

Theophylline Extended-Release Capsules

DEFINITION
Theophylline Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of anhydrous theophylline (C₇H₈N₄O₂).

- IDENTIFICATION**
- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
 - **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 0.77 g of [ammonium acetate](#) to a 1-L volumetric flask, and dissolve in 80% of the flask volume of [water](#). Adjust with [glacial acetic acid](#) to a pH of 5.4 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	93.5	6.5
2.5	93.5	6.5
5.0	10	90
5.1	93.5	6.5
7.0	93.5	6.5

Diluent: Dilute 138 mL of [ammonium hydroxide solution](#) with [water](#) to 1 L.

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

Sample stock solution: Nominally 4 mg/mL of theophylline prepared as follows. Transfer the contents of a suitable number of Capsules to a 500-mL volumetric flask. Add 150 mL of *Diluent* and heat on a hot plate to just boiling with occasional stirring. Remove from the hot plate and sonicate for 5 min while still hot. Cool to ambient temperature and dilute with [water](#) to volume.

Sample solution: Nominally 0.2 mg/mL of theophylline from *Sample stock solution*. Centrifuge and use the supernatant.

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

Mode: LC

Detector: UV 270 nm. For *Identification A*, use a photodiode array detector in the range of 210–400 nm.

Column: 2.1-mm × 10-cm; 1.7-µm packing [L7](#)

Column temperature: 40 ± 2°

Flow rate: 0.4 mL/min

Injection volume: 1 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of theophylline ($C_7H_8N_4O_2$) in the portion of Capsules 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 = nominal concentration of theophylline in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

[NOTE—The following tests, which were assigned numbers chronologically, are placed in groups corresponding to product dosing intervals.

Thus, individual tests do not necessarily appear in numerical order.]

For products labeled for dosing every 12 h

Test 1: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1*. Proceed as directed for [Dissolution \(711\)](#), [Procedure, Apparatus 1 and 2](#), [Delayed-Release Dosage Forms, Method B Procedure](#) except to use [Acceptance Table 2](#).

Medium: pH 1.2 [simulated gastric fluid](#) (without pepsin) for the first hour; pH 6.0 phosphate buffer (see [Reagents, Indicators, and Solutions—Buffer Solutions](#)); 900 mL

Apparatus 2: 50 rpm

Times: 1, 2, 4, 6, and 8 h

Standard solution: A known concentration of [USP Theophylline RS](#) in *Medium*

Sample solution: Filtered portions of the solution under test. Dilute with *Medium*, if necessary, to a concentration that is similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 271 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of theophylline ($C_7H_8N_4O_2$) dissolved at each time point using the UV absorption.

Tolerances: See [Table 2](#).

Table 2

Time (h)	Amount Dissolved (%)
1	3–15
2	20–40
4	50–75
6	65–100
8	NLT 80

The percentage of the labeled amount of theophylline ($C_7H_8N_4O_2$) dissolved at the times given conforms to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Solution A: 6.8 g/L of [monobasic potassium phosphate](#). Adjust with either [1 N hydrochloric acid](#) or [1 N sodium hydroxide](#) to a pH of 4.5 ± 0.05 .

Medium: *Solution A*; 900 mL

Apparatus 2: 75 rpm

Times: 1, 2, 4, and 8 h

Analysis: Proceed as directed in *Test 1*.

Tolerances: See [Table 3](#).

Table 3

Time (h)	Amount Dissolved (%)
1	10–30
2	30–55
4	55–80
8	NLT 80

The percentage of the labeled amount of theophylline ($C_7H_8N_4O_2$) dissolved at the times given conforms to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*. Proceed as directed for [Dissolution \(711\)](#), [Procedure, Apparatus 1 and 2, Delayed-Release Dosage Forms, Method B Procedure](#) except to use [Acceptance Table 2](#).

Medium: pH 1.2 [simulated gastric fluid](#) (without pepsin) for 1 h; pH 7.5 [simulated intestinal fluid](#) (without enzyme); 900 mL

Apparatus 2: 50 rpm

Times: 1, 2, 3, 4, and 7 h

Analysis: Proceed as directed in *Test 1*.

Tolerances: See [Table 4](#).

Table 4

Time (h)	Amount Dissolved (%)
1	1–17
2	30–60
3	50–90
4	NLT 65
7	NLT 85

The percentage of the labeled amount of theophylline ($C_7H_8N_4O_2$) dissolved at the times given conforms to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 4: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*. Proceed as directed for [Dissolution \(711\)](#), [Procedure, Apparatus 1 and 2, Delayed-Release Dosage Forms, Method A Procedure](#) except to use [Acceptance Table 2](#).

Medium: pH 3.0 phosphate buffer prepared by adjusting 0.05 M potassium phosphate buffer with [phosphoric acid](#) to a pH of 3.0 ± 0.05 , for the first 3.5 h, followed by the addition of 5.3 M [sodium hydroxide](#) to adjust to a pH of 7.4 ± 0.05 ; 900 mL

Apparatus 2: 50 rpm

Times: 1, 2, 3.5, and 5 h

Analysis: Proceed as directed in *Test 1*.