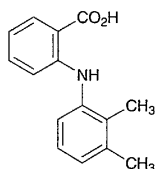


## Mefenamic Acid

メフェナム酸



$C_{15}H_{15}NO_2$ : 241.29  
2-(2,3-Dimethylphenylamino)benzoic acid [61-68-7]

Mefenamic Acid, when dried, contains not less than 99.0% of  $C_{15}H_{15}NO_2$ .

**Description** Mefenamic Acid occurs as a white to light yellow powder. It is odorless and tasteless at first, but leaves a slightly bitter aftertaste.

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

It dissolves in sodium hydroxide TS.

Melting point: about 225°C (with decomposition).

**Identification (1)** Dissolve 0.01 g of Mefenamic Acid in 1 mL of methanol by warming, cool, add 1 mL of a solution of *p*-nitrobenzene diazonium fluoroborate (1 in 1000) and 1 mL of sodium hydroxide TS, and mix thoroughly: an orange-red color is produced.

(2) Dissolve 0.01 g of Mefenamic Acid in 2 mL of sulfuric acid, and heat: the solution shows a yellow color and a green fluorescence.

(3) Dissolve 7 mg of Mefenamic Acid in a solution of hydrochloric acid in methanol (1 in 1000) to make 500 mL. Determine the absorption spectrum of the solution 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.

**Purity (1) Chloride**—To 1.0 g of Mefenamic Acid add 20 mL of sodium hydroxide TS, and dissolve by warming. Cool, add 2 mL of acetic acid (100) and water to make 100 mL, and mix well. Remove the produced precipitate by filtration, discard the first 10 mL of the filtrate, and to subsequent 25 mL of the filtrate add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.50 mL of 0.01 mol/L hydrochloric acid VS add 5 mL of sodium hydroxide TS, 0.5 mL of acetic acid (100), 6 mL of nitric acid and water to make 50 mL (not more than 0.071%).

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

(3) Arsenic—Prepare the test solution with 1.0 g of Mefenamic Acid according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.10 g of Mefenamic Acid, in 5 mL of a mixture of chloroform and methanol

(3:1), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of chloroform and methanol (3:1) to make exactly 200 mL, pipet 10 mL of this solution, add a mixture of chloroform and methanol (3:1) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 25  $\mu$ 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 a mixture of 2-methyl-1-propanol and ammonia solution (28) (3:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): 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, phosphorus (V) oxide, 4 hours).

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

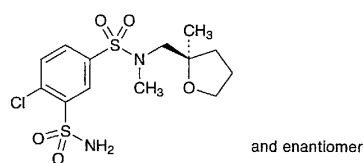
**Assay** Weigh accurately about 0.5 g of Mefenamic Acid, previously dried, and dissolve in 100 mL of ethanol (95), previously neutralized to phenol red TS with 0.1 mol/L sodium hydroxide VS, by warming gently. Cool, and titrate with 0.1 mol/L sodium hydroxide VS until the color of the solution changes from yellow through yellow-red to red-purple (indicator: 2 to 3 drops of phenol red TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L sodium hydroxide VS  
= 24.129 mg of  $C_{15}H_{15}NO_2$

**Containers and storage** Containers—Well-closed containers.

## Mefruside

メフルシド



and enantiomer

$C_{13}H_{19}ClN_2O_5S_2$ : 382.88  
4-Chloro-*N*-methyl-*N*-[(*RS*)-2-methyltetrahydrofuran-2-ylmethyl]-3-sulfamoylbenzenesulfonamide [7195-27-9]

Mefruside, when dried, contains not less than 98.5% of  $C_{13}H_{19}ClN_2O_5S_2$ .

**Description** Mefruside occurs as a white crystalline powder.

It is very soluble in dimethylformamide, freely soluble in acetone, soluble in methanol, sparingly soluble in ethanol (95), and practically insoluble in water.

A solution of Mefruside in dimethylformamide (1 in 10) has no optical rotation.

**Identification (1)** Determine the absorption spectrum of a solution of Mefruside in methanol (1 in 40,000) as directed under the Ultraviolet-visible Spectrophotometry, and com-

pare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Mefruside, 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.

(3) Perform the test with Mefruside as directed under the Flame Coloration Test (2): a green color appears.

**Melting point** 149 – 152°C

**Purity** (1) Heavy metals—Dissolve 1.0 g of Mefruside in 30 mL of acetone, and add 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 2.0 mL of Standard Lead Solution add 30 mL of acetone, 2 mL of dilute acetic acid and water to make 50 mL (not more than 20 ppm).

(2) Arsenic—Prepare the test solution with 1.0 g of Mefruside according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(3) Related substances—Dissolve 0.20 g of Mefruside in 10 mL of acetone, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add acetone to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10  $\mu$ 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 a mixture of chloroform and acetone (5:2) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): 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, 105°C, 2 hours).

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

**Assay** Weigh accurately about 0.5 g of Mefruside, previously dried, dissolve in 80 mL of *N,N*-dimethylformamide, and titrate with 0.1 mol/L tetramethylammonium hydroxide VS (potentiometric titration). Separately, perform a blank determination with a solution prepared by adding 13 mL of water to 80 mL of *N,N*-dimethylformamide, and make any necessary correction.

Each mL of 0.1 mol/L tetramethylammonium hydroxide VS  
= 38.289 mg of  $C_{13}H_{19}ClN_2O_5S_2$

**Containers and storage** Containers—Well-closed containers.

## Mefruside Tablets

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Mefruside Tablets contain not less than 95% and not more than 105% of the labeled amount of mefruside

( $C_{13}H_{19}ClN_2O_5S_2$ ; 382.88).

**Method of preparation** Prepare as directed under Tablets, with Mefruside.

**Identification** (1) Weigh a quantity of powdered Mefruside Tablets, equivalent to 0.3 g of Mefruside according to the labeled amount, shake with 15 mL of heated methanol for 20 minutes, and filter. Add 25 mL of water to the filtrate, and allow to stand while ice-cooling for 30 minutes. Filter the white precipitate formed, wash with water, and dry at 105°C for 2 hours: the precipitate melts between 149°C and 152°C.

(2) Weigh a quantity of powdered Mefruside Tablets, equivalent to 0.01 g of Mefruside according to the labeled amount, shake with 70 mL of methanol strongly for 15 minutes, add methanol to make 100 mL, and filter. Determine the absorption spectrum of the filtrate as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 274 nm and 278 nm, and between 283 nm and 287 nm.

**Dissolution test** Perform the test with 1 tablet of Mefruside Tablets at 50 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of water as the test solution. Take 20 mL or more of the dissolved solution 45 minutes after starting the test, and filter through a filter paper for quantitative analysis (5C). Discard the first 5 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.070 g of mefruside for assay, previously dried at 105°C for 2 hours, dissolve in methanol to make exactly 50 mL. Pipet 2 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances,  $A_T$  and  $A_S$ , of the sample solution and the standard solution at 285 nm in a layer of 5 cm in length as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Mefruside Tablets in 45 minutes is not less than 85%.

Dissolution rate (%) with respect to the labeled amount of mefruside ( $C_{13}H_{19}ClN_2O_5S_2$ )

$$= W_s \times \frac{A_T}{A_S} \times \frac{1}{C} \times 36$$

$W_s$ : Amount (mg) of mefruside for assay.

$C$ : Labeled amount (mg) of mefruside ( $C_{13}H_{19}ClN_2O_5S_2$ ) in 1 tablet.

**Assay** Weigh accurately not less than 20 Mefruside Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 0.065 g of mefruside ( $C_{13}H_{19}ClN_2O_5S_2$ ), shake with 70 mL of methanol for 15 minutes, then add methanol to make exactly 100 mL, and filter. Discard the first 20 mL of the filtrate, take exactly 10 mL of the subsequent filtrate, add methanol to make exactly 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.065 g of mefruside for assay, previously dried at 105°C for 2 hours, and dissolve in methanol to make exactly 100 mL. Pipet 10 mL of this solution, add methanol to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances,  $A_T$  and  $A_S$ , of the sample solution and the standard solution at 285 nm as directed under the Ultraviolet-visible Spectrophotometry.