10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution. Place the plate in a chamber filled with iodine vapor for 10 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (1 g, in vacuum, phosphorus (V) oxide, 50°C, 3 hours).

**Residue on ignition** Not more than 0.20% (1 g).

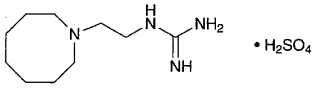
**Assay** Weigh accurately about 0.25 g of Guanabenz Acetate, previously dried, dissolve in 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 29.114 mg of $C_8H_8Cl_2N_4.C_2H_4O_2$

**Containers and storage** Containers—Tight containers.
Storage—Light-resistant.

# Guanethidine Sulfate

硫酸グアネチジン



$C_{10}H_{22}N_4.H_2SO_4$: 296.39
1-[2-(Hexahydroazocin-1(2*H*)-yl)ethyl]guanidine monosulfate [*645-43-2*]

Guanethidine Sulfate, when dried, contains not less than 98.5% of $C_{10}H_{22}N_4.H_2SO_4$.

**Description** Guanethidine Sulfate occurs as white crystals or crystalline powder. It is odorless or has a slight, characteristic odor and a bitter taste.

It is very soluble in formic acid, freely soluble in water, and practically insoluble in ethanol (95) and in diethyl ether.

Melting point: 251 – 256°C (an evacuated sealed capillary tube, with decomposition).

**Identification** (1) To 4 mL of a solution of Guanethidine Sulfate (1 in 4000) add 2 mL of 1-naphthol TS, 1 mL of diacetyl TS and 15 mL of water, and allow to stand for 30 minutes: a red color develops.

(2) Determine the infrared absorption spectrum of Guanethidine Sulfate, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) A solution of Guanethidine Sulfate (1 in 10) responds to the Qualitative Tests for sulfate.

**pH** Dissolve 1.0 g of Guanethidine Sulfate in 50 mL of water: the pH of the solution is between 4.7 and 5.7.

**Purity** (1) Clarity and color of solution—Dissolve 1.0 g of Guanethidine Sulfate in 50 mL of water: the solution is clear and colorless.

(2) Methylisothiourea sulfate—Dissolve 2.0 g of Guanethidine Sulfate in 80 mL of sodium hydroxide TS, and allow to stand for 10 minutes. Add 60 mL of hydrochloric acid, 2 g of sodium bromide and water to make 200 mL. Then, to this solution add 0.70 mL of 1/60 mol/L potassium bromate VS and 2 mL of zinc iodide-starch paste TS: a blue color develops.

(3) Heavy metals—Proceed with 2.0 g of Guanethidine Sulfate according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

**Loss on drying** Not more than 0.5% (1 g, 105°C, 4 hours).

**Residue on ignition** Not more than 0.20% (1 g).

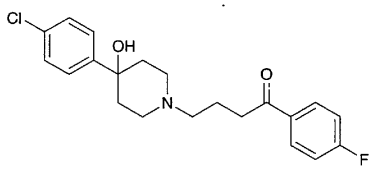
**Assay** Weigh accurately about 0.5 g of Guanethidine Sulfate, previously dried, dissolve in 2 mL of formic acid, add 70 mL of a mixture of acetic anhydride and acetic acid (100) (6:1), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 29.639 mg of $C_{10}H_{22}N_4.H_2SO_4$

**Containers and storage** Containers—Tight containers.
Storage—Light-resistant.

# Haloperidol

ハロペリドール



$C_{21}H_{23}ClFNO_2$: 375.86
4-[4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)butan-1-one [*52-86-8*]

Haloperidol, when dried, contains not less than 99.0% of $C_{21}H_{23}ClFNO_2$.

**Description** Haloperidol occurs as white to pale yellow crystals or powder. It is odorless.

It is freely soluble in acetic acid (100), soluble in chloroform, sparingly soluble in methanol and in ethanol (95), slightly soluble in 2-propanol and in diethyl ether, and practically insoluble in water.

**Identification** (1) Transfer 0.02 g of Haloperidol and 0.05 g of sodium to a test tube, and heat gradually and cautiously to ignite. Cool, add 0.5 mL of methanol and 5 mL of water, and heat to boil. Filter the solution, acidify the filtrate with 2 to 3 drops of hydrochloric acid, then add 2 drops of zirconyl-alizarin red S TS: the red-purple color of the test solution disappears, and a pale yellow color develops.

(2) Dissolve 0.1 g of Haloperidol in 30 mL of diluted

hydrochloric acid (1 in 1000) by warming, cool, and add 5 mL of Reinecke salt TS: a light red precipitate is produced.

**(3)** Dissolve 0.03 g of Haloperidol in 100 mL of 2-propanol. To 5 mL of the solution add 10 mL of 0.1 mol/L hydrochloric acid TS and 2-propanol to make 100 mL. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

**(4)** Perform the test with Haloperidol as directed under the Flame Coloration Test (2): a green color appears.

**Melting point** 149 - 153°C

**Purity** **(1)** Clarity and color of solution—Dissolve 0.25 g of Haloperidol in 10 mL of chloroform: the solution is clear and is colorless to pale yellow.

**(2)** Sulfate—To 1.0 g of Haloperidol add 50 mL of water, shake, and filter. To 25 mL of the filtrate add 1 mL of dilute hydrochloric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.50 mL of 0.005 mol/L sulfuric acid VS (not more than 0.048%).

**(3)** Heavy metals—Proceed with 1.0 g of Haloperidol according to method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

**(4)** Higher condensation product—Dissolve 0.030 g of Haloperidol in 50 mL of methanol, and add 1 mL of 1 mol/L hydrochloric acid TS and methanol to make exactly 100 mL. Determine the absorbance of this solution at 335 nm as directed under Spectrophotometry: the absorbance is not more than 0.220.

**Loss on drying** Not more than 0.5% (1 g, in vacuum, 60°C, phosphorus (V) oxide, 3 hours).

**Residue on ignition** Not more than 0.10% (1 g).

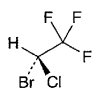
**Assay** Weigh accurately about 0.6 g of haloperidol, previously dried, and dissolve in 40 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (indicator: 1 drop of crystal violet TS). Perform a blank determination.

Each mL of 0.1 mol/L perchloric acid VS
= 37.587 mg of $C_{21}H_{23}ClFNO_2$

**Containers and storage** Containers—Tight containers.
Storage—Light-resistant.

# Halothane

ハロタン




and enantiomer

$C_2HBrClF_3$: 197.38
(*RS*)-2-Bromo-2-chloro-1,1,1-trifluoroethane [*151-67-7*]

Halothane contains not less than 0.008% and not more than 0.012% of Thymol as a stabilizer.

**Description** Halothane is a clear, colorless, and mobile liquid.

It is miscible with ethanol (95), with diethyl ether and with isooctane.

It is slightly soluble in water.

It is a volatile, nonflammable liquid, and setting fire to its heated vapor does not support combustion.

It is affected by light.

Refractive index $n_D^{20}$: 1.369 - 1.371

**Identification** Transfer about 3 μL of Halothane to a gas cell having light path 10 cm in length, and determine the infrared absorption spectrum as directed in the gas sampling method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

**Specific gravity** $d_{20}^{20}$: 1.872 - 1.877

**Purity** **(1)** Acid or alkali—Shake 60 mL of Halothane with 60 mL of freshly boiled and cooled water vigorously for 3 minutes. Separate the water layer, and use this as the sample solution. To 20 mL of the sample solution add 1 drop of bromocresol purple TS and 0.10 mL of 0.01 mol/L sodium hydroxide VS: a red-purple color develops. To 20 mL of the sample solution add 1 drop of bromocresol purple TS and 0.6 mL of 0.01 mol/L hydrochloric acid VS: a yellow color is produced.

**(2)** Halide and halogen—To 5 mL of the sample solution obtained in (1) add 1 drop of nitric acid and 0.20 mL of silver nitrate TS: no turbidity is produced. To 10 mL of the sample solution obtained in (1) add 1 mL of potassium iodide TS and 2 drops of starch TS, and allow to stand for 5 minutes: no blue color develops.

**(3)** Phosgene—Transfer 50 mL of Halothane to a dried 300-mL conical flask, suspend a strip of phosgene test paper vertically inside the flask with the lower end about 10 mm above the surface of the liquid, insert the stopper, and allow to stand in a dark place for 20 to 24 hours: the test paper shows no yellow color.

**(4)** Residue on evaporation—Pipet 50 mL of Halothane, evaporate on a water bath, and dry the residue at 105°C for 2 hours: the mass of the residue is not more than 1.0 mg.

**(5)** Volatile related substances—To 100 mL of Halothane add exactly 5.0 μL of the internal standard, and use this solution as the sample solution. Perform the test with 5 μL of the sample solution as directed under the Gas Chromatography, and determine each peak area by the automatic integration method: the total area of the peaks other than those of halothane and the internal standard is not larger than the peak area of the internal standard.

*Internal standard*—1,1,2-Trichloro-1,2,2-trifluoroethane.

*Operating conditions*—

Detector: A hydrogen flame-ionization detector.

Column: A column about 3 mm in inside diameter and 3 m in length, at the first 2 m from the injection port, having macrogol 400 coated in the ratio of 30% on siliceous earth for gas chromatography (180 to 250 μm in particle diameter), and at the remaining 1 m, having dinonyl phthalate coated in the ratio of 30% on siliceous earth for gas chromatography (180 to 250 μm in particle diameter).

Column temperature: A constant temperature of about 50°C