

$$\begin{aligned} & \text{Amount (mg) of } C_{19}H_{17}NOS \\ &= \text{amount (mg) of Tolnaftate Reference Standard} \\ & \quad \times \frac{A_T}{A_S} \end{aligned}$$

Containers and storage Containers—Tight containers.

Tolnaftate Solution

トルナフトート液

Tolnaftate Solution contains not less than 90% and not more than 110% of the labeled amount of tolinaftate ($C_{19}H_{17}NOS$: 307.41).

Method of preparation Prepare as directed under Liquids and Solutions, with Tolnaftate.

Identification (1) Spot 1 drop of Tolnaftate Solution on filter paper. Spray hydrogen hexachloroplatinate (IV)-potassium iodide TS on the paper: a light yellow color develops in the spot.

(2) To a volume of Tolnaftate Solution, equivalent to 0.02 g of Tolnaftate according to the labeled amount, add chloroform to make 10 mL, and use this solution as the sample solution. Separately, dissolve 0.02 g of Tolnaftate 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 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 toluene to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spot from the sample solution and that from the standard solution show the same R_f value.

Assay Pipet a volume of Tolnaftate Solution, equivalent to about 0.02 g of tolinaftate ($C_{19}H_{17}NOS$), add exactly 4 mL of the internal standard solution, then add chloroform to make 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.4 g of Tolnaftate Reference Standard, previously dried in vacuum at a pressure not exceeding 0.67 kPa at 65°C for 3 hours, and dissolve in chloroform to make exactly 100 mL. Pipet 5 mL of this solution, add exactly 4 mL of the internal standard solution, then add chloroform to make 50 mL, and use this solution as the standard solution. Perform the test with 10 μ L each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S , of the peak area of tolinaftate to that of the internal standard, respectively.

$$\begin{aligned} & \text{Amount (mg) of tolinaftate } (C_{19}H_{17}NOS) \\ &= \text{amount (mg) of Tolnaftate Reference Standard} \\ & \quad \times \frac{Q_T}{Q_S} \times \frac{1}{20} \end{aligned}$$

Internal standard solution—A solution of diphenyl phthalate in chloroform (3 in 200).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column about 4 mm in inside diameter and 15 to 30 cm in length, packed with octadecylsilylanized silica gel for liquid chromatography (5 to 10 μ m in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: A mixture of methanol and water (7:3).

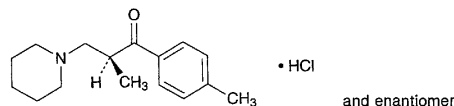
Flow rate: Adjust the flow rate so that the retention time of tolinaftate is about 14 minutes.

Selection of column: Proceed with 10 μ L of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of the internal standard and tolinaftate in this order with the resolution between these peaks being not less than 5.

Containers and storage Containers—Tight containers.

Tolperisone Hydrochloride

塩酸トルペリゾン



$C_{16}H_{23}NO \cdot HCl$: 281.82
(*RS*)-2-Methyl-1-(4-methylphenyl)-3-piperidin-1-ylpropan-1-one monohydrochloride [3644-61-9]

Tolperisone Hydrochloride, when dried, contains not less than 98.5% of $C_{16}H_{23}NO \cdot HCl$.

Description Tolperisone Hydrochloride occurs as a white, crystalline powder. It has a slight, characteristic odor.

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

It is hygroscopic.

The pH of a solution of Tolperisone Hydrochloride (1 in 20) is between 4.5 and 5.5.

Melting point: 167 – 174°C

Identification (1) Dissolve 0.2 g of Tolperisone Hydrochloride in 2 mL of ethanol (95), add 2 mL of 1,3-dinitrobenzene TS and 2 mL of sodium hydroxide TS, and heat: a red color develops.

(2) To 5 mL of a solution of Tolperisone Hydrochloride (1 in 20) add 2 to 3 drops of iodine TS: a red-brown precipitate is produced.

(3) Dissolve 0.5 g of Tolperisone Hydrochloride in 5 mL of water, add 2 mL of ammonia TS, and filter. Acidify 5 mL of the filtrate with dilute nitric acid: the solution responds to the Qualitative tests for chloride.

Absorbance $E_{1\text{cm}}^{1\%}$ (257 nm): 555 – 585 (after drying, 5 mg, ethanol (95), 500 mL).

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Tolperisone Hydrochloride in 10 mL of water: the solution is clear and colorless.

(2) Sulfate—Perform the test using 4.0 g of Tolperisone

Hydrochloride. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.005%).

(3) Heavy metals—Proceed with 1.0 g of Tolperisone Hydrochloride 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).

(4) Piperidine hydrochloride—Dissolve 0.20 g of Tolperisone Hydrochloride in water to make exactly 10 mL, and use this solution as the sample solution. Separately, dissolve 0.020 g of piperidine hydrochloride in water to make exactly 1000 mL, and use this solution as the standard solution. Transfer 5.0 mL each of the sample solution and the standard solution to different separators, add 0.1 mL each of a solution of copper (II) sulfate pentahydrate (1 in 20), then add 0.1 mL each of ammonia solution (28) and exactly 10 mL each of a mixture of isooctane and carbon disulfide (3:1), and shake vigorously for 30 minutes. Immediately after allowing to stand, separate the isooctane-carbon disulfide mixture layer, and dehydrate with anhydrous sodium sulfate. Perform the test with these solutions as directed under the Ultraviolet-visible Spectrophotometry: the absorbance of the sample solution at 438 nm is not more than that of the standard solution.

Loss on drying Not more than 0.5% (1 g, in vacuum, silica gel, 3 hours).

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

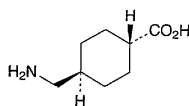
Assay Weigh accurately about 0.5 g of Tolperisone Hydrochloride, previously dried, dissolve in 70 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

$$\begin{aligned} \text{Each mL of 0.1 mol/L perchloric acid VS} \\ = 28.183 \text{ mg } C_{16}H_{23}NO \cdot HCl \end{aligned}$$

Containers and storage Containers—Well-closed containers.

Tranexamic Acid

トランエキサム酸



$C_8H_{15}NO_2$: 157.21

trans-4-(Aminomethyl)cyclohexanecarboxylic acid
[1197-18-8]

Tranexamic Acid, when dried, contains not less than 99.0% of $C_8H_{15}NO_2$.

Description Tranexamic Acid occurs as white crystals or crystalline powder. It is odorless, and has a bitter taste.

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

It dissolves in sodium hydroxide TS.

Identification (1) To 5 mL of a solution of Tranexamic Acid (1 in 100) add 1 mL of ninhydrin TS and heat for 3 minutes: a deep purple color is produced.

(2) To 5 mL of a solution of Tranexamic Acid (1 in 10) add 5 mL of a solution of *p*-toluenesulfonic acid (1 in 10), shake, and allow to stand for 30 minutes: a white precipitate is formed. Collect the precipitate by filtration, wash with two 10-mL portions of water, and dry at 105°C for 1 hour: the precipitate melts between 262°C and 267°C (with decomposition).

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

(2) Chloride—Perform the test with 1.0 g of Tranexamic Acid. Prepare the control solution with 0.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.014%).

(3) Heavy metals—Dissolve 2.0 g of Tranexamic Acid in 30 mL of water, add 12 mL of 1 mol/L hydrochloric acid VS and water to make 50 mL, and perform the test with this solution as the test solution. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

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

(5) Readily carbonizable substances—Perform the test with 0.5 g of Tranexamic Acid: no color develops.

(6) *Cis*-4-aminomethylcyclohexane-1-carboxylic acid—Dissolve 0.10 g of Tranexamic Acid in 2.5 mL of sodium hydroxide TS, and add 0.18 mL of acetic anhydride dropwise with shaking in ice water over 5 minutes. Allow to stand in ice water for 30 minutes, add 2.5 mL of 1 mol/L hydrochloric acid TS, and evaporate the solution under reduced pressure on a water bath to dryness between 40°C and 50°C for 15 to 20 minutes. Add 10 mL of methanol to the residue, add gently 0.10 mL of thionyl chloride along a wall of the vessel, and heat on a water bath between 80°C and 90°C for 20 minutes under a reflux condenser. After cooling, add slowly about 0.2 g of powdered anhydrous sodium carbonate with shaking to neutralize, and then evaporate under reduced pressure on a water bath between 40°C and 50°C to dryness. Add 8 mL of acetone to the residue, stir well, and filter by suction using a glass filter (G4). Repeat this operation twice with 8 mL of acetone. Collect the filtrate, and evaporate under reduced pressure on a water bath between 40°C and 50°C to dryness. After drying, the residue in a desiccator (in vacuum, silica gel) for 12 hours, and dissolve in 1.0 mL of methanol. Add exactly 1 mL of the internal standard solution to the solution, and use this solution as the sample solution. Perform the test with 1 μL of the sample solution as directed under the Gas Chromatography according to the following conditions: the ratio of the peak height of *cis*-4-aminomethylcyclohexane-1-carboxylic acid to the peak height of the internal standard is not more than 0.8.

Internal standard solution—A solution of 4-aminoacetophenone in methanol (1 in 1000).

Operating conditions—

Detector: A hydrogen flame-ionization detector.

Column: A column about 3 mm in inside diameter and about 2 m in length, packed with 2.5% of polyethylene glycol 20 mol/L coated on siliceous earth for gas chromatography (180 to 250 μm in particle diameter).