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Ergotamine Tartrate and Caffeine Suppositories

DEFINITION

Ergotamine Tartrate and Caffeine Suppositories contain NLT 90.0% and NMT 110.0% of the labeled amounts of ergotamine tartrate $[(C_{33}H_{35}N_5O_5)_2 \cdot C_4H_6O_6]$ and caffeine ($C_8H_{10}N_4O_2$).

IDENTIFICATION

• **A.**

Solution A: 10 mg/mL of tartaric acid in water

Sample solution: Melt 1 Suppository in 10 mL of hot *Solution A*. Chill the mixture until the layer of oil has hardened, then filter, divide the filtrate into two parts, and use one part. Reserve the other part of this filtrate for use in *Identification* test *B*.

Analysis

Sample: *Sample solution*

To one portion of the *Sample solution*, add 10 mL of *p*-dimethylaminobenzaldehyde TS.

Acceptance criteria: A blue color develops (presence of ergotamine).

• **B.**

Sample solution: Use the remaining portion of the *Sample solution* from *Identification* test *A*.

Analysis

Sample: *Sample solution*

Transfer the *Sample solution* to a small evaporating dish, and evaporate to dryness on a steam bath. Add 1 mL of hydrochloric acid and 100 mg of potassium chlorate, and evaporate. Invert the dish over a vessel containing ammonium hydroxide.

Acceptance criteria: The residue acquires a purple color, which disappears upon the addition of 1 N sodium hydroxide (presence of caffeine).

ASSAY

• **Procedure**

Protect all solutions from light.

Solution A: Acetonitrile, water, and triethylamine (150:850:0.5) adjusted by the dropwise addition of fluorometric grade sulfuric acid to a pH of 3.1 ± 0.1

Solution B: Acetonitrile, water, and triethylamine (620:1380:1) adjusted by the dropwise addition of fluorometric grade sulfuric acid to a pH of 3.1 ± 0.1. Make any necessary adjustments in pH to meet relative retention times, and make other adjustments if necessary.

Solution C: 10 mg/mL of tartaric acid in water

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
NLT 3[a]	0	100
23	100	0
25	100	0

[a] Do not switch to using 100% of *Solution B* until 3 min after the injection of a sample or until after the caffeine peak has eluted, whichever occurs last.

Diluent: Methanol and *Solution C* (50:50)

Standard stock solution: 40 µg/mL of USP Ergotamine Tartrate RS in *Diluent*

Standard solution: 20 µg/mL of USP Ergotamine Tartrate RS from *Standard stock solution* and 1 mg/mL of USP Caffeine RS in *Diluent*

System suitability solution: 10 µg/mL of USP Ergotamine Tartrate RS and 0.5 mg/mL of USP Caffeine RS from *Standard solution* and 2 µg/mL of USP Ergotaminine RS in *Diluent*

Sample solution: Nominally 20 µg/mL of ergotamine tartrate from NLT 20 Suppositories prepared as follows. Weigh NLT 20 Suppositories, and grind to a fine mesh. Transfer a portion of the ground mass, equivalent to 2 mg of ergotamine tartrate, to a suitable glass-stoppered flask. Add 100.0 mL of *Diluent*, insert the stopper in the flask, and place it in a water bath maintained at 40°. Shake vigorously for 5 min, or longer if necessary, until the specimen is completely melted. Sonicate for 30 min, and transfer to a freezer for 45 min. Pass through a glass fiber filter of 0.7-µm pore size, and discard the first 5–10 mL of the filtrate.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 244 nm (for caffeine), in series with a fluorometric detector (for ergotamine tartrate) with excitation at 229 nm and detection at 435 nm

Column: 4.6-mm × 25-cm; packing L7

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Samples: *Standard solution* and *System suitability solution*

[NOTE—The relative retention times for caffeine, ergotamine, and ergotaminine are 1.0, 4, and 4.5, respectively.]

Suitability requirements

Resolution: NLT 3.0 between ergotamine and ergotaminine, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of caffeine ($C_8H_{10}N_4O_2$) in the portion of Suppositories taken:

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

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

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

C_S = concentration of USP Caffeine RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of the labeled amount of ergotamine tartrate [$(C_{33}H_{35}N_5O_5)_2 \cdot C_4H_6O_6$] in the portion of Suppositories taken:

$$\text{Result} = (I_U/I_S) \times (C_S/C_U) \times 100$$

I_U = fluorometric response of ergotamine from the *Sample solution*

I_S = fluorometric response of ergotamine from the *Standard solution*

C_S = concentration of USP Ergotamine Tartrate RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of ergotamine tartrate in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0% of the labeled amounts of ergotamine tartrate [$(C_{33}H_{35}N_5O_5)_2 \cdot C_4H_6O_6$] and caffeine ($C_8H_{10}N_4O_2$)

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, at a temperature not above 25°. Do not expose unwrapped Suppositories to sunlight.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Caffeine RS

USP Ergotamine Tartrate RS

USP Ergotaminine RS

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

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

Chromatographic Database Information: Chromatographic Database

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