Triclofos Sodium Syrup

Monosodium Trichloroethyl Phosphate Syrup

トリクロホスナトリウムシロップ

Triclofos Sodium Syrup contains not less than 90% and not more than 110% of the labeled amount of triclofos sodium ($C_2H_3Cl_3NaO_4P$: 251.37).

Method of preparation Prepare as directed under Syrups, with Triclofos Sodium.

Identification **(1)** Weigh a portion of Triclofos Sodium Syrup, equivalent to 0.25 g of Triclofos Sodium according to the labeled amount, add 40 mL of water, shake well, add 5 mL of diluted sulfuric acid (3 in 50), and extract with 25 mL of 3-methyl-1-butanol. Take 5 mL of the extract, evaporate on a water bath to dryness, and add 1 mL of diluted sulfuric acid (1 in 2) and 1 mL of a solution of potassium permanganate (1 in 20) to the residue. Heat in a water bath for 5 minutes, add 7 mL of water, and then add a solution of oxalic acid dihydrate (1 in 20) until the color of the solution disappears. To 1 mL of this solution add 1 mL of pyridine and 1 mL of a solution of sodium hydroxide (1 in 5), and heat in a water bath, while shaking, for 1 minute: a light red color develops in the pyridine layer.

(2) Take 10 mL of the extract obtained in (1), evaporate on a water bath to dryness, add 1 g of anhydrous sodium carbonate to the residue, and heat for 10 minutes. After cooling, dissolve the residue in 40 mL of water, filter if necessary, and render the filtrate acidic with dilute nitric acid: the solution responds to the Qualitative Tests (2) for chloride. The remainder of the filtrate responds to the Qualitative Tests (1) for chloride and to the Qualitative Tests for phosphate.

pH 6.0 - 6.5

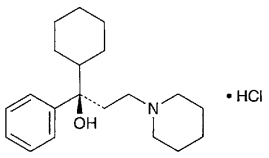
Assay Weigh accurately a portion of Triclofos Sodium Syrup, equivalent to 0.13 g of Triclofos Sodium according to the labeled amount, add 15 mL of water, 1 mL of sodium hydroxide TS and 15 mL of diethyl ether, shake for 1 minute, and separate the water layer. Wash the diethyl ether layer with 1 mL of water, and combine the washing with above water layer. To this solution add 2.5 mL of diluted sulfuric acid (3 in 50), and extract with four 10-mL portions of 3-methyl-1-butanol. Combine the 3-methyl-1-butanol extracts, and add 3-methyl-1-butanol to make exactly 50 mL. Measure exactly 10 mL each of this solution, and dilute with potassium hydroxide-ethanol TS. Place in a glass ampule, fire-seal, mix, and heat at 120°C for 2 hours in an autoclave. After cooling, transfer the contents to a flask, add 20 mL of diluted nitric acid (63 in 500) and exactly 25 mL of 0.02 mol/L silver nitrate VS, shake well, and titrate the excess silver nitrate with 0.02 mol/L ammonium thiocyanate VS (indicator: 2 to 3 drops of ammonium iron (III) sulfate TS). Perform a blank determination.

Each mL of 0.02 mol/L silver nitrate VS
= 1.676 mg of $C_2H_3Cl_3NaO_4P$

Containers and storage Containers—Tight containers.
Storage—In a cold place.

Trihexyphenidyl Hydrochloride

塩酸トリヘキシフェニジル



and enantiomer

$C_{20}H_{31}NO.HCl$: 337.93
(*RS*)-1-Cyclohexyl-1-phenyl-3-(piperidin-1-yl)propan-1-ol monohydrochloride [*52-49-3*]

Trihexyphenidyl Hydrochloride, when dried, contains not less than 98.5% of $C_{20}H_{31}NO.HCl$.

Description Trihexyphenidyl Hydrochloride occurs as a white, crystalline powder. It is odorless, and has a bitter taste.

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

Melting point: about 250°C (with decomposition).

Identification **(1)** Dissolve 1 g of Trihexyphenidyl Hydrochloride in 100 mL of water by warming, and cool. Use this solution as the sample solution. To 5 mL of the sample solution add 1 mL of a solution of 2,4,6-trinitrophenol in chloroform (1 in 50), and shake vigorously: a yellow precipitate is formed.

(2) To 20 mL of the sample solution obtained in (1) add 2 mL of sodium hydroxide TS: a white precipitate is formed. Collect the precipitate, wash with a small amount of water, recrystallize from methanol, and dry in a desiccator (in vacuum, silica gel) for 2 hours: the crystals so obtained melt between 113°C and 117°C.

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

pH Dissolve 1.0 g of Trihexyphenidyl Hydrochloride in 100 mL of water by warming, and cool: the pH of this solution is between 5.0 and 6.0.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Trihexyphenidyl Hydrochloride in 100 mL of water by warming: the solution is clear and colorless.

(2) Heavy metals—Dissolve 1.5 g of Trihexyphenidyl Hydrochloride in 60 mL of water by warming on a water bath at 80°C, cool, and filter. To 40 mL of the filtrate add 2 mL of dilute acetic acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 2.0 mL of Standard Lead Solution, 2 mL of dilute acetic acid and water to make 50 mL (not more than 20 ppm).

(3) Piperidylpropiophenone—Dissolve 0.10 g of Trihexyphenidyl Hydrochloride in 40 mL of water and 1 mL of 1 mol/L hydrochloric acid VS by warming, cool, and add water to make 100 mL. Determine the absorbance of this solution at 247 nm as directed under the Ultraviolet-visible Spectrophotometry: the absorbance is not more than 0.50.

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 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-