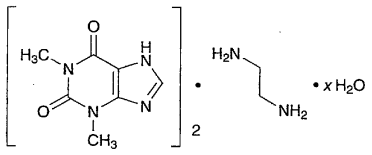
stopper tightly, heat in a water bath at 70°C for 30 minutes. After cooling, add 2 mL of acetic acid (100). When the procedure is run with 20 μL of this solution under the above operating conditions, amikacin derivative and kanamycin derivative are eluted in this order with the resolution between these peaks being not less than 5.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak height of amikacin derivative is not more than 2.0%.

Containers and storage Containers—Hermetic containers.

Aminophylline

アミノフィリン



$C_{14}H_{16}N_8O_4.C_2H_8N_2.xH_2O$
3,7-Dihydro-1,3-dimethyl-1*H*-purine-2,6-dione hemi(ethylenediamine) hydrate [*5877-66-5*, dihydrate]

Aminophylline contains not less than 84.0% and not more than 86.0% of theophylline ($C_7H_8N_4O_2$: 180.17), and not less than 14.0% and not more than 15.0% of ethylenediamine ($C_2H_8N_2$: 60.10), calculated on the anhydrous basis.

Description Aminophylline occurs as white to pale yellow granules or powder. It is odorless or slightly ammonia-like odor, and has a bitter taste.

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

To 1 g of Aminophylline add 5 mL of water, and shake: it dissolves almost completely. Separation of crystals begins in 2 to 3 minutes, and these crystals dissolve on the addition of a small amount of ethylenediamine.

It is gradually affected by light, and gradually loses ethylenediamine in air.

Identification **(1)** Dissolve 0.75 g of Aminophylline in 30 mL of water, and use this solution as the sample solution. To 20 mL of the sample solution add 1 mL of dilute hydrochloric acid: a precipitate is gradually formed. Filter the precipitate, recrystallize from water, and dry at 105°C for 1 hour: the crystals so obtained melt between 271°C and 275°C.

(2) Dissolve 0.1 g of the crystals obtained in (1) in 50 mL of water, and to 2 mL of this solution add tannic acid TS dropwise: a white precipitate is produced, and this precipitate dissolves upon dropwise addition of tannic acid TS.

(3) To 0.01 g of the crystals obtained in (1) add 10 drops of hydrogen peroxide TS and 1 drop of hydrochloric acid, and evaporate on a water bath to dryness: the residue shows a yellow-red color. Invert the dish containing the residue over a vessel containing 2 to 3 drops of ammonia TS: the color of the residue changes to red-purple, which is destroyed on the addition of 2 to 3 drops of sodium hydroxide TS.

(4) Dissolve 0.01 g of the crystals obtained in (1) in 5 mL of water, add 3 mL of ammonia-ammonium chloride buffer solution, pH 8.0, and 1 mL of copper (II) sulfate-pyridine TS, and mix. Add 5 mL of chloroform to the mixture, and shake: the chloroform layer develops a green color.

(5) To 5 mL of the sample solution obtained in (1) add 2 drops of copper (II) sulfate TS: a purple color develops. Add 1 mL of copper (II) sulfate TS: the color changes to blue, and green precipitates are formed on standing.

pH Dissolve 1.0 g of Aminophylline in 25 mL of water: the pH of the solution is between 8.0 and 9.5.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Aminophylline in 10 mL of hot water: the solution is clear and colorless to pale yellow.

(2) Heavy metals—Proceed with 1.0 g of Aminophylline 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).

Water Not more than 7.9% (0.3 g, direct titration).

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

Assay **(1)** Theophylline—Weigh accurately about 0.25 g of Aminophylline, and dissolve in 50 mL of water and 8 mL of ammonia TS by gentle warming on a water bath. Add exactly 20 mL of 0.1 mol/L silver nitrate VS, warm on a water bath for 15 minutes, allow to stand between 5°C and 10°C for 20 minutes, collect the precipitate by suction, and wash with three 10-mL portions of water. Combine the filtrate and washings, and add dilute nitric acid to make neutral. Add 3 mL of dilute nitric acid, and titrate the excess silver nitrate with 0.1 mol/L ammonium thiocyanate VS (indicator: 2 mL of ammonium iron (III) sulfate TS). Perform a blank determination.

Each mL of 0.1 mol/L silver nitrate VS
= 18.017 mg of $C_7H_8N_4O_2$

(2) Ethylenediamine—Weigh accurately about 0.5 g of Aminophylline, dissolve in 30 mL of water, and titrate with 0.1 mol/L hydrochloric acid VS (indicator: 3 drops of bromophenol blue TS).

Each mL of 0.1 mol/L hydrochloric acid VS
= 3.0049 mg of $C_2H_8N_2$

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

Aminophylline Injection

アミノフィリン注射液

Aminophylline Injection is an aqueous solution for injection. It contains not less than 75% and not more than 86% of the labeled amount of theophylline ($C_7H_8N_4O_2$: 180.17), and not less than 13% and not more than 20% of ethylenediamine ($C_2H_8N_2$: 60.10).

The concentration of Aminophylline Injection is expressed as the quantity of aminophylline ($C_{16}H_{24}N_{10}O_4.2H_2O$: 456.46).

Method of preparation Prepare as directed under Injections, with Aminophylline. It may be prepared with Theophylline and its equivalent Ethylenediamine, instead of Aminophylline.

It may contain not more than 0.060 g of Ethylenediamine as a stabilizer for each g of Aminophylline.

Description Aminophylline Injection is a clear and colorless liquid. It has a slightly bitter taste.

It gradually changes in color by light.

pH: 8.0 - 10.0

Identification To a volume of Aminophylline Injection, equivalent to 0.75 g of Aminophylline according to the labeled amount, add water to make 30 mL. Proceed with this solution as directed in the Identification under Aminophylline.

Assay **(1)** Theophylline—To an accurately measured volume of Aminophylline Injection, equivalent to about 0.2 g of theophylline ($C_7H_8N_4O_2$) (about 0.25 g of Aminophylline), add 15 mL of water, 8 mL of ammonia TS and 20 mL of silver nitrate TS, and warm on a water bath for 15 minutes. Cool to between 5°C and 10°C for 20 minutes, filter the precipitate through a glass filter (G4), and wash with three 10-mL portions of water. Dissolve the precipitate in 5 mL of nitric acid, and wash the filter with three 10-mL portions of water. Combine the nitric acid solution and washings, and titrate with 0.1 mol/L ammonium thiocyanate VS (indicator: 2 mL of ammonium iron (III) sulfate TS).

Each mL of 0.1 mol/L ammonium thiocyanate VS
= 18.017 mg of $C_7H_8N_4O_2$

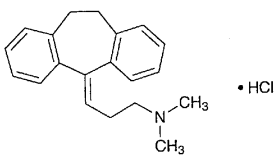
(2) Ethylenediamine—To an accurately measured volume of Aminophylline Injection, equivalent to about 0.03 g of ethylenediamine ($C_2H_8N_2$) (about 0.2 g of Aminophylline), add water to make 30 mL, and titrate with 0.1 mol/L hydrochloric acid VS (indicator: 2 to 3 drops of bromophenol blue TS).

Each mL of 0.1 mol/L hydrochloric acid VS
= 3.0049 mg of $C_2H_8N_2$

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

Amitriptyline Hydrochloride

塩酸アミトリプチリン



$C_{20}H_{23}N.HCl$: 313.86

N-[3-(10,11-Dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-ylidene)propyl]-*N*,*N*-dimethylamine monohydrochloride [*549-18-8*]

Amitriptyline Hydrochloride, when dried, contains not less than 99.0% of $C_{20}H_{23}N.HCl$.

Description Amitriptyline Hydrochloride occurs as colorless crystals or a white to pale yellow crystalline powder. It has a bitter taste and a numbing effect.

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

The pH of a solution of Amitriptyline Hydrochloride (1 in 20) is between 4.0 and 5.0.

Identification **(1)** Dissolve 5 mg of Amitriptyline Hydrochloride in 3 mL of sulfuric acid: a red color develops. Add 5 drops of potassium dichromate TS to this solution: it turns dark brown.

(2) Acidify 1 mL of a solution of Amitriptyline Hydrochloride (1 in 500) with 0.5 mL of dilute nitric acid, and add 1 drop of silver nitrate TS: a white, opalescent precipitate is produced.

(3) Determine the absorption spectrum of a solution of Amitriptyline Hydrochloride (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Amitriptyline Hydrochloride Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

Melting point 195 - 198°C

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

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

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 0.5 g of Amitriptyline Hydrochloride, previously dried, dissolve in 50 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
= 31.387 mg of $C_{20}H_{23}N.HCl$

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

Amitriptyline Hydrochloride Tablets

塩酸アミトリプチリン錠

Amitriptyline Hydrochloride Tablets contain not