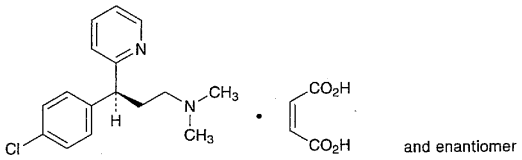
TS, and warm at 70°C for 40 minutes. After cooling, add 100 mL of ethanol (95), and titrate the excess potassium hydroxide with 0.1 mol/L hydrochloric acid VS until the color of the solution changes from blue through blue-green to yellow (indicator: 1 mL of thymol blue TS). Perform a blank determination.

Each mL of 0.1 mol/L potassium hydroxide-ethanol TS
= 24.566 mg of $C_{10}H_{12}ClNO_4$

Containers and storage Containers—Tight containers.

Chlorpheniramine Maleate

マレイン酸クロルフェニラミン



and enantiomer

$C_{16}H_{19}ClN_2.C_4H_4O_4$: 390.86
N-[(*RS*)-3-(4-Chlorophenyl)-3-pyridin-2-ylpropyl]-*N*,*N*-dimethylamine monomaleate [*113-92-8*]

Chlorpheniramine Maleate, when dried, contains not less than 98.0% of *dl*-chlorpheniramine maleate ($C_{16}H_{19}ClN_2.C_4H_4O_4$).

Description Chlorpheniramine Maleate occurs as white, fine crystals. It is odorless, and has a bitter taste.

It is very soluble in acetic acid (100), freely soluble in water, in ethanol (95) and in chloroform, and practically insoluble in diethyl ether.

Identification (1) Dissolve 1 mg of Chlorpheniramine Maleate in 5 mL of water, add 2 mL of Dragendorff's TS, and shake: a red-orange precipitate is produced.

(2) Dissolve 0.5 g of Chlorpheniramine Maleate in 5 mL of water, add 2 mL of ammonia solution (28), and extract with three 5-mL portions of chloroform. Separate the water layer, evaporate to dryness, add about 1.5 mL of dilute sulfuric acid and 5 mL of water, and extract with four 25-mL portions of diethyl ether. Combine the diethyl ether extracts, and evaporate on a water bath at a temperature of about 35°C with the aid of a current of air: the residue melts between 128°C and 136°C.

(3) Determine the infrared absorption spectrum of Chlorpheniramine Maleate, previously dried, as directed in the paste 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.

Absorbance $E^{1\%}_{1cm}$ (265 nm): 210 - 220 (after drying, 5 mg, 0.25 mol/L sulfuric acid TS, 250 mL).

pH Dissolve 1.0 g of Chlorpheniramine Maleate in 100 mL of water: the pH of this solution is between 4.0 and 5.5.

Melting point 130 - 135°C

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Chlorpheniramine Maleate in 20 mL of water: the solution is clear and colorless.

(2) Readily carbonizable substances—Weigh 0.025 g of Chlorpheniramine Maleate, and perform the test: no color develops.

(3) Related substances—Dissolve 0.10 g of Chlorpheniramine maleate in 2 mL of chloroform, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add chloroform to make exactly 10 mL. Pipet 1 mL of this solution, add chloroform again to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 2 μL each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate, methanol and dilute acetic acid (31) (5:3:2) to a distance of about 10 cm, and air-dry the plate. Spray evenly Dragendorff's TS for spraying on the plate: 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, 105°C, 3 hours).

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

Assay Dissolve about 0.4 g of Chlorpheniramine Maleate, previously dried and accurately weighed, in 20 mL of acetic acid (100). Titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue-green to green (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 19.543 mg of $C_{16}H_{19}ClN_2.C_4H_4O_4$

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

Chlorpheniramine Maleate Injection

マレイン酸クロルフェニラミン注射液

Chlorpheniramine Maleate Injection is an aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of *dl*-chlorpheniramine maleate ($C_{16}H_{19}ClN_2.C_4H_4O_4$: 390.86).

Method of preparation Prepare as directed under Injections, with Chlorpheniramine Maleate.

Description Chlorpheniramine Maleate Injection is a clear, colorless liquid.
pH: 4.5 - 7.0

Identification (1) Take a volume of Chlorpheniramine Maleate Injection, equivalent to 1 mg of Chlorpheniramine Maleate According to the labeled amount, add 5 mL of water and 2 mL of Dragendorff's TS, and shake: a red-orange precipitate is produced.

(2) Transfer a volume of Chlorpheniramine Maleate In-

jection, equivalent to 0.05 g of Chlorpheniramine Maleate According to the labeled amount, to a beaker, adjust with 0.1 mol/L hydrochloric acid TS or dilute sodium hydroxide TS to a pH between 4.8 and 5.2, if necessary, and evaporate on a water bath to dryness cautiously. Add 20 mL of ethanol (99.5) to the residue, stir thoroughly, and filter. Evaporate the filtrate on a water bath to dryness, and dissolve the residue with 10 mL of water. Transfer the solution to a separator, and extract with two 20-mL portions of chloroform. Combine the chloroform extracts, add 0.01 g of activated charcoal, shake for several minutes, and filter. Evaporate the filtrate with the aid of a current of air by warming in a water bath at about 40°C. Add 0.2 to 0.3 mL of 2-propanol to the residue, shake vigorously, add 10 mL of diethyl ether, rub the inside wall of the beaker with a glass rod, if necessary, and allow to stand. Discard the supernatant liquid, and dry the residue in a desiccator (in vacuum, silica gel) for 1 hour: the residue melts between 128°C and 135°C.

(3) Take a volume of Chlorpheniramine Maleate Injection, equivalent to 0.025 g of Chlorpheniramine Maleate according to the labeled amount, add 5 mL of dilute sodium hydroxide TS, and extract with 20 mL of hexane. Wash the hexane layer with 10 mL of water, shake with 0.5 g of anhydrous sodium sulfate for several minutes, and filter. Evaporate the filtrate in a water bath at about 50°C under a reduced pressure, and determine the infrared absorption spectrum of the residue as directed in the liquid film method under the Infrared Spectrophotometry: it exhibits absorption at the wave numbers of about 2940 cm^{-1}, 2810 cm^{-1}, 2770 cm^{-1}, 1589 cm^{-1}, 1491 cm^{-1}, 1470 cm^{-1}, 1434 cm^{-1}, 1091 cm^{-1} and 1015 cm^{-1}.

Assay Transfer an exactly measured volume of Chlorpheniramine Maleate Injection, equivalent to about 3 mg of chlorpheniramine maleate ($C_{16}H_{19}ClN_2.C_4H_4O_4$), to a 100-mL separator, add 20 mL of water and 2 mL of sodium hydroxide TS, and extract with two 50-mL portions of diethyl ether. Combine diethyl ether extracts, wash with 20 mL of water, and then extract with 20-mL, 20-mL and 5-mL portions of 0.25 mol/L sulfuric acid TS successively. Combine all acid extracts, and add 0.25 mol/L sulfuric acid TS to make exactly 50 mL. Pipet 10 mL of this solution, and add 0.25 mol/L sulfuric acid TS to make exactly 25 mL. Determine the absorbance A of this solution at a wavelength of the maximum absorbance at about 265 nm as directed under the Ultraviolet-visible Spectrophotometry.

$$\text{Amount (mg) of chlorpheniramine maleate } (C_{16}H_{19}ClN_2.C_4H_4O_4) = \frac{A}{210} \times 1250$$

Containers and storage Containers—Hermetic containers. Storage—Light-resistant.

Chlorpheniramine Maleate Powder

マレイン酸クロルフェニラミン散

Chlorpheniramine Maleate Powder contains not less than 93% and not more than 107% of the labeled amount of *dl*-chlorpheniramine maleate ($C_{16}H_{19}ClN_2.C_4H_4O_4$: 390.86).

Method of preparation Prepare as directed under Powders, with Chlorpheniramine Maleate.

Identification **(1)** Weigh a portion of Chlorpheniramine Maleate Powder, equivalent to 0.05 g of Chlorpheniramine Maleate according to the labeled amount, shake with 40 mL of 0.1 mol/L hydrochloric acid TS, and filter. Transfer the filtrate to a separator, and wash with 40 mL of chloroform. Add 10 mL of sodium hydroxide TS, and extract with 20 mL of hexane. Wash the hexane layer with 5 mL of water. Centrifuge, if necessary, shake the hexane extract with 0.5 g of anhydrous sodium sulfate for several minutes, and filter. To 5 mL of the filtrate [the remaining filtrate to be used in (3)] add 2 mL of Dragendorff's TS, and shake: a red-orange precipitate is produced.

(2) Transfer a portion of Chlorpheniramine Maleate Powder, equivalent to 0.05 g of Chlorpheniramine Maleate according to the labeled amount, to a glass-stoppered flask, add 20 mL of diethyl ether, allow to stand for 10 minutes with frequent shaking, decant, and discard the diethyl ether. Add 20 mL of diethyl ether to the residue, allow to stand for 10 minutes with frequent shaking, decant, and discard the diethyl ether. Repeat the same procedure once more. Dissolve the residue in 20 mL of water, shake for 15 minutes, and centrifuge. Transfer the supernatant liquid to a separator, and extract with two 40-mL portions of chloroform. Combine the chloroform extracts, add 0.01 g of activated charcoal, shake for several minutes, and filter. Evaporate the filtrate with the aid of a current of air by warming in a water bath at about 40°C. Add 0.2 to 0.3 mL of 2-propanol to the residue, shake vigorously, add 10 mL of diethyl ether, rub the inside wall of the beaker with a glass rod, if necessary, and allow to stand. Discard the supernatant liquid, and dry the residue in a desiccator (in vacuum, silica gel) for 1 hour: the residue melts between 128°C and 135°C.

(3) Evaporate the remaining filtrate obtained in (1), in a water bath at about 50°C under a reduced pressure, and determine the infrared absorption spectrum of the residue as directed in the liquid film method under the Infrared Spectrophotometry: it exhibits absorption at the wave numbers of about 2940 cm^{-1}, 2810 cm^{-1}, 2770 cm^{-1}, 1589 cm^{-1}, 1491 cm^{-1}, 1470 cm^{-1}, 1434 cm^{-1}, 1091 cm^{-1} and 1015 cm^{-1}.

Assay Weigh accurately a portion of Chlorpheniramine Maleate Powder, equivalent to about 3 mg of chlorpheniramine maleate ($C_{16}H_{19}ClN_2.C_4H_4O_4$), transfer to a 100-mL separator, add 20 mL of 0.05 mol/L sulfuric acid TS, and shake for 5 minutes. Add 20 mL of diethyl ether, and allow to stand for 5 minutes with frequent shaking. Centrifuge, if necessary, and filter the water layer through a dry filter paper into a second separator. Extract the diethyl ether layer with two 10-mL portions of 0.05 mol/L sulfuric acid TS, filter the acid extracts, and combine the washings with the filtrate. Wash the filter paper with a small amount of 0.05 mol/L, and combine the washings with the filtrate. Add sodium hydroxide TS, and extract with two 50-mL portions of diethyl ether, combine the diethyl ether extracts, wash with 20 mL of eater, and extract with 20-mL, 20-mL and 5-mL portions of 0.25 mol/L sulfuric acid TS successively. Combine all acid extracts, and add 0.25 mol/L sulfuric acid TS to make exactly 50 mL. Pipet 10 mL of this solution, trans-