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).

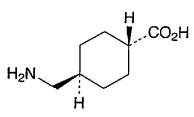
Assay Weigh accurately about 0.5 g of Tolperisone Hydrochloride, previously dried, dissolve in 70 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 28.183 mg $C_{16}H_{23}NO.HCl$

Containers and storage Containers—Well-closed containers.

Tranexamic Acid

トラネキサム酸



$C_8H_{15}NO_2$: 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).

Column temperature: A constant temperature of about 215°C.

Carrier gas: Nitrogen

Flow rate: Adjust the flow rate so that the retention time of the internal standard is about 8 minutes. The retention times of *cis*-4-aminomethylcyclohexane-1-carboxylic acid and tranexamic acid are about 11 minutes and 14 minutes, respectively.

Selection of column: Proceed with 1 μL of the sample solution under the above operating conditions, and calculate the resolution. Use a column giving elution of the internal standard, *cis*-4-aminomethylcyclohexane-1-carboxylic acid and tranexamic acid in this order with the resolution between the peaks of the internal standard and tranexamic acid being not less than 4.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of the internal standard from 1 μL of the sample solution composes 30% to 60% of the full scale.

Loss on drying Not more than 0.5% (1 g, 105°C, 2 hours).

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

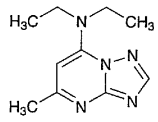
Assay Weigh accurately about 0.3 g of Tranexamic Acid, previously dried, dissolve in 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue to blue-green (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 15.721 mg of $C_8H_{15}NO_2$

Containers and storage Containers—Well-closed containers.

Trapidil

トラピジル



$C_{10}H_{15}N_5$: 205.26

7-Diethylamino-5-methyl[1,2,4]triazolo[1,5-*a*]pyrimidine

[*15421-84-8*]

Trapidil, when dried, contains not less than 98.5% of $C_{10}H_{15}N_5$.

Description Trapidil occurs as a white to pale yellowish white, crystalline powder.

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

The pH of a solution of Trapidil (1 in 100) is between 6.5 and 7.5.

Identification (1) To 5 mL of a solution of Trapidil (1 in 50) add 3 drops of Dragendorff's TS: an orange color develops.

(2) Determine the absorption spectrum of a solution of Trapidil (1 in 125,000) 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.

Absorbance $E^{1\%}_{1cm}$ (307 nm): 860 - 892 (after drying, 0.02 g, water, 2500 mL).

Melting point 101 - 105°C

Purity (1) Clarity and color of solution—Dissolve 2.5 g of Trapidil in 10 mL of water: the solution is clear and colorless to pale yellow.

(2) Chloride—Perform the test with 0.5 g of Trapidil. Prepare the control solution with 0.25 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.018%).

(3) Ammonium—Place 0.05 g of Trapidil in a glass-stoppered conical flask, thoroughly moisten with 10 drops of sodium hydroxide TS, and stopper the flask. Allow it to stand at 37°C for 15 minutes: the gas evolved does not change moistened red litmus paper to blue.

(4) Heavy metals—Dissolve 1.0 g of Trapidil in 40 mL of water, and add 1.5 mL of dilute hydrochloric acid, 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 1.0 mL of Standard Lead Solution add 2 mL of dilute acetic acid and water to make 50 mL (not more than 10 ppm).

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

(6) Related substances—Dissolve 0.10 g of Trapidil in 4 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add methanol to make exactly 20 mL. Pipet 1 mL of this solution, add methanol 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 20 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, ethanol (95) and acetic acid (100) (85:13:2) to a distance of about 10 cm, and air-dry the plate. Allow the plate to stand in iodine vapor for 60 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 0.5% (1 g, in vacuum, silica gel, 60°C, 3 hours).

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

Assay Weigh accurately about 0.2 g of Trapidil, previously dried, dissolve in 20 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 20.526 mg of $C_{10}H_{15}N_5$

Containers and storage Containers—Tight containers.