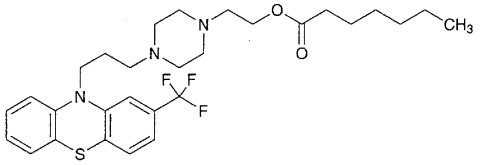
Fluphenazine Enanthate

エナント酸フルフェナジン



$C_{29}H_{38}F_3N_3O_2S$: 549.69
2-(4-{3-[2-(Trifluoromethyl)phenothiazin-10-yl]propyl}piperazin-1-yl)ethyl heptanoate [*2746-81-8*]

Fluphenazine Enanthate, when dried, contains not less than 98.5% of $C_{29}H_{38}F_3N_3O_2S$.

Description Fluphenazine Enanthate is a light yellow to yellowish orange viscous liquid. It is generally clear, and can be opaque by producing crystals.

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

Identification (1) Prepare the test solution with 0.01 g of Fluphenazine Enanthate 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: the test solution responds to the Qualitative Tests for fluoride.

(2) Dissolve 2 mg of Fluphenazine Enanthate in 200 mL of a solution of hydrochloric acid in methanol (17 in 2000). 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.

(3) Determine the infrared absorption spectrum of Fluphenazine Enanthate as directed in the liquid firm 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.

Purity (1) Heavy metals—Proceed with 1.0 g of Fluphenazine Enanthate according to Method 2, and perform the test. Prepare the control solution with 3.0 mL of Standard Lead Solution (not more than 30 ppm).

(2) Related substances—Dissolve 0.25 g of Fluphenazine Enanthate 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 20 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 acetone, hexane and ammonia solution (28) (16:6:1) to a distance of about 15 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. Then spray evenly diluted sulfuric acid (1 in 2) on the plate: 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, in vacuum, 60°C, 3 hours).

Residue on ignition Not more than 0.20% (1 g).

Assay Weigh accurately about 0.5 g of Fluphenazine Enanthate, previously dried, dissolve in 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (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
= 27.485 mg of $C_{29}H_{38}F_3N_3O_2S$

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

Flurazepam

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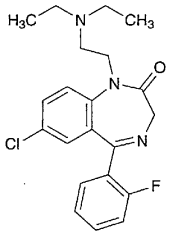

$C_{21}H_{23}ClFN_3O$: 387.88
7-Chloro-1-[2-(diethylamino)ethyl]-5-(2-fluorophenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one [*17617-23-1*]

Flurazepam, when dried, contains not less than 99.0% of $C_{21}H_{23}ClFN_3O$.

Description Flurazepam occurs as white to light yellow crystals or crystalline powder.

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

Identification (1) Dissolve 0.01 g of Flurazepam in 3 mL of sulfuric acid: the solution shows a greenish yellow fluorescence under ultraviolet light (main wavelength: 365 nm).

(2) Dissolve 0.01 g of Flurazepam in 3 mL of citric acid-acetic acid TS, and heat in a water bath for 4 minutes: a dark red color develops.

(3) Prepare the test solution with 0.01 g of Flurazepam 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.

(4) Determine the absorption spectrum of a solution of Flurazepam in methanol (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, determine the absorption spectrum of a

solution of Flurazepam in methanol (1 in 10,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 2: both spectra exhibit similar intensities of absorption at the same wavelengths.

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

Melting point 79 - 83°C

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Flurazepam in 10 mL of ethanol (95): the solution is clear and colorless to light yellow.

(2) Chloride—Dissolve 1.0 g of Flurazepam in 50 mL of diethyl ether, add 46 mL of water and 4 mL of sodium carbonate TS, shake, separate the water layer, wash with two 20-mL portions of diethyl ether, and filter the water layer. Neutralize 20 mL of the filtrate with dilute nitric acid, and 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 with 0.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.036%).

(3) Sulfate—Neutralize 20 mL of the filtrate obtained in (2) with dilute hydrochloric acid, and add 1 mL of dilute hydrochloric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.048%).

(4) Heavy metals—Proceed with 2.0 g of Flurazepam 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).

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

(6) Related substances—Dissolve 0.20 g of Flurazepam in 20 mL of chloroform, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add chloroform to make exactly 20 mL. Pipet 3 mL of this solution, add chloroform 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 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 cyclohexane, acetone and ammonia solution (28) (60:40:1) 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 0.20% (1 g, in vacuum, 60°C, 2 hours).

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

Assay Weigh accurately about 0.3 g of Flurazepam, previously dried, dissolve in 50 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS to the second equivalence point (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 19.394 mg of $C_{21}H_{23}ClFN_3O$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Flurazepam Capsules

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Flurazepam Capsules contain not less than 93% and not more than 107% of the labeled amount of flurazepam ($C_{21}H_{23}ClFN_3O$: 387.88).

Method of preparation Prepare as directed under Capsules, with Flurazepam.

Identification **(1)** Powder the contents of Flurazepam Capsules. To a quantity of the powder, equivalent to 0.1 g of Flurazepam according to the labeled amount, add 100 mL of 0.1 mol/L hydrochloric acid TS, stir, and filter. To 40 mL of the filtrate add 80 mL of a solution of sodium hydroxide (1 in 250) and 100 mL of hexane, extract by shaking well, and use the hexane layer as the sample solution. Evaporate 25 mL of the sample solution on a water bath to dryness. Dissolve the residue in 3 mL of sulfuric acid: the solution shows a greenish yellow fluorescence under ultraviolet light.

(2) Evaporate 25 mL of the sample solution obtained in (1) on a water bath to dryness. Dissolve the residue in 3 mL of citric acid-acetic acid TS, and heat in a water bath for 4 minutes: a dark red color develops.

(3) Determine the absorption spectrum of the sample solution obtained in the Assay as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 315 nm and 319 nm, and a minimum between 297 nm and 301 nm.

Assay Weigh accurately the contents of not less than 20 Flurazepam Capsules, and powder the combined contents. Weigh accurately a portion of the powder, equivalent to about 0.05 g of flurazepam ($C_{21}H_{23}ClFN_3O$), add 30 mL of methanol, stir well for 10 minutes, and add methanol to make exactly 50 mL. Filter this solution, discard the first 20 mL of the filtrate, pipet 6 mL of the subsequent filtrate, add methanol to make exactly 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of flurazepam for assay, previously dried in vacuum at 60°C for 2 hours, and dissolve in methanol to make exactly 50 mL. Pipet 6 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 317 nm as directed under the Ultraviolet-visible Spectrophotometry.

Amount (mg) of flurazepam ($C_{21}H_{23}ClFN_3O$)
= amount (mg) of flurazepam for assay
$\times \frac{A_T}{A_S}$

Containers and storage Containers—Tight containers.