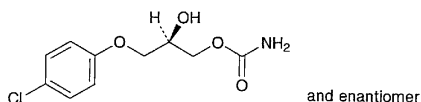


$$\begin{aligned} & \text{Amount (mg) of } C_{23}H_{29}ClO_4 \\ & = \text{amount (mg) of Chlormadinone Acetate} \\ & \quad \text{Reference Standard} \\ & \quad \times \frac{A_T}{A_S} \end{aligned}$$

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

Chlorphenesin Carbamate

カルバミン酸クロルフェネシン



$C_{10}H_{12}ClNO_4$: 245.66
(*RS*)-3-(4-Chlorophenoxy)-2-hydroxypropyl carbamate
[886-74-8]

Chlorphenesin Carbamate, when dried, contains not less than 98.0% and not more than 102.0% of $C_{10}H_{12}ClNO_4$.

Description Chlorphenesin Carbamate occurs as white crystals or crystalline powder. It is odorless, and has a slightly bitter taste.

It is freely soluble in methanol, in ethanol (95) and in pyridine, soluble in 2-propanol, sparingly soluble in diethyl ether, slightly soluble in water, and practically insoluble in hexane.

A solution of Chlorphenesin Carbamate in ethanol (95) (1 in 20) shows no optical rotation.

Identification (1) Determine the absorption spectrum of a solution of Chlorphenesin Carbamate in ethanol (95) (3 in 200,000) 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.

(2) Determine the infrared absorption spectrum of Chlorphenesin Carbamate, 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) Perform the test with Chlorphenesin Carbamate as directed under the Flame Coloration Test (2): a green color appears.

Melting point 88 – 91°C

Purity (1) Heavy metals—Dissolve 2.0 g of Chlorphenesin Carbamate in 20 mL of ethanol (95), and add 2 mL of dilute acetic acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 2.0 mL of Standard Lead Solution add 20 mL of ethanol (95), 2 mL of dilute acetic acid and water to make 50 mL (not more than 10 ppm).

(2) Arsenic—Prepare the test solution with 1.0 g of Chlorphenesin Carbamate according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(3) Related substances—(i) Chlorphenesin-2-carba-

mate: Dissolve 0.10 g of Chlorphenesin Carbamate in 20 mL of a mixture of hexane for liquid chromatography and 2-propanol (7:3), and use this solution as the sample solution. Perform the test with 10 μ L of the sample solution as directed under the Liquid Chromatography according to the following conditions. Determine the peak area, A_a , of chlorphenesin carbamate and the peak area, A_b , of chlorphenesin-2-carbamate by the automatic integration method: the ratio, $A_b/(A_a + A_b)$, is not larger than 0.007.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 30 cm in length, packed with silica gel for liquid chromatography (5 μ m in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: A mixture of hexane for liquid chromatography, 2-propanol and acetic acid (100) (700:300:1).

Flow rate: Adjust the flow rate so that the retention time of chlorphenesin carbamate is about 9 minutes.

Detection sensitivity: Pipet 1 mL of the sample solution, add a mixture of *n*-hexane for liquid chromatography and 2-propanol (7:3) to make exactly 100 mL. Adjust the detection sensitivity so that the peak height of chlorphenesin carbamate from 10 μ L of this solution is about 20 to 40% of the full scale.

Selection of column: Dissolve 0.1 g of Chlorphenesin Carbamate in methanol to make 50 mL. To 25 mL of this solution add 25 mL of sodium hydroxide TS, and warm at 60°C for 20 minutes. To 20 mL of this solution add 5 mL of 1 mol/L hydrochloric acid TS, shake well with 20 mL of ethyl acetate, and allow to stand to separate the ethyl acetate layer. Proceed with 10 μ L of this layer under the above operating conditions, and calculate the resolution. Use a column giving elution of chlorphenesin, chlorphenesin carbamate and chlorphenesin-2-carbamate in this order, with the ratios of the retention time of chlorphenesin and chlorphenesin-2-carbamate to chlorphenesin carbamate are about 0.7 and about 1.2, respectively, and with the resolution between the peaks of chlorphenesin and chlorphenesin carbamate being not less than 2.0.

(ii) Other related substances: Dissolve 0.10 g of Chlorphenesin Carbamate in 10 mL of ethanol (95), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add ethanol (95) to make exactly 20 mL. Pipet 2 mL of this solution, add ethanol (95) to make exactly 20 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 50 μ L each of the sample solution and the standard solution on a plate of silica gel for liquid chromatography. Develop the plate with a mixture of ethyl acetate, methanol and ammonia solution (28) (17:2:1) to a distance of about 10 cm, and air-dry the plate. Allow to stand in iodine vapor for 20 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 0.20% (1 g, in vacuum, silica gel, 4 hours).

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

Assay Weigh accurately about 0.5 g of Chlorphenesin Carbamate, previously dried, dissolve in 20 mL of pyridine, add exactly 50 mL of 0.1 mol/L potassium hydroxide-ethanol

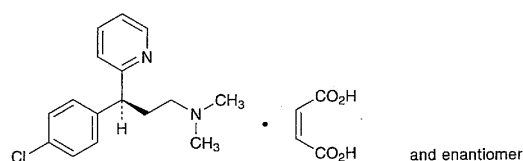
TS, and warm at 70°C for 40 minutes. After cooling, add 100 mL of ethanol (95), and titrate the excess potassium hydroxide with 0.1 mol/L hydrochloric acid VS until the color of the solution changes from blue through blue-green to yellow (indicator: 1 mL of thymol blue TS). Perform a blank determination.

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



$C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$: 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 ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$).

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 $E_{1\text{cm}}^{1\%}$ (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 $C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$

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 ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$: 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-