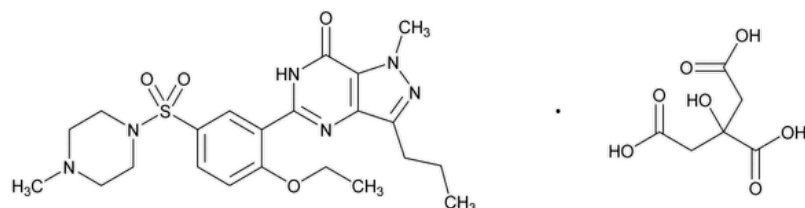


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Sildenafil Citrate



$C_{22}H_{30}N_6O_4S \cdot C_6H_8O_7$ 666.70

Piperazine, 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxyphenyl]sulfonyl]-4-methyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1);

1-[[3-(6,7-Dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxyphenyl]sulfonyl]-4-methylpiperazine citrate (1:1) CAS RN®: 171599-83-0; UNII: BW9B0ZE037.

Sildenafil

$C_{22}H_{30}N_6O_4S$ 474.58 CAS RN®: 139755-83-2; UNII: 3M70B98Y7H.

DEFINITION

Sildenafil Citrate contains NLT 98.0% and NMT 102.0% of sildenafil citrate ($C_{22}H_{30}N_6O_4S \cdot C_6H_8O_7$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

- A. [▲SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K▲](#) (CN 1-MAY-2020)

ASSAY

• PROCEDURE

Buffer: Dilute 7 mL of triethylamine with water to 1 L. Stir, and adjust with phosphoric acid to a pH of 3.0 ± 0.1 .

Mobile phase: Buffer, methanol, and acetonitrile (58:25:17)

Standard solution: 0.028 mg/mL of [USP Sildenafil Citrate RS](#) in Mobile phase

Sample solution: 0.028 mg/mL of Sildenafil Citrate in Mobile phase

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 290 nm

Column: 3.9-mm × 15-cm; 5-μm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection size: 20 μL

System suitability

Sample: Standard solution

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 0.85% for six replicate injections

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of sildenafil citrate ($C_{22}H_{30}N_6O_4S \cdot C_6H_8O_7$) in the portion of the sample taken.



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$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of sildenafil from the *Sample solution*

r_S = peak response of sildenafil from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

C_U = concentration of the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#)

Sample: NLT 0.5 g

Acceptance criteria: NMT 0.1%

• LIMIT OF IMIDAZOLE

Diluent: Methanol, water, and ammonium hydroxide (15:5:1)

Standard solution 1: 0.035 mg/mL of [USP Imidazole RS](#) in *Diluent*

Standard solution 2: 0.0175 mg/mL of [USP Imidazole RS](#) in *Diluent* from *Standard solution 1*

Sample solution: 17.5 mg/mL of Sildenafil Citrate in *Diluent*

System suitability solution: Mix equal volumes of *Sample solution* and *Standard solution 1*.

Chromatographic system

(See [Chromatography \(621\)](#), [Thin-Layer Chromatography](#).)

Mode: TLC

Adsorbent: 0.2-mm layer of chromatographic silica gel mixture with a particle size of 2–10 µm (HPTLC plates)

Application volume: 10 µL. [NOTE—Apply as 6-mm bands.]

Developing solvent system: Methylene chloride, ethyl acetate, alcohol, and ammonium hydroxide (50:30:20:1)

System suitability

Sample: *System suitability solution*

Suitability requirements: The chromatogram shows two clearly separated zones.

Analysis:

Samples: *Standard solution 2* and *Sample solution*

Develop the plate over a distance of about two-thirds of the length of the plate. Dry at 100° for about 15 min, and cool. Expose the plate to iodine vapor until the plate is light brown, and examine the plate under UV light at 254 nm. [NOTE—The retardation factors for citrate, imidazole, and sildenafil are about 0, 0.25, and 0.4, respectively.]

Acceptance criteria: Any spot corresponding to imidazole in the *Sample solution* is not more intense than the principal spot from *Standard solution 2* (0.1%).

• ORGANIC IMPURITIES

Buffer, Mobile phase, and Chromatographic system: Proceed as directed in the Assay, except to run the chromatograph for 3 times the retention time of sildenafil.

Identification solution: 7.5 µg/mL of [USP Sildenafil Related Compound A RS](#) in *Mobile phase*

System suitability solution: Dissolve 70 mg of Sildenafil Citrate in 1 mL of a solution of hydrogen peroxide and anhydrous formic acid (2:1).

Allow to stand for at least 10 min to generate sildenafil *N*-oxide, and then dilute with *Mobile phase* to 250 mL.

Sample solution: 0.7 mg/mL of Sildenafil Citrate in *Mobile phase*

Diluted sample solution: 1.4 µg/mL of sildenafil citrate in *Mobile phase* from the *Sample solution*

Sensitivity solution: 0.35 µg/mL of sildenafil citrate in *Mobile phase* from the *Diluted sample solution*

System suitability

Samples: *Diluted sample solution*, *Sensitivity solution*, and *System suitability solution*

[NOTE—The relative retention times for sildenafil, sildenafil *N*-oxide, and sildenafil related compound A are about 1.0, 1.2, and 1.7, respectively.]

Suitability requirements

Resolution: NLT 2.5 between sildenafil *N*-oxide and sildenafil, *System suitability solution*

Tailing factor: NMT 1.5 for the sildenafil peak, *Diluted sample solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Identification solution*, *Diluted sample solution*, and *Sample solution*

[NOTE—Identify sildenafil related compound A from the *Identification solution*.]