

Status: Currently Official on 14-Feb-2025
 Official Date: Official as of 01-May-2023
 Document Type: NF Monographs
 DocId: GUID-F5154FF7-0933-4BE2-AA30-536E958C1BEC_7_en-US
 DOI: https://doi.org/10.31003/USPNF_M39303_07_01
 DOI Ref: mvy7g

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Hypromellose Phthalate

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DEFINITION

Hypromellose Phthalate is a monophthalic acid ester of hydroxypropyl methylcellulose. It contains methoxy ($-\text{OCH}_3$), hydroxypropoxy ($-\text{OCH}_2\text{CHOHCH}_3$), and phthalyl (o-carboxybenzoyl; $\text{C}_8\text{H}_5\text{O}_3$) groups. It contains NLT 21.0% and NMT 35.0% of phthalyl groups, calculated on the anhydrous basis.

IDENTIFICATION

- ♦ **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K. Do not dry specimens. ♦

ASSAY

♦ PHTHALYL CONTENT

Sample: 1 g

Analysis: Transfer the *Sample* to a conical flask, dissolve in 50 mL of a mixture of [alcohol](#), [acetone](#), and water (2:2:1), add phenolphthalein TS, and titrate with [0.1 N sodium hydroxide VS](#). Perform a blank determination (see [Titrimetry \(541\)](#)).

Calculate the percentage of phthalyl groups in the portion of Hypromellose Phthalate taken:

$$\text{Result} = [0.01 \times M_{r1} \times (V/W)] - [2 \times (M_{r1}/M_{r2}) \times P]$$

M_{r1} = molecular weight of the phthalyl group, 149.1

V = volume of 0.1 N sodium hydroxide consumed after correction for the blank (mL)

W = weight of Hypromellose Phthalate taken, calculated on the anhydrous basis (g)

M_{r2} = molecular weight of phthalic acid, 166.1

P = percentage of free phthalic acid found as directed in the test for *Limit of Free Phthalic Acid*

Acceptance criteria: 21.0%–35.0% on the anhydrous basis

IMPURITIES

- ♦ **RESIDUE ON IGNITION (281):** NMT 0.20%

- ♦ **CHLORIDE AND SULFATE (221), Chloride**

Sample solution: Dissolve 1.0 g in 40 mL of [0.2 N sodium hydroxide](#), add 1 drop of [phenolphthalein TS](#), and add [2 N nitric acid](#) dropwise, with stirring, until the red color is discharged. Add an additional 20 mL of [2 N nitric acid](#) with stirring. Heat on a water bath, with stirring, until the gel-like precipitate formed becomes granular. Cool the mixture, and centrifuge. Separate the liquid phase, and wash the residue with three successive 20-mL portions of water, separating the washings by centrifuging. Dilute the combined liquids with water to 200 mL, mix, and filter.

Standard solution: Treat 0.50 mL of [0.01 N hydrochloric acid](#) with 10 mL of [0.2 N sodium hydroxide](#), add 7 mL of [2 N nitric acid](#), and dilute with water to 50 mL.

Analysis: Add 1 mL of [silver nitrate TS](#) to the *Standard solution*. Add 1 mL of silver nitrate TS to a 50-mL portion of the *Sample solution*. After mixing, allow each solution to stand for 5 min protected from direct sunlight. Compare the turbidity of the solutions.

Acceptance criteria: A 50-mL portion of the *Sample solution* shows no more chloride than the *Standard solution* (0.07%).

Change to read:

♦ LIMIT OF FREE PHTHALIC ACID

Mobile phase: 0.1% [trifluoroacetic acid](#) and [acetonitrile](#) (90:10)

Standard solution: Weigh accurately and transfer 12.5 mg of [phthalic acid](#) to a 250-mL volumetric flask, and add 125 mL of [acetonitrile](#). Add 25 mL of water, and dilute with [acetonitrile](#) to volume.

Sample solution: Weigh accurately and transfer 200 mg of Hypromellose Phthalate to a 100-mL volumetric flask. Add 50 mL of [acetonitrile](#), and sonicate to dissolve partially. Add 10 mL of water, and sonicate to dissolve. Cool to room temperature, and dilute with [acetonitrile](#) to volume.

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 4.6-mm × 25-cm; packing L1 with a high carbon load

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.0% for ▲5▲ (NF 1-May-2023) replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phthalic acid in the portion of Hypromellose Phthalate taken:

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

r_U = peak response of phthalic acid from the *Sample solution*

r_S = peak response of phthalic acid from the *Standard solution*

C_S = concentration of phthalic acid in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 1.0%

SPECIFIC TESTS

• [WATER DETERMINATION \(921\), Method I:](#) NMT 5.0%

• [VISCOSITY—CAPILLARY METHODS \(911\).](#)

Sample solution: Dissolve 10 g, previously dried at 105° for 1 h, in 90 g of a mixture of [methanol](#) and [methylene chloride](#) (1:1 w/w) by mixing and shaking.

Analysis: Determine the viscosity at 20 ± 0.1°.

Acceptance criteria: 80%–120% of that indicated by the label

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- ♦ **LABELING:** Label it to indicate its viscosity and nominal phthalyl content. ♦
- ♦ [USP REFERENCE STANDARDS \(11\).](#)
[USP Hypromellose Phthalate RS](#)
- ♦

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
HYPROMELLOSE PHTHALATE	Documentary Standards Support	CE2020 Complex Excipients

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

Pharmacopeial Forum: Volume No. PF 30(3)

Current DocID: GUID-F5154FF7-0933-4BE2-AA30-536E958C1BEC_7_en-US

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