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Hypromellose Acetate Succinate

Hydroxypropyl methylcellulose acetate succinate;
Cellulose, 2-hydroxypropyl methyl ether, acetate hydrogen butanedioate;
Cellulose, 2-hydroxypropyl methyl ether, acetate succinate
CAS RN®: 71138-97-1.

DEFINITION

Hypromellose Acetate Succinate is a mixture of acetic acid and monosuccinic acid esters of hydroxypropyl methylcellulose. It contains NLT 12.0% and NMT 28.0% of methoxy groups ($-\text{OCH}_3$), NLT 4.0% and NMT 23.0% of hydroxypropoxy groups ($-\text{OCH}_2\text{CHOHCH}_3$), NLT 2.0% and NMT 16.0% of acetyl groups ($-\text{COCH}_3$), and NLT 4.0% and NMT 28.0% of succinoyl groups ($-\text{COC}_2\text{H}_4\text{COOH}$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197A ▲](#) (CN 1-MAY-2020)

Sample: Neat. Do not dry specimen.

Analysis: Use a Fourier transform IR spectrophotometer fitted with a suitable accessory for single bounce attenuated total reflectance (see [Mid-Infrared Spectroscopy \(854\)](#)) with a diamond or germanium crystal. Acquire a background single-beam spectrum with a clean diamond or germanium crystal sampling plate in place. Place the sample on the diamond or germanium crystal sampling surface with a microspatula or equivalent. For best results, the sample should cover the crystal surface under the pressure point tip. Using the pressure device, apply pressure to the sample, making sure the sample remains centered under the pressure tip. Acquire a single-beam spectrum of the sample, and make the necessary corrections for the background. Release the pressure device, and clear it from the sample area. Wipe the sample off the crystal and pressure device tip, and rinse both with acetone.

Acceptance criteria: The IR spectrum of the *Sample* exhibits maxima only at the same wavelengths as a similarly obtained spectrum of [USP Hypromellose Acetate Succinate RS](#).

ASSAY

• ACETYL AND SUCCINOYL GROUPS

Phosphoric acid solution: 1.25 M phosphoric acid and water (2:98)

Buffer: 2.72 g/L of monobasic potassium phosphate

Diluent: Adjust the *Buffer* with 1 N sodium hydroxide to a pH of 7.5.

Acetic acid stock solution: Add approximately 20 mL of water to a stoppered, 100-mL volumetric flask, place the flask on a balance, and tare. Transfer 2.0 mL of glacial acetic acid to the flask, and record the weight of the acid added. Fill the flask with water to volume. Transfer 6 mL of the resulting solution into a 100-mL volumetric flask, and dilute with water to volume.

Succinic acid stock solution: 1.3 mg/mL of succinic acid

Mobile phase: Adjust the *Buffer* to a pH of 2.8 by the dropwise addition of 6 M phosphoric acid. Pass through a 0.22- μm nylon filter.

Standard solution 1: Transfer 4.0 mL of the *Acetic acid stock solution* and 4.0 mL of the *Succinic acid stock solution* to a 25-mL volumetric flask. Dilute with *Mobile phase* to volume, and mix.

Standard solution 2: Prepare as directed for *Standard solution 1*. This solution is prepared as a duplicate.

Sample solution: Weigh 12.4 mg of Hypromellose Acetate Succinate into a glass vial. Transfer 4.0 mL of 1.0 N sodium hydroxide to the vial, and stir the solution for 4 h. Then, add 4.0 mL of 1.25 M phosphoric acid to the same vial to bring the pH of the solution to 3 or less. Invert the test *Sample solution* vial several times to ensure complete mixing, and pass through a filter of 0.22- μm pore size. Use the clear filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm $\times$ 15-cm; 5- μm packing L1

Column temperature: 20°–30°

Flow rate: 1 mL/min

Run time: 15 min

Injection volume: 10 μL

System suitability**Samples:** *Standard solution 1* and *Standard solution 2***Suitability requirements****Column efficiency:** NLT 8000 theoretical plates, determined from the succinic acid peak, *Standard solution 1***Tailing factor:** 0.9–1.5 for the succinic acid peak, *Standard solution 1***Relative standard deviation:** NMT 2.0% for each peak from six replicate injections, *Standard solution 1***Peak difference:** The difference in peak areas between *Standard solution 1* and *Standard solution 2* for both acetic and succinic acids peaks does not exceed 2%.

[NOTE—After each run sequence, the column should be flushed first by 50% water and 50% acetonitrile for 60 min and then by 100% methanol for 60 min. The column should be stored in 100% methanol.]

Analysis**Samples:** *Standard solution 1* and *Sample solution*Calculate the percentage of acetic acid, *A*, in the portion of Hypromellose Acetate Succinate taken:

$$A = (r_{UA}/r_{SA}) \times (C_A/C_U) \times 100$$

 r_{UA} = peak response for acetic acid from the *Sample solution* r_{SA} = peak response for acetic acid from *Standard solution 1* C_A = concentration of acetic acid in *Standard solution 1* (mg/mL) C_U = concentration of Hypromellose Acetate Succinate in the *Sample solution* (mg/mL)Calculate the percentage of acetyl groups ($-\text{COCH}_3$) in the portion of Hypromellose Acetate Succinate taken:

$$\text{Result} = (A - A_{\text{free}}) \times (M_{r1}/M_{r2})$$

 A = defined above A_{free} = percentage of free acetic acid, as determined in the test for *Limit of Free Acetic and Succinic Acids* M_{r1} = molecular weight of the acetyl group, 43.04 M_{r2} = molecular weight of acetic acid, 60.05Calculate the percentage of succinic acid, *S*, in the portion of Hypromellose Acetate Succinate taken:

$$S = (r_{US}/r_{SS}) \times (C_S/C_U) \times 100$$

 r_{US} = peak response for succinic acid from the *Sample solution* r_{SS} = peak response for succinic acid from *Standard solution 1* C_S = concentration of succinic acid in *Standard solution 1* (mg/mL) C_U = concentration of Hypromellose Acetate Succinate in the *Sample solution* (mg/mL)Calculate the percentage of succinoyl groups ($-\text{COC}_2\text{H}_4\text{COOH}$) in the portion of Hypromellose Acetate Succinate taken:

$$\text{Result} = (S - S_{\text{free}}) \times (M_{r1}/M_{r2})$$

 S = defined above S_{free} = percentage of free succinic acid, as determined in the test for *Limit of Free Acetic and Succinic Acids* M_{r1} = molecular weight of the succinoyl group, 101.08 M_{r2} = molecular weight of succinic acid, 118.09**Acceptance criteria****Acetyl groups ($-\text{COCH}_3$):** 2.0%–16.0% on the dried basis**Succinoyl groups ($-\text{COC}_2\text{H}_4\text{COOH}$):** 4.0%–28.0% on the dried basis**• CONTENT OF METHOXY AND 2-HYDROXYPROPOXY GROUPS**[CAUTION—Hydriodic acid and its reaction byproducts are highly toxic. Perform all steps in the preparation of the *Sample solution* and the *Standard solution* in a properly functioning hood. Specific safety practices to be followed are to be identified to the analyst performing this test.]