of Oral Solution taken; and \( r_2 \) and \( r_1 \) are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.

**Hyoscyamine Sulfate Tablets**

Hyoscyamine Sulfate Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of hyoscyamine sulfate \([\text{C}_{17}\text{H}_{23}\text{NO}_3\text{H}_2\text{SO}_4\cdot 2\text{H}_2\text{O}]\).

**Packaging and storage**—Preserve in tight, light-resistant containers.

**USP Reference standards** (11)—

**USP Hyoscyamine Sulfate RS**

**Identification**—

A: The retention time of the major peak in the chromatogram of the Assay preparation corresponds to that in the chromatogram of the Standard preparation, as obtained in the Assay.

B: A filtered solution of Tablets meets the requirements of the tests for Sulfate (191).

**Disintegration** (701): 15 minutes.

**Uniformity of dosage units** (905): meet the requirements.

**Assay**—


Tropic acid solution—Dissolve an accurately weighed quantity of trocic acid in Diluent to obtain a solution having a concentration of about 3 \( \mu \)g of trocic acid per mL.

System suitability preparation—Transfer 3.0 mL of the Standard stock preparation into a 100-mL volumetric flask, add 40 mL of the Tropic acid solution, dilute with Diluent, to volume and mix.

**Assay preparation**—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed quantity of the powder, equivalent to about 0.125 mg of hyoscyamine sulfate, to a 25-mL volumetric flask. Add about 20 mL of the Diluent, and sonicate for 15 minutes with occasional swirling. Allow to cool to room temperature, dilute with Diluent to volume, and mix. Pass an aliquot through a 0.45-\( \mu \)m filter, discarding the first 5 mL of the filtrate.

Chromatographic system—The liquid chromatograph is equipped with a 205-nm detector and a 4.6-mm \( \times \) 15-cm column that contains 4-\( \mu \)m packing L11 and a 3-mm \( \times \) 4-mm guard column that contains packing L11. The flow rate is about 1.0 mL per minute. The column temperature is maintained at 30°. Chromatograph the System suitability preparation, and record the peak responses as directed for Procedure: the elution order is the trocic acid peak, followed by the hyoscyamine peak; the resolution, \( R \), between trocic acid and hyoscyamine is not less than 1.5; the tailing factor for the hyoscyamine peak is not more than 1.8; and the relative standard deviation for six replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 \( \mu \)L) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in mg, of hyoscyamine sulfate \([\text{C}_{17}\text{H}_{23}\text{NO}_3\text{H}_2\text{SO}_4\cdot 2\text{H}_2\text{O}]\) in the portion of Tablets taken by the formula:

\[
25 \times 1.053 \times C = \frac{C_{(\text{R2})}}{r_1 - r_2}
\]

in which 1.053 is the ratio of the molecular weight of hydrated hyoscyamine sulfate to that of anhydrous hyoscyamine sulfate; \( C \) is as defined under Standard preparation; and \( r_1 \) and \( r_2 \) are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.

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**Hyromellose**

<table>
<thead>
<tr>
<th>Attribute</th>
<th>JP</th>
<th>EP</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
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<tr>
<td>Labeling</td>
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<tr>
<td>Assay</td>
<td>+</td>
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</tr>
</tbody>
</table>

**Legend:** + will adopt and implement; − will not stipulate

**Nonharmonized attributes:** Packaging and Storage

**Specific local attributes:** Appearance of solution (EP), Description (JP), Limit of glyoxal (EP)

**Cellulose, 2-hydroxypropyl methyl ether:**

**Cellulose hydroxypropyl methyl ether** [9004-65-3].

**DEFINITION**

Hyromellose is a methyl and hydroxypropyl mixed ether of cellulose. It contains, calculated on the dried basis, methoxy (–OCH₃: 31.03) and hydroxypropoxy (–OC₃H₆OH: 75.09) groups conforming to the limits for the types of Hyromellose (hydroxypropyl methylcellulose) set forth in the table below.

<table>
<thead>
<tr>
<th>Substitution Type</th>
<th>Methoxy (%)</th>
<th>Hydroxypropoxy (%)</th>
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<tbody>
<tr>
<td>1828</td>
<td>16.5</td>
<td>20.0</td>
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<td>2208</td>
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<tr>
<td>2910</td>
<td>28.0</td>
<td>30.0</td>
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</table>

**IDENTIFICATION**

- **A. PROCEDURE**
  
  **Sample:** 1 g
  
  **Analysis:** Gently add the Sample to the top of 100 mL of water in a beaker, and allow to disperse over the surface, tapping the top of the container to ensure an even dispersion of the substance. Allow the beaker to stand for 1–2 min.
  
  **Acceptance criteria:** The powdered material aggregates on the surface.

- **B. PROCEDURE**
  
  **Sample:** 1 g
  
  **Analysis:** Add the Sample to 100 mL of boiling water, and stir the mixture using a magnetic stirrer with a bar 25 mm long.
  
  **Acceptance criteria:** A slurry is formed, but the powdered material does not dissolve. Cool the slurry to 10°, and stir using a magnetic stirrer; the resulting liquid is a clear or slightly turbid solution with thickness dependent on the viscosity grade.

- **C. PROCEDURE**
  
  **Solution A:** Sulfuric acid and water (9:1). [ NOTE—Carefully add sulfuric acid to water.]
  
  **Sample solution:** 0.1 mL of the solution prepared for Identification test B
  
  **Analysis:** To the Sample solution, add 9 mL of Solution A, and shake. Heat in a water bath for exactly 3 min, immedi-
Hypromellose / Official Monographs

Mode: GC
Detector: Thermal conductivity or hydrogen flame-ionization
Column: 3- to 4-mm × 1.8- to 3-m glass column packed with 20% liquid phase G28 on 100- to 120-mesh support

Result = 21.864 × (R Ua/R Sa) × (W Sa/WU)

R Ua = peak area ratio of methyl iodide to n-octane from the Sample solution
R Sa = peak area ratio of methyl iodide to n-octane from the Standard solution
W Sa = weight of methyl iodide in the Standard solution (mg)
WU = weight of Hypromellose, calculated on the dried basis, taken for the Sample solution (mg)

Result = 44.17 × (R Ub/R Sb) × (W Sb/WU)

R Ub = peak area ratio of isopropyl iodide to n-octane from the Sample solution
R Sb = peak area ratio of isopropyl iodide to n-octane from the Standard solution
W Sb = weight of isopropyl iodide in the Standard solution (mg)
WU = weight of Hypromellose, calculated on the dried basis, taken for the Sample solution (mg)

Acceptance criteria: See the limits, calculated on the dried basis, in the Table in the Definition.

ASSAY

• Procedure
  [CAUTION—Hydriodic acid and its reaction byproducts are highly toxic. Perform all steps in the preparation of the Standard solution and the Sample solution in a properly functioning hood. Specific safety practices to be followed are to be identified to the analyst per forming this test.]

Apparatus: For the reaction vial, use a 5-mL pressure-tight serum vial, 50 mm in height, 20 mm in outside diameter, and 13 mm in inside diameter at the mouth. The vial is equipped with a pressure-tight septum having a polytetrafluoroethylene-faced butyl rubber and an airtight seal using an aluminum crimp or any sealing system that provides sufficient airtightness. Use a heater having a heating module that has a square-shape aluminum block with holes 20 mm in diameter and 32 mm in depth, into which the reaction vial fits. The heating module is also equipped with a magnetic stirrer capable of mixing the contents of the vial, or use a reciprocal shaker that per forms a reciprocating motion of about 100 times/min.

Hydriodic acid: Use a reagent having a typical concentration of HI of about 57%.

Internal standard solution: 30 mg/mL of n-octane in o-xylene

Standard solution: Into a suitable serum vial, weigh between 60 and 100 mg of adipic acid, and add 2.0 mL of Hydriodic acid and 2.0 mL of Internal standard solution. Close the vial securely with a suitable septum stopper. W eigh the vial and contents, add between 15 µL and 22 µL of isopropyl iodide through the septum with a syringe, weigh again, and calculate the weight of isopropyl iodide added, by difference. Add 45 µL of methyl iodide similarly, weigh again, and calculate the weight of methyl iodide added, by difference. Shake the reaction vial well, and allow the layers to separate. Use the upper layer as the Standard solution.

Sample solution: Transfer 0.065 g of dried Hypromellose to a 5-mL thick-walled reaction vial equipped with a pressure-tight septum-type closure, add between 60 and 100 mg of adipic acid, and pipet 2.0 mL of Internal standard solution into the vial. Cautiously pipet 2.0 mL of Hydriodic acid into the mixture, immediately cap the vial tightly, and weigh. Using the magnetic stirrer equipped in the heating module, or use a reciprocal shaker, mix the contents of the vial continuously, heating and maintaining the temperature of the contents at 130 ± 2°C for 60 min. If a reciprocal shaker or magnetic stirrer cannot be used, shake the vial well by hand at 5-min intervals during the initial 30 min of the heating time. Allow the vial to cool, and weigh. If the weight loss is ≥0.50% of the contents or there is evidence of a leak, discard the mixture, and prepare another Sample solution.

Chromatographic system
(See Chromatography (621), System Suitability.)
PACKAGING AND STORAGE:

ADDITIONAL REQUIREMENTS

LABELING:

Hypromellose Ophthalmic Solution

- Hypromellose Ophthalmic Solution is a sterile solution of Hypromellose. It contains not less than 85.0 percent and not more than 115.0 percent of the labeled amount of Hypromellose (hydroxypropyl methylcellulose). It may contain suitable antimicrobial, buffering, and stabilizing agents.

Packaging and storage—Preserve in tight containers.

USP Reference standards

Identification—

A: Pour a few mL of Ophthalmic Solution onto a glass plate, and allow the water to evaporate: a thin, self-sustaining film results.

B: Heat 5 mL of Ophthalmic Solution in a test tube over a low flame: the warm solution turns cloudy but clears upon chilling.

Sterility (71): meets the requirements.

pH (791): between 6.0 and 7.8.

Assay—

Standard preparation—Dissolve a suitable quantity of USP Hypromellose RS, accurately weighed, in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 100 µg per mL.

Assay preparation—Dilute an accurately measured volume of Ophthalmic Solution quantitatively with water to obtain a solution having an equivalent concentration of about 100 µg of hypromellose per mL.

Procedure—Pipet 2 mL each of the Standard preparation, the Assay preparation, and water to provide a blank, into separate, glass-stoppered test tubes. To each tube add 5.0 mL of diphenylamine solution (prepared by dissolving 3.75 g of colorless diphenylamine crystals in 150 mL of glacial acetic acid and diluting the solution with 90 mL of hydrochloric acid), mix, and immediately insert the tubes into an oil bath at 105 °C for 30 minutes, the temperature being kept uniform within 0.1 °C during heating. Remove the tubes, and place them in an ice-water bath for 10 minutes or until thoroughly cool. At room temperature and using a suitable spectrophotometer, concomitantly determine the absorbances of the solutions from the Standard preparation and the Assay preparation at 635 nm, using the water solution as the blank. Calculate the quantity, in µg of hypromellose in each mL of the Ophthalmic Solution taken by the formula:

\[
0.001 \frac{C}{d}(A_1 / A_2)
\]

in which \(C\) is the concentration, in µg per mL, of USP Hypromellose RS in the Standard preparation; \(d\) is the dilution factor used to obtain the Assay preparation; and \(A_1\) and \(A_2\) are the absorbances of the solutions from the Assay preparation and the Standard preparation, respectively.