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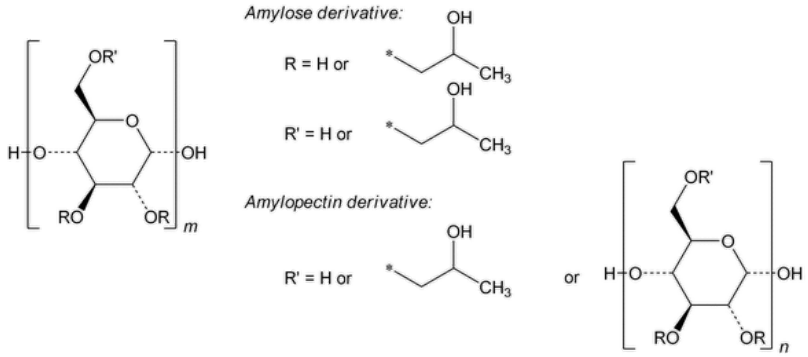
Hydroxypropyl Potato Starch



For the Amylose derivative, *m* is about 300–1000.

DEFINITION

Hydroxypropyl Potato Starch is partially substituted 2-hydroxypropylether obtained from potato starch by a chemical modification of etherification with propylene oxide. In addition, this starch may be partially hydrolyzed using acids or enzymes to obtain thinned starch. It contains NLT 2.0% and NMT 7.0% of hydroxypropyl groups, on the dried basis.

IDENTIFICATION

- **A. Procedure**

Analysis: Examine under a microscope, using NLT 20× magnification and a mixture of glycerin and water (1:1) as a mounting agent.

Acceptance criteria: It presents granules, either irregularly shaped, ovoid or pear-shaped, usually 30–100 µm in size, but occasionally exceeding 100 µm, or rounded 10–35 µm in size. There are occasional compound granules having 2–4 components. The ovoid and pear-shaped granules have an eccentric hilum, and the rounded granules have a centric or slightly eccentric hilum. All granules show clearly visible concentric striations. Between crossed nicol prisms, the Hydroxypropyl Potato Starch granules show a distinct black cross intersecting at the hilum.

- **B. Procedure**

Sample solution: Suspend 1 g of Hydroxypropyl Potato Starch in 50 mL of water, boil for 1 min, and cool.

Acceptance criteria: A translucent or clear mucilage is formed.

- **C. Procedure**

Analysis: To 1 mL of the *Sample solution* obtained in *Identification* test *B* add 0.05 mL of iodine and potassium iodide TS 2.

Acceptance criteria: An orange-red to dark blue color is produced, which disappears upon heating.

- **D. Procedure**

Ninhydrin solution: Dissolve 3 g of ninhydrin in 100 mL of a 45.5-g/L solution of sodium metabisulfite.

Diluted sulfuric acid: 98 g/L of H_2SO_4

Sample: 100 mg of Hydroxypropyl Potato Starch

Analysis: Transfer the *Sample* to a 100-mL volumetric flask, and add 12.5 mL of *Diluted sulfuric acid*. Place the flask in a water bath, and heat until the *Sample* is dissolved. Cool, and dilute with water to 100 mL. [**Caution—**When sulfuric acid is miscible with water, it produces intense heat.]

Pipet 1 mL of this solution to a glass-stoppered, 25-mL graduated test-tube and, with the tube immersed in cold water, add drop-wise 8 mL of sulfuric acid. Mix well, and place the tube in a boiling water bath for exactly 3 min. Immediately transfer the tube to an ice bath until the solution is chilled. Add 0.6 mL of *Ninhydrin solution*, carefully allowing the reagent to run down the walls of the test tube. Immediately shake the tube well, and place it in a water bath at 25° for 100 min. Dilute with sulfuric acid to 25 mL [**Caution—**Use sulfuric acid cautiously.], and mix by inverting the tube several times. Do not shake.

Acceptance criteria: A violet color develops within 5 min due to the presence of hydroxypropyl groups (starch ether).

ASSAY

• **Procedure for Hydroxypropyl Groups**

Deuterium chloride solution: Dilute 1 mL of deuterium chloride (38% w/w) with 5 mL of deuterium oxide.

Internal standard solution: Dissolve 50.0 mg of sodium 3-trimethylsilyl-1-propane sulfonate in about 5 g of deuterium oxide, weighed to the nearest 0.1 mg. Store in a sealed bottle.

Sample solution: Disperse 20 g of Hydroxypropyl Potato Starch in 200.0 mL of carbon dioxide-free water at room temperature. Agitate for 15 min, and filter. Repeat the operation two more times. If poor dispersibility or slow filtration is observed, use refrigerated carbon dioxide-free water for the washing operation. Dry the washed starch for NLT 4 h in vacuum at 30 ± 5°. Determine the moisture content (B) on 5 g of the washed and dried starch following the *Loss on Drying* test. Weigh 12.0 mg of the washed and dried starch in a 5-mm NMR tube. Add 0.75 mL of deuterium oxide and 0.1 mL of *Deuterium chloride solution*. Cap the tube, mix, and place it in a boiling water bath until a clear solution is obtained. [Note—It may take 3 min–1 h.] When a clear solution is obtained, allow to cool to room temperature. Dry the exterior of the tube, and weigh to the nearest 0.1 mg. Add 0.05 mL of *Internal standard solution*, and weigh to the nearest 0.1 mg. Determine the mass of the *Internal standard solution* added. Mix thoroughly.

Nuclear magnetic resonance spectrometry

(See *Nuclear Magnetic Resonance Spectroscopy ⟨761⟩, Quantitative Applications*.)

Apparatus: FT-NMR spectrometer at minimum 300 MHz

Acquisition of ^{1}H NMR spectra: The following parameters may be used.

Sweep width: 8 ppm (about −1.0 to +7 ppm)

Irradiation frequency offset: None

Time domain: NLT 64 K

Pulse width: 90 degree

Pulse delay: 10 s

Dummy scans: 0

Number of scans: 8

Use the CH_3 signal of the internal standard for shift referencing. Set the shift of the peak of the singlet to 0 ppm. Record the FID signal.

Analysis

Samples: *Internal standard solution* and *Sample solution*

Call the integration sub-routine after phase corrections and baseline correction between −0.5 and +6 ppm.

Measure the peak areas of the doublet from the methyl groups of the hydroxypropyl function at +1.2 ppm (A_2), and of the methyl groups at 0 ppm of the internal standard (A_1) without ^{13}C-satellites.

Measure the signal coming from the 3 protons of the methyl group in the hydroxypropyl function.

Calculate the content of hydroxypropyl groups as a percentage (w/w, dried basis):

$$\text{Result} = (N \times A_2/A_1) \times (C_i \times W_i/W) \times (M_{r2}/M_{r1}) \times [100/(100 - B)] \times 100$$

N = numerical value representing the 3 methyl groups in the internal standard (sodium 3-trimethylsilyl-1-propane sulfonate), 3

A_2 = area of the methyl groups of hydroxypropyl in Hydroxypropyl Potato Starch

A_1 = area of the methyl groups in the internal standard (sodium 3-trimethylsilyl-1-propane sulfonate)

C_i = concentration of the internal standard in the *Internal standard solution* (mg/g)

W_i = weight of the *Internal standard solution* in the NMR tube (g)

W = weight of the washed and dried Hydroxypropyl Potato Starch in the NMR tube (mg)

M_{r1} = molecular weight of the internal standard, 218.32 g/mol

M_{r2} = molar mass of hydroxypropyl group, 59.09 g/mol

B = moisture content of the washed and dried Hydroxypropyl Potato Starch used in the *Sample solution*, as a percentage (w/w)

Acceptance criteria: The content of hydroxypropyl groups is 2.0%–7.0% on the dried basis.

IMPURITIES

Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.6%, determined on a 1.0-g test specimen

Change to read:

- **Limit of Iron**

Standard iron stock solution: Prepare a solution containing the equivalent of 10 µg/mL of iron, as directed under ▲*Iron ⟨241⟩, Procedures, Procedure 1*▲ (CN 1-Jun-2023) ·

Diluted standard iron solution: Immediately before use, dilute an accurately measured volume of *Standard iron stock solution* quantitatively with water to obtain a solution containing the equivalent of 1 µg/mL of iron.

Standard solution: Transfer 10 mL of the *Diluted standard iron solution* to a test tube. Add 2 mL of citric acid solution (2 in 10) and 0.1 mL of thioglycolic acid, and mix. Add 10 N ammonium hydroxide until the solution is distinctly alkaline to litmus, dilute with water to 20 mL, and mix.

Sample solution: Shake 1.0 g of Hydroxypropyl Potato Starch with 20 mL of 2 N hydrochloric acid, and filter. Transfer 10 mL of the filtrate to a test tube. Add 2 mL of citric acid solution (2 in 10) and 0.1 mL of thioglycolic acid, and mix. Add 10 N ammonium hydroxide until the solution is distinctly alkaline to litmus, dilute with water to 20 mL, and mix.

Acceptance criteria: After 5 min, any pink color in the *Sample solution* is not more intense than that in the *Standard solution*, corresponding to a limit of 20 µg/g of iron.

- **Limit of Sulfur Dioxide, *Method IV* ⟨525⟩:** NMT 50 ppm

Organic Impurities

- **Procedure 1: Limit of Oxidizing Substances**

Sample: 4.0 g of Hydroxypropyl Potato Starch

Analysis: Transfer the *Sample* to a glass-stoppered, 125-mL conical flask, and add 50.0 mL of water. Insert the stopper, and swirl for 5 min. Transfer to a glass-stoppered, 50-mL centrifuge tube, and centrifuge to clarify. Transfer 30.0 mL of the clear supernatant to a glass-stoppered, 125-mL conical flask. Add 1 mL of glacial acetic acid and 0.5–1.0 g of potassium iodide. Insert the stopper, swirl, and allow to stand for 25–30 min in the dark. Add 1 mL of starch TS, and titrate with 0.002 N sodium thiosulfate VS to the disappearance of the starch-iodine color. Perform a blank determination, and make any necessary correction. Each mL of 0.002 N sodium thiosulfate VS is equivalent to 34 µg of oxidant, calculated as hydrogen peroxide.

Acceptance criteria: NMT 1.4 mL of 0.002 N sodium thiosulfate VS is required (20 µg/g, calculated as H_2O_2).

- **Procedure 2: Foreign Matter**

Sample: 50 mg/mL of Hydroxypropyl Potato Starch in a mixture of glycerin and water (1:1)

Analysis: Examine under a microscope, using NLT 20× magnification and a mixture of glycerin and water (1:1) as a mounting agent.

Acceptance criteria: NMT traces of matter other than Hydroxypropyl Potato Starch granules are present.

SPECIFIC TESTS

- **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^3 cfu/g, the total combined molds and yeasts count does not exceed 10^2 cfu/g, and it meets the requirements of the test for the absence of *Escherichia coli*.

- **pH ⟨791⟩**

Sample solution: Suspend 5.0 g of Hydroxypropyl Potato Starch in 25.0 mL of carbon dioxide-free water, and shake for 60 s. Allow to stand for 15 min.

Acceptance criteria: 4.5–8.0

- **Loss on Drying ⟨731⟩:** Dry about 1 g at 130° for 90 min: it loses NMT 20.0% of its weight.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

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

Topic/Question	Contact	Expert Committee
HYDROXYPROPYL POTATO STARCH	Documentary Standards Support	CE2020 Complex Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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