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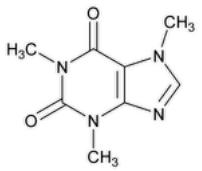
Caffeine



$C_8H_{10}N_4O_2 \cdot H_2O$ 212.21
$C_8H_{10}N_4O_2$ 194.19
1*H*-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-;
1,3,7-Trimethylxanthine CAS RN®: 58-08-2; UNII: 3G6A5W338E.
Monohydrate CAS RN®: 5743-12-4.

DEFINITION

Caffeine is anhydrous or contains one molecule of water of hydration. It contains NLT 98.5% and NMT 101.0% of $C_8H_{10}N_4O_2$, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **B.** The retention time of the caffeine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 0.82 g/L of anhydrous sodium acetate

Mobile phase: Acetonitrile, tetrahydrofuran, and *Buffer* (25:20:955). Adjust with glacial acetic acid to a pH of 4.5.

System suitability solution: 0.02 mg/mL of theophylline in *Mobile phase*. Shake, and sonicate if necessary, to dissolve.

Standard solution: Transfer 5.0 mg of USP Caffeine RS to a 25-mL volumetric flask. Add 5.0 mL of the *System suitability solution* and 10 mL of *Mobile phase*. Shake, and sonicate if necessary. Dilute with *Mobile phase* to volume, and filter.

Sample solution: 0.2 mg/mL of Caffeine in *Mobile phase*. [Note—Shake, and sonicate if necessary, to dissolve.]

Chromatographic system

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

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 15-cm; packing L1

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for theophylline and caffeine are 0.69 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6.0 between theophylline and caffeine

Tailing factor: NMT 2.0 for theophylline and caffeine peaks

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of caffeine ($C_8H_{10}N_4O_2$) in the portion of Caffeine 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 = concentration of Caffeine in the *Sample solution* (mg/mL)

Acceptance criteria: 98.5%–101.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Mobile phase, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Caffeine taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity from the *Sample solution*

r_T = sum of the responses of all the peaks from the *Sample solution*

Acceptance criteria

Individual impurities: NMT 0.1%

Total impurities: NMT 0.1%

SPECIFIC TESTS

• **Water Determination, *Method III*⟨921⟩:** Dry a sample at 80° for 4 h: the anhydrous form loses NMT 0.5% of its weight, and the hydrous form loses NMT 8.5% of its weight.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve hydrous Caffeine in tight containers. Preserve anhydrous Caffeine in well-closed containers.

• **Labeling:** Label it to indicate whether it is anhydrous or hydrous.

• **USP Reference Standards ⟨11⟩**

USP Caffeine RS

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

Topic/Question	Contact	Expert Committee
CAFFEINE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 49(2)

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