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

Assay Weigh accurately about 0.5 g of Trihexyphenidyl Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (1:1), and titrate with 0.1 mol/L perchloric acid-dioxane VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid-dioxane VS
= 33.793 mg of $C_{20}H_{31}NO.HCl$

Containers and storage Containers—Tight containers.

Trihexyphenidyl Hydrochloride Tablets

塩酸トリヘキシフェニジル錠

Trihexyphenidyl Hydrochloride Tablets contain not less than 93% and not more than 107% of the labeled amount of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO.HCl$: 337.93).

Method of preparation Prepare as directed under Tablets, with Trihexyphenidyl Hydrochloride.

Identification **(1)** Weigh a quantity of powdered Trihexyphenidyl Hydrochloride Tablets, equivalent to 0.1 g of Trihexyphenidyl Hydrochloride according to the labeled amount, add 30 mL of chloroform, shake, and filter. Evaporate the filtrate on a water bath to dryness. Dissolve the residue in 10 mL of water by warming, cool, and use this solution as the sample solution. With 5 mL of the sample solution, proceed as directed in the Identification (1) under Trihexyphenidyl Hydrochloride.

(2) Shake a quantity of powdered Trihexyphenidyl Hydrochloride Tablets, equivalent to 0.01 g of Trihexyphenidyl Hydrochloride according to the labeled amount, with 5 mL of chloroform, filter, and use the filtrate as the sample solution. Dissolve 0.02 g of Trihexyphenidyl Hydrochloride Reference Standard in 10 mL of chloroform, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 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 chloroform and methanol (9:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly hydrogen hexachloroplatinate (IV)-potassium iodide TS on the plate: the spots from the sample solution and the standard solution show a blue-purple color and the same Rf value.

(3) The sample solution obtained in (1) responds to the Qualitative Tests (2) for chloride.

Dissolution test Perform the test with 1 tablet of Trihexyphenidyl Hydrochloride Tablets at 50 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 30 minutes after starting the test, and filter through a membrane filter with pore size of not more than 0.8 μm. Discard the first 10 mL of the filtrate, and use the subsequent as the sample solution. Separately, weigh accurately about 0.01 g of Trihexyphenidyl Hydrochloride Reference Standard, previously dried at 105°C for 3 hours, and dissolve in diluted phosphate buffer solution, pH 6.8, (1 in 2) to make exactly 100 mL. Pipet 2 mL of this solution, add diluted phosphate buffer solution, pH 6.8, (1 in 2) to make exactly 100 mL, and use this solution as the standard solution. Pipet 20 mL each of the sample solution, the standard solution and diluted phosphate buffer solution, pH 6.8, (1 in 2), add exactly 1 mL of diluted acetic acid (31) (1 in 10), and immediately add 5 mL of bromocresol green-sodium hydroxide-acetic acid-sodium acetate TS, and shake. Then, add exactly 10 mL each of dichloromethane, shake well, centrifuge, and take the dichloromethane layer. Determine the absorbances, A_T, A_S and A_B, of these dichloromethane layers at 415 nm as directed under the Ultraviolet-visible Spectrophotometry, using dichloromethane as a blank.

The dissolution rate of Trihexyphenidyl Hydrochloride Tablets in 30 minutes should be not less than 70%.

Dissolution rate (%) with respect to the labeled amount of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO.HCl$)

$$= W_S \times \frac{A_T - A_B}{A_S - A_B} \times \frac{1}{C} \times 18$$

W_S: Amount (mg) of Trihexyphenidyl Hydrochloride Reference Standard.

C: Labeled amount (mg) of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO.HCl$) in 1 tablet.

Content uniformity To one tablet of Trihexyphenidyl Hydrochloride Tablets add 2 mL of dilute hydrochloric acid and 60 mL of water, disintegrate by vigorous shaking for 10 minutes, and warm on a water bath with occasional shaking for 10 minutes. Cool, add 2 mL of methannol, and add water to make exactly V mL of the solution contains about 20 μg of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO.HCl$) per ml. Centrifuge, if necessary, and use the supernatant liquid as the sample solution. Separately, dissolve about 0.02 g of Trihexyphenidyl Hydrochloride Reference Standard (determine previously its loss on drying at 105°C for 3 hours) in methanol to make exactly 20 mL. Pipet 2 mL of this solution, and add 2 mL of dilute hydrochloric acid and water to make exactly 100 mL, and use this solution as the standard solution. Pipet 10 mL each of the sample solution and the standard solution, transfer to glass-stoppered centrifuge tubes, add exactly 10 mL of bromocresol purple-dipotassium hydrogenphosphate-citric acid TS and 15 mL of chloroform, stopper tightly, shake well, and centrifuge. Pipet 10 mL each of the chloroform layers, add chloroform to make exactly 50 mL. Determine the absorbances, A_T and A_S, of the subsequent solutions of the sample solution and the standard solution at 408 nm as directed under Spectrophotometry, respectively.

Amount (mg) of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO.HCl$)
= amount (mg) of Trihexyphenidyl Hydrochlochloride Reference Standard, calculated on the dried basis

$$\times \frac{A_T}{A_S} \times \frac{V}{1000}$$

Assay Weigh accurately and powder not less than 20 Trihexyphenidyl Hydrochloride Tablets. Weigh accurately a portion of the powder, equivalent to about 5 mg of trihex-

yphenidyl hydrochloride ($C_{20}H_{31}NO.HCl$), dissolve in 2 mL of dilute hydrochloric acid and 60 mL of water by warming on a water bath for 10 minutes with occasional shaking. After cooling, add 2 mL of methanol and water to make exactly 100 mL, and use this solution as the sample solution. Dissolve about 0.05 g of Trihexyphenidyl Hydrochloride Reference Standard (determine previously its loss on drying at 105°C for 3 hours), weighed accurately, in methanol, add methanol to make exactly 20 mL. Pipet 2 mL of this solution, add 2 mL of dilute hydrochloric acid and water to make exactly 100 mL, and use this solution as the standard solution. Pipet 10 mL each of the sample solution and the standard solution into glass-stoppered centrifuge tubes, add exactly 10 mL each of bromocresol purple-dipotassium hydrogenphosphate-citric acid TS and 15 mL each of chloroform, stopper tightly, shake thoroughly, and centrifuge. Pipet 10 mL each of the chloroform layers, and add chloroform to make exactly 50 mL. Determine the absorbances, A_T and A_S, of the subsequent solutions of the sample solution and the standard solution at 408 nm as directed under Spectrophotometry, respectively.

Amount (mg) of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO.HCl$)
= amount (mg) of Trihexyphenidyl Hydrochloride Reference Standard, calculated on the dried basis $\times \frac{A_T}{A_S} \times \frac{1}{10}$

Containers and storage Containers—Tight containers.

Trimetazidine Hydrochloride

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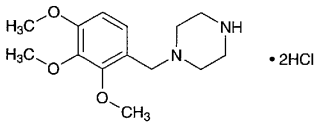

$C_{14}H_{22}N_2O_3.2HCl$: 339.26
1-(2,3,4-Trimethoxybenzyl)piperazine dihydrochloride
[13171-25-0]

Trimetazidine Hydrochloride contains not less than 98.0% of $C_{14}H_{22}N_2O_3.2HCl$, calculated on the dried basis.

Description Trimetazidine Hydrochloride occurs as a white, crystalline powder. It is odorless.

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

The pH of a solution of Trimetazidine Hydrochloride (1 in 20) is between 2.3 and 3.3.

Melting point: about 227°C (with decomposition).

Identification **(1)** Dissolve 5 mg of Trimetazidine Hydrochloride in 1 mL of water, add 1 mL of *p*-benzoquinone TS, boil gently for 2 to 3 minutes, and cool: a red color develops.

(2) Determine the absorption spectrum of a solution of Trimetazidine Hydrochloride in 0.1 mol/L hydrochloric acid TS (1 in 6250) 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.

(3) Determine the infrared absorption spectrum of Trimetazidine Hydrochloride as directed in the potassium chloride 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.

(4) A solution of Trimetazidine Hydrochloride (1 in 50) responds to the Qualitative Tests for chloride.

Purity **(1)** Clarity and color of solution—Dissolve 0.5 g of Trimetazidine Hydrochloride in 5 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 2.0 g of Trimetazidine Hydrochloride 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).

(3) Arsenic—Prepare the test solution with 1.0 g of Trimetazidine Hydrochloride according to Method 1, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.5 g of Trimetazidine Hydrochloride in 10 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL 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 cyclohexane and diethylamine (1:1) to a distance of about 10 cm, air-dry the plate, and then dry at 110°C for 1 hour. After cooling, examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot and the spot of the starting point from the sample solution are not more intense than the spot from the standard solution.

Water Not more than 1.5% (2 g, direct titration).

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

Assay Weigh accurately about 0.25 g of Trimetazidine Hydrochloride, dissolve in 20 mL of water, add 5 mL of sodium hydroxide TS, and extract with three 20-mL portions of chloroform. Filter the chloroform extract each time through a pledget of cotton with anhydrous sodium sulfate on a funnel. Combine all the extracts, and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from red-brown to green (indicator: 0.5 mL of *p*-naphtholbenzein TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 16.963 mg of $C_{14}H_{22}N_2O_3.2HCl$

Containers and storage Containers—Tight containers.