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Pregelatinized Hydroxypropyl Potato Starch

DEFINITION

Pregelatinized Hydroxypropyl Potato Starch is prepared from Hydroxypropyl Potato Starch by mechanical processing in the presence of water, with or without heat, to rupture all or some of the starch granules, and is subsequently dried. It contains NLT 2.0% and NMT 7.0% of hydroxypropyl groups on the dried basis.

IDENTIFICATION

• **A. Test for Pregelatinized State**

Sample: 1 g

Analysis: Disperse the *Sample* in 50 mL of water at a temperature NMT 25°. Shake vigorously until lumps completely disperse/solubilize or until lumps disappear. Allow to stand for 20 min.

Acceptance criteria: A translucent or clear mucilage without precipitate is formed.

• **B. Test for Starch**

Analysis: Disperse 0.5 g in 2 mL of water without heating, and add 0.05 mL of iodine and potassium iodide TS2.

Acceptance criteria: A reddish-violet or blue color is produced.

• **C. Ninhydrin Test**

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

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 dropwise 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.] 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

• **Assay for Hydroxypropyl Groups**

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

Internal standard solution: Disperse 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: Determine the moisture content (*B*) on 5 g of Pregelatinized Hydroxypropyl Potato Starch following the *Loss on Drying* test. Weigh 12.0 mg of the Pregelatinized Hydroxypropyl Potato 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—This may take from 3 min to 1 h.] When a clear solution is obtained, allow it to cool to room temperature. Dry the exterior of the tube, and weigh to the nearest 0.1 mg. Add 0.05 mL of the *Internal standard solution*. Weigh to the nearest 0.1 mg. Determine the mass of the *Internal standard solution* added. Mix thoroughly.

Instrumental conditions

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

Mode: Nuclear magnetic resonance spectrometry

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°

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 subroutine 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 originating 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 Pregelatinized 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 Pregelatinized Hydroxypropyl Potato Starch in the NMR tube (mg)

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

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

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

Acceptance criteria: 2.0%–7.0% of hydroxypropyl groups on the dried basis

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 the *Standard iron stock solution* quantitatively with water to obtain a solution containing the equivalent of 1 µg/mL of iron.

Sample solution: Shake the residue obtained from the test for *Residue on Ignition* 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.

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.

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 ppm of iron.

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

• **Limit of Propylene Glycol**

Internal standard solution: 0.5 mg/mL of 1,3-propanediol in anhydrous pyridine

Standard stock solution: 0.5 mg/mL of USP Propylene Glycol RS in *Internal standard solution*

Standard solution: Transfer 0.1 mL of the *Standard stock solution* to a 2-mL vessel with a screw cap fitted with a septum. Add 0.9 mL of anhydrous pyridine, 0.2 mL of hexamethyldisilazane, and 0.1 mL of trimethylchlorosilane. Close, and mix. Allow to stand for 15 min before injection.

Sample stock solution: Transfer 200 mg of Pregelatinized Hydroxypropyl Potato Starch to a 100-mL volumetric flask. Add 1.0 mL of the *Internal standard solution* and 9.0 mL of anhydrous pyridine. Boil under reflux using a water bath for 20 min. Allow to cool to room temperature.

Sample solution: Transfer 1.0 mL of the *Sample stock solution* to a 2-mL vessel with a screw cap fitted with a septum. Add 0.2 mL of hexamethyldisilazane and 0.1 mL of trimethylchlorosilane. Close, and mix. Allow to stand for 15 min before injection.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 30-m fused-silica capillary column; 0.25-µm layer of phase G1

Temperature

Detector: 250°

Injection port: 250°

Column: 70°. [Note—The column must be desorbed regularly. Conditions: Program from 70° to 300° at 7°/min, and maintain 10 min at 300°.]

Carrier gas: Helium

Flow rate: 3 mL/min

Injection type: Split ratio of 1:30

Injection size: 1 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for the trimethylsylilated derivative of propylene glycol and the trimethylsylilated derivative of 1,3-propanediol are 1.0 and 1.4, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the peaks due to the trimethylsylilated derivative of propylene glycol and the trimethylsylilated derivative of 1,3-propanediol

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of propylene glycol in the portion of Pregelatinized Hydroxypropyl Potato Starch taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = internal standard ratio (peak response of propylene glycol/peak response of 1,3-propanediol) from the *Sample solution*

R_S = internal standard ratio (peak response of propylene glycol/peak response of 1,3-propanediol) from the *Standard solution*

C_S = concentration of USP Propylene Glycol RS in the *Standard solution* (mg/mL)

C_U = concentration of Pregelatinized Hydroxypropyl Potato Starch in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.1%

• **Limit of Oxidizing Substances**

Sample: 4.0 g

Analysis: Transfer the *Sample* to a glass-stoppered 125-mL conical flask, and add 50.0 mL of a mixture of water and methanol (1:1). 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 ppm, calculated as H_2O_2).

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: Progressively suspend 3.0 g of Pregelatinized Hydroxypropyl Potato Starch in 100.0 mL of carbon dioxide-free water, stirring continuously. Determine the pH when all the solid is wetted.

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.

• **USP Reference Standards ⟨11⟩**

USP Propylene Glycol RS

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

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

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