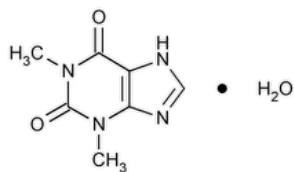


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Theophylline



$C_7H_8N_4O_2 \cdot H_2O$ 198.18
 $C_7H_8N_4O_2$ 180.17
1*H*-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-, monohydrate;
Theophylline monohydrate CAS RN[®]: 5967-84-0; UNII: C137DTR5RG.
Anhydrous CAS RN[®]: 58-55-9; UNII: 0I55128JYK.

DEFINITION
Theophylline contains one molecule of water of hydration or is anhydrous. It contains NLT 97.0% and NMT 102.0% of theophylline ($C_7H_8N_4O_2$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K ▲](#) (CN 1-MAY-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

• **PROCEDURE**

Solution A: 10 mM ammonium acetate prepared as follows. Transfer 770.8 mg of ammonium acetate to a 1-L volumetric flask, and dissolve in 80% flask volume of water. Adjust with glacial acetic acid to a pH of 5.5 and dilute with water to volume. Pass through a suitable filter of 0.2-µm pore size.

Solution B: Methanol

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	98	2
7	50	50
7.3	10	90
8.3	10	90
8.31	98	2
12	98	

Impurity stock solution: 0.2 mg/mL of [USP Theophylline Related Compound F RS](#) in water

System suitability solution: 1 mg/mL of [USP Theophylline RS](#) and 1 µg/mL of [USP Theophylline Related Compound F RS](#), from *Impurity stock solution*, in water. Sonicate as needed to aid in the dissolution.

Standard solution: 0.2 mg/mL of [USP Theophylline RS](#) in water

Sample solution: 0.2 mg/mL of Theophylline in water

Chromatographic system

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

Mode: LC

Detector: UV 270 nm

Column: 2.1-mm × 10-cm; 1.7-µm packing L1

Column temperature: 40°

Flow rate: 0.4 mL/min

Injection volume: 1 µL

System suitability

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

[NOTE—See [Table 2](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between theophylline and theophylline related compound F, *System suitability solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of theophylline ($C_7H_8N_4O_2$) in the portion of Theophylline taken:

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

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

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

C_S = concentration of [USP Theophylline RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 97.0%–102.0% on the dried basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.15%

• **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, Impurity stock solution, and System suitability solution: Proceed as directed in the Assay.

Standard stock solution: 50 µg/mL each of [USP Caffeine RS](#), [USP Theophylline RS](#), [USP Theophylline Related Compound B RS](#), [USP Theophylline Related Compound C RS](#), [USP Theophylline Related Compound D RS](#), and [USP Theophylline Related Compound F RS](#)

Standard solution: 1 µg/mL each of [USP Caffeine RS](#), [USP Theophylline RS](#), [USP Theophylline Related Compound B RS](#), [USP Theophylline Related Compound C RS](#), [USP Theophylline Related Compound D RS](#), and [USP Theophylline Related Compound F RS](#), from *Standard stock solution*, in water

Sample solution: 1.0 mg/mL of Theophylline in water

Chromatographic system

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

Mode: LC

Detector

For unspecified impurities with absorption maxima near 220 nm: UV 220 nm

For specified impurities and unspecified impurities with absorption maxima near 270 nm: UV 270 nm

Column: 2.1-mm × 10-cm; 1.7-µm packing L1

Column temperature: 40°

Flow rate: 0.4 mL/min

Injection volume: 1 µL

System suitability

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

[NOTE—See [Table 2](#) for relative retention times.]