Column temperature: A constant temperature of about 35°C.

Mobile phase: Diluted methanol (7 in 10).

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

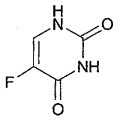
Selection of column: Proceed with 20 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of fluorometholone and the internal standard in this order with the resolution between these peaks being not less than 4.

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Fluorouracil

フルオロウラシル



$C_4H_3FN_2O_2$: 130.08

5-Fluoropyrimidine-2,4(1*H*,3*H*)-dione [*51-21-8*]

Fluorouracil, when dried, contains not less than 98.5% of $C_4H_3FN_2O_2$, and not less than 13.1% and not more than 16.1% of fluorine (F: 19.00).

Description Fluorouracil occurs as white crystals or crystalline powder. It is odorless.

It is freely soluble in *N,N*-dimethylformamide, sparingly soluble in water, slightly soluble in ethanol (95), and practically insoluble in diethyl ether.

Melting point: about 282°C (with decomposition).

Identification (1) Add 0.2 mL of bromine TS to 5 mL of a solution of Fluorouracil (1 in 500): the color of bromine TS is discharged. Further add 2 mL of barium hydroxide TS: a purple precipitate is formed.

(2) Determine the absorption spectrum of a solution of Fluorouracil in 0.1 mol/L hydrochloric acid TS (1 in 100,000) 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.

(3) Proceed with 0.01 g of Fluorouracil as directed under the Oxygen Flask Combustion Method, using a mixture of 0.5 mL of 0.01 mol/L sodium hydroxide TS and 20 mL of water as the absorbing liquid. After combustion is completed, shake well to absorb the gas evolved: the solution responds to the Qualitative Tests for fluoride.

Purity (1) Clarity and color of solution—Add 20 mL of water to 0.20 g of Fluorouracil, and dissolve by warming: the solution is clear and colorless.

(2) Fluoride—Dissolve 0.10 g of Fluorouracil in 10.0 mL of diluted 0.01 mol/L sodium hydroxide TS (1 in 20). Transfer 5.0 mL of this solution to a 20-mL volumetric flask, add 10 mL of a mixture of alizarin complexone TS, acetic acid-potassium acetate buffer solution, pH 4.3, and cerium (III) nitrate TS (1:1:1), and add water to make 20 mL. Allow to stand for 1 hour, and use this solution as the sample solution. Separately, transfer 1.0 mL of Standard Fluorine Solution to a 20-mL volumetric flask, add 5.0 mL of diluted 0.01 mol/L sodium hydroxide TS (1 in 20), and add 10 mL of a mixture of alizarin complexone TS, acetic acid-potassium acetate buffer solution, pH 4.3, and cerium (III) nitrate TS (1:1:1). Proceed in the same manner as directed for the preparation of the sample solution, and use this solution as the standard solution. Perform the test as directed under the Ultraviolet-visible Spectrophotometry, using a solution, prepared with 5.0 mL of diluted 0.01 mol/L sodium hydroxide TS (1 in 20) in the same manner, as the blank: the absorbance of the sample solution at 600 nm is not larger than that of the standard solution (not more than 0.012%).

(3) Heavy metals—Proceed with 1.0 g of Fluorouracil 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) Arsenic—To 1.0 g of Fluorouracil in a crucible add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 10), ignite the ethanol to burn, and incinerate by strong heating at 750°C to 850°C. If a carbonized substance remains in this method, moisten with a small amount of nitric acid, and incinerate by strong heating. Cool, add 10 mL of dilute hydrochloric acid to the residue, dissolve it by warming on a water bath, use this solution as the test solution, and perform the test using Apparatus B (not more than 2 ppm).

(5) Related substances—Dissolve 0.10 g of Fluorouracil in 10 mL of water, and use this solution as the sample solution. Measure exactly 1 mL of this solution, add water 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 μL 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 ethyl acetate, acetone and water (7:4:1) to a distance of about 12 cm, air-dry the plate, and 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, 80°C, 4 hours).

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

Assay (1) Fluorouracil—Weigh accurately about 0.2 g of Fluorouracil, previously dried, dissolve in 20 mL of *N,N*-dimethylformamide, and titrate with 0.1 mol/L tetramethylammonium hydroxide VS until the color of the solution changes from yellow through blue-green to blue (indicator: 3 drops of thymol blue-dimethylformamide TS). Perform a blank determination.

Each mL of 0.1 mol/L tetramethylammonium hydroxide VS
= 13.008 mg of $C_4H_3FN_2O_2$

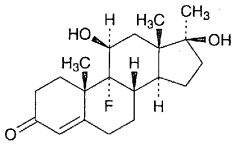
(2) Fluorine—Weigh accurately about 4 mg of Fluorouracil, previously dried, and proceed as directed in the determination of fluorine under the Oxygen Flask Combustion Method, using a mixture of 0.5 mL of 0.01 mol/L

sodium hydroxide TS and 20 mL of water as the absorbing liquid.

Containers and storage Containers—Tight containers.

Fluoxymesterone

フルオキシメステロン



$C_{20}H_{29}FO_3$: 336.44

9-Fluoro-11β,17β-dihydroxy-17-methylandrost-4-en-3-one [*76-43-7*]

Fluoxymesterone, when dried, contains not less than 97.0% and not more than 102.0% of $C_{20}H_{29}FO_3$.

Description Fluoxymesterone occurs as white crystals or crystalline powder. It is odorless.

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

Identification (1) Dissolve 5 mg of Fluoxymesterone in 2 mL of sulfuric acid: a yellow color develops.

(2) Prepare the test solution with 0.01 g of Fluoxymesterone as directed under the Oxygen Flask Combustion Method, using a mixture of 0.5 mL of 0.01 mol/L sodium hydroxide TS and 20 mL of water as an absorbing liquid: the test solution responds to the Qualitative Tests (2) for fluoride.

(3) Determine the absorption spectrum of a solution of Fluoxymesterone in ethanol (95) (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 Fluoxymesterone Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(4) Determine the infrared absorption spectrum of Fluoxymesterone, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of previously dried Fluoxymesterone Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears between the spectra, dissolve Fluoxymesterone and Fluoxymesterone Reference Standard in ethanol (99.5), respectively, then evaporate the ethanol to dryness, and repeat the test on the residues.

Optical rotation $[\alpha]_D^{20}$: +104 – +112° (after drying, 0.1 g, ethanol (95), 10 mL, 100 mm).

Purity (1) Heavy metals—Proceed with 0.5 g of Fluoxymesterone according to Method 2, and perform the test. Prepare the control solution with 1.5 mL of Standard Lead Solution (not more than 30 ppm).

(2) Other steroids—Dissolve 0.03 g of Fluoxymesterone in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample 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 10 μL 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 toluene, ethanol (95) and ethyl acetate (3:1:1) to a distance of about 12 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 1.0% (1 g, 105°C, 3 hours).

Residue on ignition Not more than 0.2% (0.5 g, platinum crucible).

Assay Weigh accurately about 0.025 g each of Fluoxymesterone and Fluoxymesterone Reference Standard, previously dried, dissolve each in the internal standard solution to make exactly 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10 μL 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 fluoxymesterone to that of the internal standard, respectively.

$$\text{Amount (mg) of fluoxymesterone } (C_{20}H_{29}FO_3) = \text{amount (mg) of Fluoxymesterone Reference Standard} \times \frac{Q_T}{Q_S}$$

Internal standard solution—A solution of methylprednisolone in a mixture of chloroform and methanol (19:1) (1 in 5000).

Operating conditions—

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

Column: A stainless steel column 4.6 mm in inside diameter and 30 cm in length, packed with silica gel for liquid chromatography (5 μm in particle diameter).

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

Mobile phase: A mixture of *n*-butyl chloride, water-saturated *n*-butyl chloride, tetrahydrofuran, methanol and acetic acid (100) (95:95:14:7:6).

Flow rate: Adjust the flow rate so that the retention time of fluoxymesterone is about 9 minutes.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, fluoxymesterone and the internal standard are eluted in this order with the resolution between these peaks being not less than 6.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of fluoxymesterone to that of the internal standard is not more than 1.5%.

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.