. Pass through a filter having a 0.5-µm porosity.

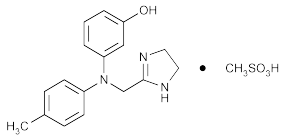
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.5 for caffeine and 1.0 for phentermine; the resolution, *R,* between caffeine and phentermine is not less than 4; the column efficiency determined from the analyte peak is not less than 2000 theoretical plates; and 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 phentermine hydrochloride ($C_{10}H_{15}N \cdot HCl$) in the portion of Tablets taken by the formula:

$$10C(R_U / R_S)$$

in which C is the concentration, in mg per mL, of USP Phentermine Hydrochloride RS in the *Standard preparation;* and R_U and R_S are the peak response ratios of phentermine to the internal standard obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Phentolamine Mesylate



$C_{17}H_{19}N_3O \cdot CH_4O_3S$ 377.46

Phenol, 3-[[(4,5-dihydro-1*H*-imidazol-2-yl)methyl](4-methylphenyl)amino]-, monomethanesulfonate (salt).

m-[*N*-(2-Imidazolin-2-ylmethyl)-*p*-toluidino]phenol monomethanesulfonate (salt) [65-28-1].

» Phentolamine Mesylate contains not less than 98.0 percent and not more than 102.0 percent of $C_{17}H_{19}N_3O \cdot CH_4O_3S$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers. Store at 25°, excursions permitted between 15° and 30°.

USP Reference standards ⟨11⟩**—**
USP Phentolamine Mesylate RS

Identification—

A: *Infrared Absorption* ⟨197M⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 20 µg per mL.

Medium: water.

C: The R_F value of the principal spot in the chromatogram of the *Identification preparation* corresponds to that of *Standard preparation A* as obtained in the test for *Chromatographic purity.*

Loss on drying ⟨731⟩**—**Dry it in vacuum at 60° for 4 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Sulfate ⟨221⟩**—**A 0.10-g portion shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid (0.2%).

Chromatographic purity—

Standard preparations—Dissolve USP Phentolamine Mesylate RS in methanol, and mix to obtain *Standard preparation A* having a known concentration of 50 µg per mL. Quantitatively dilute with methanol to obtain *Standard preparations,* designated below by letter, having the following compositions:

Standard preparation	Dilution	Concentration (µg RS per mL)	Percentage (%, for comparison with test specimen)
A	(undiluted)	50	0.5
B	(3 in 5)	30	0.3
C	(1 in 5)	10	0.1

Test preparation—Dissolve an accurately weighed quantity of Phentolamine Mesylate in methanol to obtain a solution containing 10 mg per mL.

Identification preparation—Dilute a portion of the *Test preparation* quantitatively with methanol to obtain a solution containing 50 µg per mL.

Detection reagent—Prepare (1) a solution of 1 g of potassium ferricyanide in 20 mL of water, and (2) a solution of 1.9 g of ferric chloride in 20 mL of water. Just prior to use, mix equal volumes of the solutions.

Procedure—Apply separately 5 µL of the *Test preparation,* 5 µL of the *Identification preparation,* and 5 µL of each *Standard preparation* to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel, and allow to dry. Position the plate in a chromatographic chamber, and develop the chromatograms in a solvent system consisting of a mixture of chloroform, diethylamine, and methanol (15:3:2) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and dry the plate at 100° for 1 hour. Spray the plate with *Detection reagent.* Within 15 minutes after spraying, compare the intensities of any secondary spots observed in the chromatogram of the *Test preparation* with those of the principal spots in the chromatograms of the *Standard preparations:* no secondary spot from the chromatogram of the *Test preparation* is larger or more intense than the principal spot obtained from *Standard preparation A* (0.5%), and the sum of the intensities of all secondary spots obtained from the *Test preparation* corresponds to not more than 1.0%.

Assay—

0.1 N Tetrabutylammonium hydroxide in isopropyl alcohol—Dilute with dehydrated isopropyl alcohol a commercially available 25% solution of tetrabutylammonium hydroxide in methanol, and standardize as directed under *Tetrabutylammonium Hydroxide, Tenth-Normal (0.1 N)* (see *Volumetric Solutions* in the section *Reagents, Indicators, and Solutions*), using dehydrated isopropyl alcohol instead of dimethylformamide.

Procedure—Dissolve with the aid of sonication, if necessary, about 300 mg of Phentolamine Mesylate, accurately weighed, in 100 mL of dehydrated isopropyl alcohol. Titrate in an atmosphere of nitrogen with *0.1 N Tetrabutylammonium hydroxide in isopropyl alcohol,* determining the endpoint potentiometrically, using a glass electrode and a calomel electrode containing a saturated solution of tetramethylammonium chloride in dehydrated isopropyl alcohol (see *Titrimetry* ⟨541⟩). Perform a blank determination, and make any necessary correction. Each mL of 0.1 N tetrabutylammonium hydroxide is equivalent to 37.75 mg of $C_{17}H_{19}N_3O \cdot CH_4O_3S$.

Phentolamine Mesylate for Injection

» Phentolamine Mesylate for Injection is sterile Phentolamine Mesylate or a sterile mixture of Phentolamine Mesylate with a suitable buffer or suitable diluents. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{17}H_{19}N_3O \cdot CH_4O_3S$.

Packaging and storage—Preserve in *Containers for Sterile Solids* as described under *Injections* ⟨1⟩.

USP Reference standards ⟨11⟩**—**
USP Endotoxin RS
USP Phentolamine Mesylate RS

Constituted solution—At the time of use, it meets the requirements for *Constituted Solutions* under *Injections* ⟨1⟩.

Identification—Mix a portion of it, equivalent to about 40 mg of phentolamine mesylate, with about 15 mL of chloroform. Filter into a beaker, and evaporate to dryness, taking precautions against introducing moisture: the residue so obtained responds to *Identification* test *A* under *Phentolamine Mesylate.*

Bacterial endotoxins ⟨85⟩**—**It contains not more than 5.8 USP Endotoxin Units per mg of phentolamine mesylate.

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

Procedure for content uniformity—Dissolve the contents of 1 container in water to provide a solution containing about 20 µg of phentolamine mesylate per mL. Concomitantly determine the absorbances of this solution and of a solution of USP Phentolamine Mesylate RS, in the same medium, at a concentration of about 20 µg per mL, in 1-cm cells at the wavelength of maximum absorbance at about 278 nm, with a suitable spectrophotometer, using water as the blank. Calculate the quantity, in mg, of $C_{17}H_{19}N_3O \cdot CH_4O_3S$ in the Phentolamine Mesylate for Injection taken by the formula:

$$(T / D)C(A_U / A_S)$$

in which T is the labeled quantity, in mg, of phentolamine mesylate in the Phentolamine Mesylate for Injection, D is the concentration, in µg per mL, of phentolamine mesylate in the solution from the Phentolamine Mesylate for Injection, based on the labeled quantity per container and the extent of dilution, C is the concentration, in µg per mL, of USP Phentolamine Mesylate RS in the Standard solution, and A_U and A_S are the absorbances of the solution from the Phentolamine Mesylate for Injection and the Standard solution, respectively.

pH ⟨791⟩: between 4.5 and 6.5, in a freshly prepared solution having a concentration of about 1 in 100.

Other requirements—It meets the requirements for *Sterility Tests* ⟨71⟩ and *Labeling* under *Injections* ⟨1⟩.

Assay—

Standard preparation—Transfer about 25 mg of USP Phentolamine Mesylate RS, accurately weighed, to a 50-mL volumetric flask, add water to volume, and mix.

Assay preparation—Dissolve the contents of 10 containers of Phentolamine Mesylate for Injection in a volume of water corresponding to the volume of solvent specified in the labeling. Transfer an aliquot, equivalent to about 25 mg of phentolamine mesylate, to a 50-mL volumetric flask, add water to volume, and mix.

Procedure—Pipet 5-mL portions, respectively, of the *Standard preparation*, *Assay preparation*, and water to provide a blank, into separate 125-mL separators. Into each separator pipet 5-mL portions of 0.1 N hydrochloric acid and saturated picric acid solution. Extract with three 25-mL portions of chloroform, filtering each portion through chloroform-washed cotton into a 100-mL volumetric flask. Dilute with chloroform to volume, and mix. Concomitantly determine the absorbances of the solutions from the *Assay preparation* and the *Standard preparation* in 1-cm cells at the wavelength of maximum absorbance at about 410 nm, with a suitable spectrophotometer, against the blank. Calculate the quantity, in mg, of $C_{17}H_{19}N_3O \cdot CH_4O_3S$ in the aliquot of Phentolamine Mesylate for Injection taken by the formula:

$$50C(A_U / A_S)$$

in which C is the concentration, in mg per mL, of USP Phentolamine Mesylate RS in the *Standard preparation*, and A_U and A_S