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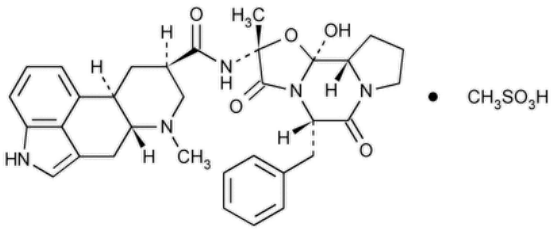
Dihydroergotamine Mesylate



$C_{33}H_{37}N_5O_5 \cdot CH_4O_3S$ 679.78

Ergotaman-3',6',18-trione, 9,10-dihydro-12'-hydroxy-2'-methyl-5'-(phenylmethyl)-, (5'α)-, monomethanesulfonate (salt).

Dihydroergotamine monomethanesulfonate CAS RN®: 6190-39-2; UNII: 81AXN7R2QT.

» Dihydroergotamine Mesylate contains not less than 97.0 percent and not more than 103.0 percent of $C_{33}H_{37}N_5O_5 \cdot CH_4O_3S$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed, light-resistant containers.

USP Reference standards ⟨11⟩—

USP Dihydroergotamine Mesylate RS

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests ⟨197⟩, Infrared Spectroscopy: 197K*▲ (CN 1-May-2020) ·

Change to read:

B: ▲*Spectroscopic Identification Tests ⟨197⟩, Ultraviolet-Visible Spectroscopy: 197U*▲ (CN 1-May-2020) —

Solution: 50 µg per mL.

Medium: 70% alcohol.

Absorptivities at 280 nm, calculated on the dried basis, do not differ by more than 3.0%.

C: The principal spot from the *Test preparation* found in the test for *Related alkaloids* corresponds in R_F value to that obtained from the *Standard preparation*.

Specific rotation ⟨781S⟩**:** between −16.7° and −22.7°.

Test solution: 25 mg per mL, in a mixture of chloroform, alcohol, and ammonium hydroxide (10:10:1).

pH ⟨791⟩**:** between 4.4 and 5.4, in a solution (1 in 1000).

Loss on drying ⟨731⟩—Dry it in vacuum at 100° to constant weight: it loses not more than 4.0% of its weight.

Related alkaloids—

Solvent mixture—Mix 10 volumes of chloroform, 10 volumes of methanol, and 1 volume of ammonium hydroxide.

Test solution—Prepare a solution of Dihydroergotamine Mesylate in *Solvent mixture* to contain 20 mg per mL.

Standard solution and *Standard dilutions*—Prepare a solution of USP Dihydroergotamine Mesylate RS in *Solvent mixture* to contain 20 mg per mL *(Standard solution)*. Prepare a series of dilutions of the *Standard solution* in *Solvent mixture* to contain 0.40 mg, 0.20 mg, and 0.10 mg per mL *(Standard dilutions)*.

Procedure—In a suitable chromatographic chamber arranged for thin-layer chromatography place a volume of a solvent system consisting of a mixture of chloroform and alcohol (9:1) sufficient to develop the chromatogram, cover, and allow to equilibrate for 30 minutes. Apply 5-µL portions of the *Test solution,* the *Standard solution,* and each of the three *Standard dilutions* to a suitable thin-layer chromatographic plate coated with a 0.25-mm layer of chromatographic silica gel. Allow the spots to dry, and develop the chromatogram until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots on the plate by lightly spraying with a solution prepared by dissolving 800 mg of *p*-dimethylaminobenzaldehyde in a cooled mixture of 80 g of alcohol and 20 g of sulfuric acid. The R_F value of the principal spot obtained from the *Test solution* corresponds to that obtained from the *Standard solution*. Estimate the concentration of any other spots observed in the lane for the *Test solution* by comparison with the *Standard dilutions*. The spots from the 0.40-, 0.20-, and 0.10-mg-per-mL dilutions are equivalent to 2.0%, 1.0%, and 0.50% of impurities, respectively. The sum of the impurities is not greater than 2.0%.

Change to read:

Assay—

Diluent 1—Prepare a solution of 0.1 mL of phosphoric acid in 1000 mL of water.

▲▲ (ERR 1-May-2020)

Solution A—Prepare a filtered and degassed mixture of water, 25 percent ammonia water, and 98% formic acid (1000:10:5). Adjust the pH to 8.50.

Solution B—Prepare a filtered and degassed mixture of acetonitrile and *Solution A* (80:20).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments to either solution as necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Dihydroergotamine Mesylate RS in acetonitrile, and dilute quantitatively, and stepwise if necessary, with *Diluent 1* to obtain a solution having a known concentration of about 0.6 mg per mL. [NOTE—The final ratio of acetonitrile and *Diluent 1* should be similar to the final ratio obtained in the *Assay preparation*.]

Assay preparation—Transfer about 30 mg of Dihydroergotamine Mesylate, accurately weighed, to a 50-mL volumetric flask, dissolve in 20 mL of acetonitrile, dilute with *Diluent 1* to volume, and mix.

Chromatographic system (see *CHROMATOGRAPHY* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and 4.0-mm × 25-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	Solution A (%)	Solution B (%)	Elution
0	60	40	equilibration
0–12	60→50	40→50	linear gradient
12–20	50→15	50→85	linear gradient
20–24	15	85	isocratic
24–25	15→60	85→40	linear gradient
25–31	60	40	re-equilibration

Chromatograph the *Standard preparation,* and record the peak areas as directed for *Procedure:* the tailing factor is between 0.8 and 1.5; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the analyte peaks. Calculate the quantity, in mg, of $C_{33}H_{37}N_5O_5 \cdot CH_4O_3S$ in the portion of Dihydroergotamine Mesylate taken by the formula:

$$50C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Dihydroergotamine Mesylate RS in the *Standard preparation;* and r_U and r_S are the peak areas obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
DIHYDROERGOTAMINE MESYLATE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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