

(2) Dissolve 0.2 g of Perphenazine in 2 mL of methanol, add this solution to 10 mL of a warm solution of 2,4,6-trinitrophenol in methanol (1 in 25), and allow to stand for 4 hours. Collect the crystals, wash with a small volume of methanol, and dry at 105°C for 1 hour: the crystals so obtained melt between 237°C and 244°C (with decomposition).

(3) Determine the absorption spectrum of a solution of Perphenazine in 0.1 mol/L hydrochloric acid TS (1 in 200,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1 or the spectrum of a solution of Perphenazine Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, to 10 mL of the solution add 10 mL of water. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 2 or the spectrum of a solution of Perphenazine Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

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

Melting point 95 – 100°C

Purity (1) Heavy metals—Proceed with 1.0 g of Perphenazine 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).

(2) Related substances—Perform the test in the current of nitrogen in light-resistant containers under the protection from sunlight. Dissolve 0.10 g of Perphenazine in 10 mL of ethanol (95), and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add ethanol (95) to make exactly 10 mL. Pipet 1 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 solution as directed under the Thin-layer Chromatography. Spot 10 μ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of 1-butanol and 1 mol/L ammonia TS (5:1) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): any spot other than the principal spot from the sample solution is not more intense than that from the standard solution.

Loss on drying Not more than 0.5% (1 g, in vacuum, phosphorus (V) oxide, 65°C, 4 hours).

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

Assay Weigh accurately about 0.4 g of Perphenazine, previously dried, dissolve in 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue-purple to blue-green (indicator: 3 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 20.199 mg of $C_{21}H_{26}ClN_3OS$

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

Perphenazine Tablets

ペルフェナジン錠

Perphenazine Tablets contain not less than 90% and not more than 110% of the labeled amount of perphenazine ($C_{21}H_{26}ClN_3OS$: 403.97).

Method of preparation Prepare as directed under Tablets, with Perphenazine.

Identification (1) Shake well a quantity of powdered Perphenazine Tablets, equivalent to 0.025 g of Perphenazine according to the labeled amount, with 10 mL of methanol, and filter. Evaporate 2 mL of the filtrate on a water bath to dryness. With the residue, proceed as directed in the Identification (1) under Perphenazine.

(2) Add 5 mL of the filtrate obtained in the Identification (1) to 10 mL of a warm solution of 2,4,6-trinitrophenol in methanol (1 in 25), and proceed as directed in the Identification (2) under Perphenazine.

(3) Determine the absorption spectrum of the filtrate obtained in the Assay as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 309 nm and 313 nm. Add 30 mL of methanol to another 10 mL of the filtrate, and determine the absorption spectrum: it exhibits a maximum between 256 nm and 260 nm.

Dissolution test Perform the test with 1 tablet of Perphenazine Tablets at 100 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of diluted phosphate buffer solution, pH 6.8, (1 in 2) as the test solution. Take 30 mL or more of the dissolved solution 90 minutes after start of the test, and filter through a membrane filter with pore size of not more than 0.8 μ m. Discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.01 g of Perphenazine Reference Standard, previously dried in vacuum with phosphorus (V) oxide at 65°C for 4 hours, dissolve in 5 mL of 0.1 mol/L hydrochloric acid TS, and add diluted phosphate buffer solution, pH 6.8, (1 in 2) to make exactly 250 mL. Pipet 5 mL of this solution, add diluted phosphate buffer solution, pH 6.8, (1 in 2) to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S , of the sample solution and the standard solution at 255 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Perphenazine Tablets in 90 minutes is not less than 70%.

Dissolution rate (%) with respect to the
labeled amount of perphenazine ($C_{21}H_{26}ClN_3OS$)

$$= W_S \times \frac{A_T}{A_S} \times \frac{1}{C} \times 36$$

W_S : Amount (mg) of Perphenazine Reference Standard.

C : Labeled amount (mg) of perphenazine ($C_{21}H_{26}ClN_3OS$) in 1 tablet.

Content uniformity Disintegrate 1 Perphenazine Tablet by shaking with 5 mL of water, shake well with 70 mL of methanol, and add methanol to make exactly 100 mL. Centrifuge this solution, pipet x mL of the supernatant liquid, add methanol to make exactly V mL of a solution containing about 4 μ g of perphenazine ($C_{21}H_{26}ClN_3OS$) in each mL,

and use this solution as the sample solution. Separately, weigh accurately about 0.01 g of perphenazine for assay, previously dried in vacuum over phosphorus (V) oxide at 65°C for 4 hours, dissolve in methanol to make exactly 250 mL. Pipet 5 mL of this solution, add methanol to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S , of the sample solution and the standard solution at 258 nm as directed under the Ultraviolet-visible Spectrophotometry.

$$\begin{aligned} & \text{Amount (mg) of perphenazine (C}_{21}\text{H}_{26}\text{ClN}_3\text{OS)} \\ &= \text{amount (mg) of perphenazine for assay} \\ & \times \frac{A_T}{A_S} \times \frac{V}{25} \times \frac{1}{x} \end{aligned}$$

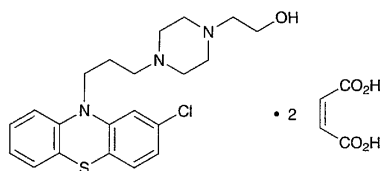
Assay Weigh accurately and powder not less than 20 Perphenazine Tablets. Weigh accurately a portion of the powder, equivalent to about 4 mg of perphenazine ($\text{C}_{21}\text{H}_{26}\text{ClN}_3\text{OS}$), add 70 mL of methanol, shake well, and add methanol to make exactly 100 mL. Filter the solution, and discard the first 20 mL of the filtrate. Pipet 5 mL of the subsequent filtrate, add methanol to make exactly 50 mL, and use this solution as the sample solution. Weigh accurately about 0.01 g of perphenazine for assay, previously dried in vacuum over phosphorus (V) oxide at 65°C for 4 hours, and dissolve in methanol to make exactly 250 mL. Pipet 5 mL of this solution, add methanol to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S , of the sample solution and the standard solution at 258 nm as directed under the Ultraviolet-visible Spectrophotometry.

$$\begin{aligned} & \text{Amount (mg) of perphenazine (C}_{21}\text{H}_{26}\text{ClN}_3\text{OS)} \\ &= \text{amount (mg) of perphenazine for assay} \\ & \times \frac{A_T}{A_S} \times \frac{2}{5} \end{aligned}$$

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

Perphenazine Maleate

マレイン酸ペルフェナジン



$\text{C}_{21}\text{H}_{26}\text{ClN}_3\text{OS} \cdot 2\text{C}_4\text{H}_4\text{O}_4$; 636.11
2-[4-[3-(2-Chlorophenothiazin-10-yl)propyl]piperazin-1-yl]ethanol dimaleate [58-39-9, Perphenazine]

Perphenazine Maleate, when dried, contains not less than 98.0% of $\text{C}_{21}\text{H}_{26}\text{ClN}_3\text{OS} \cdot 2\text{C}_4\text{H}_4\text{O}_4$.

Description Perphenazine Maleate occurs as a white to light yellow powder. It is odorless.

It is sparingly soluble in acetic acid (100), slightly soluble in water and in ethanol (95), and practically insoluble in chloroform.

It dissolves in dilute hydrochloric acid.

It is gradually colored by light.

Melting point: about 175°C (with decomposition).

Identification (1) Dissolve 8 mg of Perphenazine Maleate in 5 mL of sulfuric acid: a red color is produced, which becomes deep red-purple on warming.

(2) Dissolve 0.3 g of Perphenazine Maleate in 3 mL of dilute hydrochloric acid, add 2 mL of water and 3 mL of ammonia solution (28), shake, and extract with three 10-mL portions of chloroform. [Reserve the aqueous layer, and use for test (5)]. Evaporate the combined chloroform extracts on a water bath to dryness, dissolve the residue in 20 mL of methanol, and pour into 10 mL of a warm solution of 2,4,6-trinitrophenol in methanol (1 in 25). Allow to stand for 4 hours, collect the crystals, wash with a small amount of methanol, and dry at 105°C for 1 hour: the crystals melt between 237°C and 244°C (with decomposition).

(3) Determine the absorption spectrum of a solution of Perphenazine Maleate (1 in 20,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, to 10 mL of the solution add 30 mL of water. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 2: both spectra exhibit similar intensities of absorption at the same wavelengths.

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

(5) Evaporate the aqueous layer reserved in (2) to dryness. To the residue add 1 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 in a water bath at about 35°C with the aid of a current of air: the residue melts between 128°C and 136°C.

Purity (1) Heavy metals—Proceed with 2.0 g of perphenazine maleate according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

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

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 Weigh accurately about 0.5 g of Perphenazine Maleate, previously dried, dissolve in 70 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue to blue-green (indicator: 3 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

$$\begin{aligned} & \text{Each mL of 0.1 mol/L perchloric acid VS} \\ &= 31.806 \text{ mg of } \text{C}_{21}\text{H}_{26}\text{ClN}_3\text{OS} \cdot 2\text{C}_4\text{H}_4\text{O}_4 \end{aligned}$$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.