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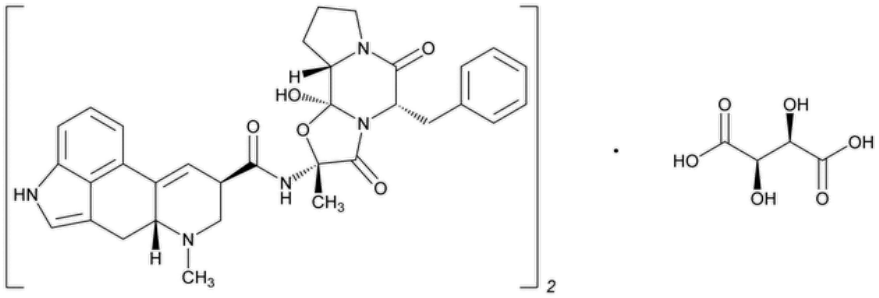
Ergotamine Tartrate



$(C_{33}H_{35}N_5O_5)_2 \cdot C_4H_6O_6$ 1313.41

Ergotaman-3',6',18-trione, 12'-hydroxy-2'-methyl-5'-(phenylmethyl)-, (5'α)-,[*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (2:1) (salt);

Ergotamine tartrate (2:1) (salt) CAS RN®: 379-79-3; UNII: MRU5XH3B48.

DEFINITION

Ergotamine Tartrate contains NLT 97.0% and NMT 100.5% of ergotamine tartrate $[(C_{33}H_{35}N_5O_5)_2 \cdot C_4H_6O_6]$, calculated on the dried basis.

IDENTIFICATION

• **A.** The chromatogram of the *Sample solution* prepared as directed in the test for *Related Alkaloids*, exhibits its principal fluorescent spot and principal blue spot at the same R_F values as the corresponding principle spots of the *Standard solution*.

ASSAY

• **Procedure**

Diluent: Acetic anhydride and glacial acetic acid (6:100)

Sample: 200 mg of Ergotamine Tartrate

Titrimetric system

Mode: Direct titration

Titrant: 0.05 N perchloric acid VS

Blank: 15 mL of *Diluent*

Endpoint detection: Visual

Analysis

Samples: *Sample* and *Blank*

Dissolve the *Sample* in 15 mL of *Diluent.* Add 1 drop of crystal violet TS, and titrate with *Titrant* from a 10-mL buret. Perform a blank determination, and make any necessary correction. Each mL of 0.05 N perchloric acid is equivalent to 32.84 mg of ergotamine tartrate $[(C_{33}H_{35}N_5O_5)_2 \cdot C_4H_6O_6]$.

Acceptance criteria: 97.0%–100.5% on the dried basis

IMPURITIES

• **Related Alkaloids**

Conduct this test without exposure to daylight and with the minimum necessary exposure to artificial light.

Solution A: A mixture of 5.5 mL of hydrochloric acid and 4.5 mL of water

Diluent: Chloroform and methanol (90:10)

Standard solution: 10 mg/mL of USP Ergotamine Tartrate RS in *Diluent*

Diluted standard solutions: USP Ergotamine Tartrate RS from the *Standard solution* diluted with *Diluent* as listed in *Table 1*

Table 1

Diluted standard solution	Concentration (mg/mL)	Percentage (%, for comparison with Sample)
A	0.2	2.0
B	0.1	1.0
C	0.05	0.5
D	0.025	0.25

Sample solution: 10 mg/mL of Ergotamine Tartrate in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel

Application volume: 5 µL

Developing solvent system: Ether, dimethylformamide, chloroform, and dehydrated alcohol (70:15:10:5)

Spray reagent: 200 mg of *p*-(dimethylamino)benzaldehyde in *Solution A*. Use a freshly prepared solution.

Analysis

Samples: *Standard solution*, *Diluted standard solutions*, and *Sample solution*

Line the chamber with filter paper, and allow it to equilibrate for 15 min. Place each spot over an opened bottle of ammonium hydroxide for 20 s, then allow the plate to dry in a current of cold air for 20 s. Develop the chromatogram until the solvent front has moved about 17 cm. Remove the plate from the developing chamber, allow the solvent to evaporate in a current of cold air for approximately 2 min, and spray with *Spray reagent*. Dry the plate at 60° for about 5 min, and compare the chromatograms.

Acceptance criteria: The R_F value of the principal spot from the *Sample solution* corresponds to that from the *Standard solution*; the sum of the intensities of any secondary spots from the *Sample solution* is NMT the intensity of the principal spot from *Diluted standard solution A*; and the intensity of NMT one of the secondary spots is greater than that of the principal spot from *Diluted standard solution B*.

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation*⟨781S⟩

Solution A: 10 g/L of tartaric acid in water

Solution B: Use chloroform from which any alcohol present has been removed by prior washing with water

Sample solution A: Dissolve 350 mg of Ergotamine Tartrate in 25 mL of *Solution A* contained in a separator, then add 500 mg of sodium bicarbonate, and mix gently but thoroughly. Add 10 mL of *Solution B*, and shake vigorously. After the layers have separated, draw off the chloroform phase through a small filter, previously moistened with *Solution B*, into a 50-mL volumetric flask. Rapidly continue the extraction with three 10-mL portions of *Solution B*, passing the extracts through the same filter. Place the flask in a bath at 20° for 10 min. Dilute with *Solution B* at 20° to 50.0 mL.

Sample solution B: Evaporate a 25.0-mL aliquot of *Sample solution A* on a rotary evaporator to dryness, maintaining the temperature of the bath below 45°. Dissolve the residue in 25 mL of glacial acetic acid.

Titrimetric system

Mode: Direct titration

Titrant: 0.05 N perchloric acid VS

Blank: 25 mL of glacial acetic acid

Endpoint detection: Visual

Analysis

Samples: *Sample solution A*, *Sample solution B*, and *Blank*

Add 1 drop of crystal violet TS to *Sample solution B*, and titrate with 0.05 N perchloric acid VS to an emerald-green endpoint. Perform a blank determination, make any necessary correction, and calculate the concentration of the ergotamine base. Each mL of 0.05 N perchloric acid is equivalent to 29.08 mg of ergotamine ($C_{33}H_{35}N_5O_5$).

Determine the specific rotation of the ergotamine base from the angular rotation at 20° of *Sample solution A* and the concentration of the ergotamine base.

Acceptance criteria: −155° to −165°

- **Loss on Drying** ⟨731⟩

Sample: 100 mg of Ergotamine Tartrate

Analysis: Dry the *Sample* under vacuum at 60° for 4 h.

Acceptance criteria: NMT 5.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed, light-resistant containers in a cold place.
- **USP Reference Standards** ⟨11⟩

  USP Ergotamine Tartrate RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ERGOTAMINE TARTRATE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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