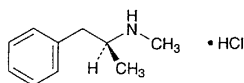


## Methamphetamine Hydrochloride

塩酸メタンフェタミン



$C_{10}H_{15}N \cdot HCl$ : 185.69

(2*S*)-*N*-Methyl-1-phenylpropan-2-amine  
monohydrochloride [51-57-0]

Methamphetamine Hydrochloride, when dried, contains not less than 98.5% of  $C_{10}H_{15}N \cdot HCl$ .

**Description** Methamphetamine Hydrochloride occurs as colorless crystals or a white, crystalline powder. It is odorless.

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

The pH of a solution of Methamphetamine Hydrochloride (1 in 10) is between 5.0 and 6.0.

**Identification (1)** To 5 mL of a solution of Methamphetamine Hydrochloride (1 in 100) add 0.5 mL of hydrogen hexachloroplatinate (IV) TS: an orange-yellow, crystalline precipitate is produced.

(2) To 5 mL of a solution of Methamphetamine Hydrochloride (1 in 100) add 0.5 mL of iodine TS: a brown precipitate is produced.

(3) To 5 mL of a solution of Methamphetamine Hydrochloride (1 in 100) add 0.5 mL of 2,4,6-trinitrophenol TS: a yellow, crystalline precipitate is produced.

(4) A solution of Methamphetamine Hydrochloride (1 in 20) responds to the Qualitative Tests for chloride.

**Optical rotation**  $[\alpha]_D^{20}$ : +16 – +19° (after drying, 0.2 g, water, 10 mL, 100 mm).

**Melting point** 171 – 175°C

**Purity (1)** Acid or alkali—Dissolve 2.0 g of Methamphetamine Hydrochloride in 40 mL of freshly boiled and cooled water, add 2 drops of methyl red TS, and use this solution as the sample solution.

(i) To 20 mL of the sample solution add 0.20 mL of 0.01 mol/L sulfuric acid VS: a red color develops.

(ii) To 20 mL of the sample solution add 0.20 mL of 0.02 mol/L sodium hydroxide VS: a yellow color develops.

(2) Sulfate—Dissolve 0.05 g of Methamphetamine Hydrochloride in 40 mL of water, add 1 mL of dilute hydrochloric acid and 1 mL of barium chloride TS, and allow to stand for 10 minutes: the solution remains unchanged.

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

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

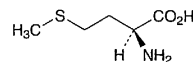
**Assay** Weigh accurately about 0.4 g of Methamphetamine Hydrochloride, previously dried, and dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3). Titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 18.570 mg of  $C_{10}H_{15}N \cdot HCl$

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

## L-Methionine

L-メチオニン



$C_5H_{11}NO_2S$ : 149.21

(2*S*)-2-Amino-4-(methylsulfanyl)butanoic acid  
[63-68-3]

L-Methionine, when dried, contains not less than 98.5% of  $C_5H_{11}NO_2S$ .

**Description** L-Methionine occurs as white crystals or crystalline powder. It has a characteristic odor.

It is freely soluble in formic acid, soluble in water, and very slightly soluble in ethanol (95).

It dissolves in dilute hydrochloric acid.

**Identification** Determine the infrared absorption spectrum of L-Methionine, previously dried, as directed in the potassium bromide 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.

**Optical rotation**  $[\alpha]_D^{20}$ : +21.0 – +25.0° (after drying, 0.5 g, 6 mol/L hydrochloric acid TS, 25 mL, 100 mm).

**pH** Dissolve 0.5 g of L-Methionine in 20 mL of water: the pH of this solution is between 5.2 and 6.2.

**Purity (1)** Clarity and color of solution—Dissolve 0.5 g of L-Methionine in 20 mL of water: the solution is clear and colorless.

(2) Chloride—Dissolve 0.5 g of L-Methionine in 20 mL of water, and add 6 mL of dilute nitric acid and water to make 40 mL. Perform the test using this solution as the test solution.

Prepare the control solution with 0.30 mL of 0.01 mol/L hydrochloric acid VS, 6 mL of dilute nitric acid and water to make 40 mL. In this test, to the test solution and the control solution add 10 mL each of silver nitrate TS (not more than 0.021%).

(3) Sulfate—Perform the test with 0.6 g of L-Methionine. Prepare the control solution with 0.35 mL of 0.005 mol/L sulfuric acid VS (not more than 0.028%).

(4) Ammonium—Perform the test with 0.25 g of L-Methionine. Prepare the control solution with 5.0 mL of Standard Ammonium Solution (not more than 0.02%).

(5) Heavy metals—Dissolve 1.0 g of L-Methionine in 40 mL of water and 2 mL of dilute acetic acid, dissolve by warming, cool, and add water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 2.0 mL of Standard Lead Solution add 2 mL of dilute acetic acid and water to make 50 mL (not more than 20 ppm).

(6) Arsenic—Transfer 1.0 g of L-Methionine to a 100-mL decomposition flask, add 5 mL of nitric acid and 2 mL of sulfuric acid, put a small funnel on the mouth of the flask, and heat carefully until white fumes are evolved. After cooling, add two 2-mL portions of nitric acid, heat, add 2-mL portions of hydrogen peroxide (30) several times, and heat until the solution becomes colorless or pale yellow. After cooling, add 2 mL of saturated ammonium oxalate monohydrate solution, and heat again until white fumes are evolved. After cooling, add water to make 5 mL, and perform the test with this solution as the test solution using Apparatus B (not more than 2 ppm).

(7) Other amino acids—Dissolve 0.10 g of L-Methionine in 10 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add water to make exactly 50 mL. Pipet 5 mL of this solution, add water to make exactly 20 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5  $\mu$ L each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. After air-drying, immediately develop the plate with a mixture of 1-butanol, water and acetic acid (100) (3:1:1) to a distance of about 10 cm, and dry the plate at 80°C for 30 minutes. Spray evenly a solution of ninhydrin in acetone (1 in 50) on the plate, and heat at 80°C for 5 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 0.30% (1 g, 105°C, 3 hours).

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

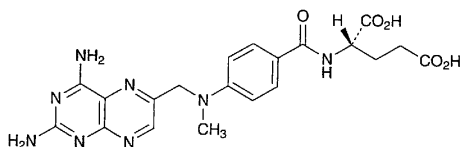
**Assay** Weigh accurately about 0.15 g of L-Methionine, previously dried, and dissolve in 3 mL of formic acid, add 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 14.921 mg of C<sub>5</sub>H<sub>11</sub>NO<sub>2</sub>S

**Containers and storage** Containers—Tight containers.

## Methotrexate

メトトレキサート



C<sub>20</sub>H<sub>22</sub>N<sub>8</sub>O<sub>5</sub>: 454.44

*N*-{4-[*N*-(2,4-Diaminopteridin-6-ylmethyl)-*N*-methylamino]-benzoyl]-L-glutamic acid [59-05-2]}

Methotrexate is a mixture of 4-amino-10-methylfolic acid and closely related compounds. It contains not less than 94.0% and not more than 102.0% of C<sub>20</sub>H<sub>22</sub>N<sub>8</sub>O<sub>5</sub>, calculated on the anhydrous basis.

**Description** Methotrexate occurs as a yellow-brown, crystalline powder.

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

It dissolves in dilute sodium hydroxide TS and in dilute sodium carbonate TS.

It is gradually affected by light.

**Identification (1)** Dissolve 1 mg of Methotrexate in 100 mL of 0.1 mol/L hydrochloric acid TS. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Methotrexate Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Methotrexate as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Methotrexate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

**Water** Take 5 mL of pyridine for water determination and 20 mL of methanol for Karl Fischer method in a dried titration flask, and titrate with water determination TS until the end point. Weigh accurately about 0.2 g of Methotrexate, immediately place in the titration flask, and add a known excess volume of Karl Fischer TS. Mix well for 30 minutes, and perform the test: the water content is not more than 12.0%.

**Residue on ignition** Not more than 0.10% (0.5 g).

**Assay** Weigh accurately about 0.025 g each of Methotrexate and Methotrexate Reference Standard, dissolve each, in the mobile phase to make exactly 250 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 10  $\mu$ L each of these solutions as directed under the Liquid Chromatography according to the following conditions, and measure the peak areas, A<sub>T</sub> and A<sub>S</sub>, of methotrexate in each solution.

Amount (mg) of C<sub>20</sub>H<sub>22</sub>N<sub>8</sub>O<sub>5</sub>  
= amount (mg) of Methotrexate Reference Standard,  
calculated on the anhydrous basis  
 $\times \frac{A_T}{A_S}$

**Operating conditions—**

**Detector:** An ultraviolet absorption photometer (wavelength: 302 nm).

**Column:** A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilylated silica gel for liquid chromatography (5 to 10  $\mu$ m in particle diameter).

**Column temperature:** Room temperature.

**Mobile phase:** A mixture of disodium hydrogenphosphate-citric acid buffer solution, pH 6.0 and acetonitrile (89:11).

**Flow rate:** Adjust the flow rate so that the retention time of methotrexate is about 8 minutes.

**Selection of column:** Dissolve 0.010 g each of Methotrexate and folic acid in 100 mL of the mobile phase.