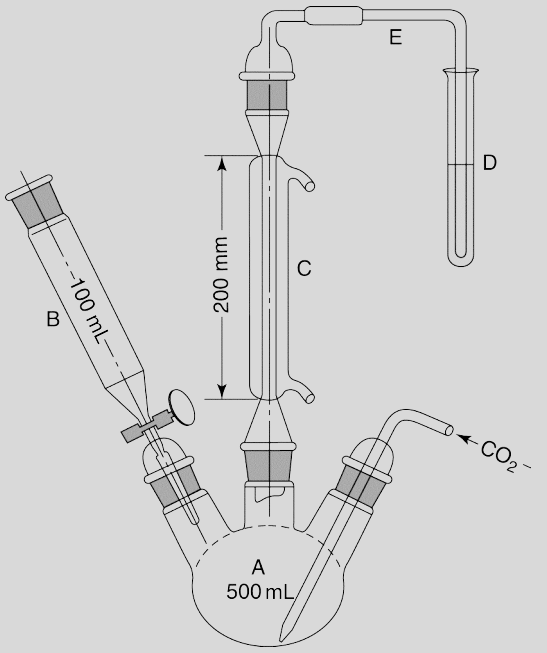
Apparatus: *Figure 1.*



In this test, the sulfur dioxide is released from the sample in a boiling acid medium and is removed by a stream of carbon dioxide. The separated gas is collected in a dilute hydrogen peroxide solution where the sulfur dioxide is oxidized to sulfuric acid and titrated with standard alkali. The apparatus consists essentially of a 500-mL three-neck, round-bottom boiling flask, a separatory funnel having a capacity of 100 mL or greater, a gas inlet tube of sufficient length to permit introduction of the carbon dioxide within 2.5 cm of the bottom of the boiling flask, a reflux condenser having a jacket length of 200 mm, and a delivery tube connecting the upper end of the reflux condenser to the bottom of a receiving test tube. Apply a thin film of stopcock grease to the sealing surfaces of all of the joints except the joint between the separatory funnel and the boiling flask, and clamp the joints to ensure tightness.

Analysis: Add 150 mL of water to the boiling flask. Close the stopcock of the separatory funnel, and begin the flow of carbon dioxide at a rate of 100 ± 5 mL/min through the *Apparatus*. Start the condenser coolant flow. Add 10 mL of *Hydrogen peroxide solution* to a receiving test tube. After 15 min, without interrupting the flow of carbon dioxide, remove the separatory funnel from the boiling flask, and transfer 25.0 g of Potato Starch into the boiling flask with the aid of 100 mL of water. Apply stopcock grease to the outer joint of the separatory funnel, and replace the separatory funnel in the boiling flask. Close the stopcock of the separatory funnel, and add 80 mL of 2 N hydrochloric acid to the separatory funnel. Open the stopcock of the separatory funnel to permit the hydrochloric acid solution to flow into the boiling flask, guarding against the escape of sulfur dioxide into the separatory funnel by closing the stopcock before the last few mL of hydrochloric acid drain out. Boil the mixture for 1 h. Remove the receiving test tube, and transfer its contents to a 200-mL wide-necked, conical flask. Rinse the receiving test tube with a small portion of water, add the rinsing to the 200-mL conical flask, and mix. Heat on a water bath for 15 min, and allow to cool.

Analysis: Add 0.1 mL of *Bromophenol blue indicator solution*, and titrate the contents with 0.1 N sodium hydroxide VS until the color changes from yellow to violet-blue. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩).

Calculate the content, in ppm, of sulfur dioxide in the *Sample solution* taken:

$$\text{Result} = 1000\ (32.03)\ VN/W$$

32.03 = milliequivalent weight of sulfur dioxide
V = volume of titrant consumed (mL)
N = normality of the titrant
W = weight of the *Sample solution* (g)

Acceptance criteria: NMT 50 ppm

- **LIMIT OF OXIDIZING SUBSTANCES**

Sample solution: Transfer 4.0 g 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.

Analysis: 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 is equivalent to 34 µg of oxidant, calculated as hydrogen peroxide.

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

SPECIFIC TESTS

- **✦MICROBIOLOGICAL EXAMINATION OF NONSTERILE PRODUCTIONS: MICROBIAL ENUMERATION TESTS** ⟨**61**⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨**62**⟩**:** The total aerobic microbial count does not exceed 1000 cfu/g; the total combined molds and yeasts count does not exceed 100 cfu/g, and it meets the requirements of the test for the absence of *Escherichia coli*.✦
- **LOSS ON DRYING** ⟨**731**⟩**:** Dry 1 g, at 130° for 90 min: it loses NMT 20.0% of its weight.
- **pH** ⟨**791**⟩**:** 5.0–8.0

Sample solution: Prepare a slurry by weighing 5.0 g of Potato Starch, transferring to a suitable nonmetallic container, and adding 25.0 mL of freshly boiled and cooled water.

Analysis: Agitate continuously at a moderate rate for 1 min. Stop the agitation, and allow to stand for 15 min. Determine the pH to the nearest 0.1 unit.

ADDITIONAL REQUIREMENTS

- **✦PACKAGING AND STORAGE:** Preserve in well-closed containers. No storage requirements specified.✦▲*NF28*

BRIEFING

Rice Starch. The European Pharmacopoeia is the coordinating pharmacopeia for the international harmonization of the compendial standards for this monograph, as part of the process of international harmonization of monographs and general analytical methods of the European, Japanese, and United States pharmacopeias. The following monograph, which represents the ADOPTION STAGE 6 document, is based on the Official Inquiry Stage 4 document, which appeared in PF 30(2). The text presented is similar to the harmonization draft for Corn Starch that appears in this issue of *Pharmacopeial Forum*, with one difference: the pH range, which is 5.0–8.0. Because there is no existing monograph for this excipient, a new monograph based on the ADOPTION STAGE 6 document is proposed.

(EM2: Kevin Moore.) RTS—C44217

Add the following:

▲Rice Starch

Attributes	EP	JP	USP
Definition	+	+	+
Identification A	+	+	+
Identification B	+	+	+
Identification C	+	+	+
pH	+	+	+
Iron	+	+	+
Oxidizing Substances	+	+	+
Sulfur dioxide	+	+	+
Loss on drying	+	+	+
Sulfated Ash [Residue on Ignition]	+	+	+

Legend: + will adopt and implement; – will not stipulate.
Nonharmonized attributes: Characters, Microbial Enumeration Tests and Tests for Specified Microorganisms, Packaging and Storage
Specific local attributes: Foreign matter (EP)
Reagents and Reference materials: Each pharmacopeia will adapt the text to take account of local reference materials and reagent specifications.

DEFINITION
Rice Starch is obtained from the caryopsis of *Oryza sativa L.*

IDENTIFICATION
- **A. PROCEDURE**
  Analysis: Examine under a microscope, using NLT 20x magnification and using a mixture of glycerin and water (1:1) as a mounting agent.
  Acceptance criteria: It appears either as angular polyhedral granules of irregular sizes with diameters ranging from 2 µm to 23 µm, or as rounded or spheroidal granules of irregular sizes with diameters ranging from 25 µm to 35 µm. The central hilum consists of a distinct cavity or two- to five-rayed cleft, and there are no concentric striations. Between orthogonally oriented polarizing plates or prisms, the starch granules show a distinct black cross intersecting at the hilum.
- **B. PROCEDURE**
  Sample solution: 20 mg/mL in water
  Analysis: Boil for 1 min, and cool.
  Acceptance criteria: A thin, cloudy mucilage is formed.
- **C. PROCEDURE**
  Sample solution: 1 mL of the mucilage obtained in *Identification* test *B*
  Analysis: Add 0.05 mL of iodine and potassium iodide TS 2 to the *Sample solution*.
  Acceptance criteria: An orange-red to dark blue color is produced, which disappears upon heating.

IMPURITIES
Inorganic Impurities
- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.6%, determined on a 1.0-g sample
- **LIMIT OF IRON**
  Sample solution: Shake 1.5 g of Rice Starch with 15 mL of 2 N hydrochloric acid, and filter. Transfer 10 mL of the filtrate to a test tube, and add 2 mL of citric acid solution (2 in 10) and 0.1 mL of thioglycolic acid. Add 10 N ammonium hydroxide until the solution is distinctly alkaline to litmus, and dilute with water to 20 mL.
  Standard iron stock solution A: Equivalent to 10 µg/mL of iron prepared as directed under *Iron* ⟨241⟩
  Standard iron stock solution B: 1 µg/mL of iron from *Standard iron stock solution A* in water
  [NOTE—Prepare immediately before use.]
  Standard iron solution: Transfer 10 mL of *Standard iron stock solution B* to a test tube, and add 2 mL of citric acid solution (2 in 10) and 0.1 mL of thioglycolic acid. Add 10 N ammonium hydroxide until the solution is distinctly alkaline to litmus, and dilute with water to 20 mL.
  Acceptance criteria: After 5 min, any pink color in the *Sample solution* is not more intense than that in the *Standard iron solution*, corresponding to a limit of 10 ppm of iron.
- **LIMIT OF SULFUR DIOXIDE**
  Carbon dioxide: Use carbon dioxide, with a flow regulator that will maintain a flow of 100 ± 10 mL/min.
  Bromophenol blue indicator solution: 0.2 mg/mL of bromophenol blue in dilute alcohol. Filter if necessary.
  Hydrogen peroxide solution: Dilute 30% hydrogen peroxide with water to obtain a 3% solution. Just before use, add 3 drops of *Bromophenol blue indicator solution*, and neutralize to a violet-blue endpoint with 0.01 N sodium hydroxide. Do not exceed the endpoint.
  Apparatus: *Figure 1.*

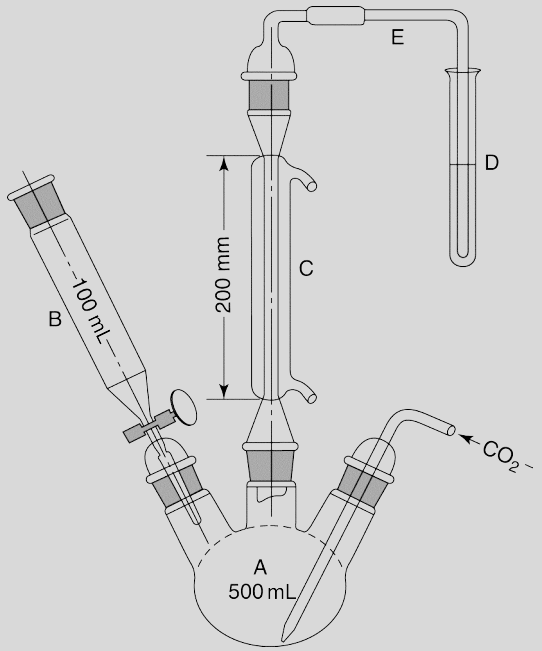


Figure 1

In this test, the sulfur dioxide is released from the sample in a boiling acid medium and is removed by a stream of carbon dioxide. The separated gas is collected in a dilute hydrogen peroxide solution where the sulfur dioxide is oxidized to sulfuric acid and titrated with standard alkali. The apparatus consists essentially of a 500-mL three-neck, round-bottom boiling flask, a separatory funnel having a capacity of 100 mL or greater, a gas inlet tube of sufficient length to permit introduction of the carbon dioxide within 2.5 cm of the bottom of the boiling flask, a reflux condenser having a jacket length of 200 mm, and a delivery tube connecting the upper end of the reflux condenser to the bottom of a receiving test tube. Apply a thin film of stopcock grease to the sealing surfaces of all of the joints except the joint between the separatory funnel and the boiling flask, and clamp the joints to ensure tightness.

Analysis
Add 150 mL of water to the boiling flask. Close the stopcock of the separatory funnel, and begin the flow of carbon dioxide at a rate of 100 ± 5 mL/min through the *Apparatus*. Start the condenser coolant flow. Add 10 mL of *Hydrogen peroxide solution* to a receiving test tube. After 15 min, without interrupting the flow of carbon dioxide, remove the separatory funnel from the boiling flask, and transfer 25.0 g of Rice Starch into the boiling flask with the aid of 100 mL of water. Apply stopcock grease to the outer joint of the separatory funnel, and replace the separatory funnel in the boiling flask. Close the stopcock of the separatory funnel, and add 80 mL of 2 N hydrochloric acid to the separatory

funnel. Open the stopcock of the separatory funnel to permit the hydrochloric acid solution to flow into the boiling flask, guarding against the escape of sulfur dioxide into the separatory funnel by closing the stopcock before the last few mL of hydrochloric acid drain out. Boil the mixture for 1 h. Remove the receiving test tube, and transfer its contents to a 200-mL wide-necked, conical flask. Rinse the receiving test tube with a small portion of water, add the rinsing to the 200-mL conical flask, and mix. Heat on a water bath for 15 min, and allow to cool.

Add 0.1 mL of *Bromophenol blue indicator solution*, and titrate the contents with 0.1 N sodium hydroxide VS until the color changes from yellow to violet-blue. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩).

Calculate the content, in ppm, of sulfur dioxide in the sample solution taken:

$$\text{Result} = 1000\ (32.03)\ VN/W$$

32.03 = milliequivalent weight of sulfur dioxide
V = volume of titrant consumed (mL)
N = normality of the titrant
W = weight of the sample solution (g)

Acceptance criteria: NMT 50 ppm

- **LIMIT OF OXIDIZING SUBSTANCES**

Sample solution: Transfer 4.0 g 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.

Analysis: 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 is equivalent to 34 µg of oxidant, calculated as hydrogen peroxide.

Acceptance criteria: NMT 1.4 mL of 0.002 N sodium thiosulfate 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 1000 cfu/g, the total combined molds and yeasts count does not exceed 100 cfu/g, and it meets the requirements of the test for the absence of *Escherichia coli*.✦
- **LOSS ON DRYING ⟨731⟩:** Dry 1 g at 130° for 90 min: it loses NMT 15.0% of its weight.
- **pH ⟨791⟩:** 5.0–8.0

Sample solution: Prepare a slurry by weighing 5.0 g of Rice Starch, transferring to a suitable nonmetallic container, and adding 25.0 mL of freshly boiled and cooled water.

Analysis: Agitate continuously at a moderate rate for 1 min. Stop the agitation, and allow to stand for 15 min. Determine the pH to the nearest 0.1 unit.

ADDITIONAL REQUIREMENTS

- **✦PACKAGING AND STORAGE:** Preserve in well-closed containers. No storage requirements specified.✦▲*NF28*

BRIEFING

Wheat Starch. The Japanese Pharmacopoeia is the coordinating pharmacopeia for the international harmonization of the compendial standards for the Wheat Starch monograph, as part of the process of international harmonization of monographs and general analytical methods of the European, Japanese, and United States pharmacopeias. The following monograph, which represents the **ADOPTION STAGE 6** document, is based on the corresponding monograph for Wheat Starch that was revised based on a request from the Japanese Pharmacopoeia. Differences between the **ADOPTION STAGE 6** document and the current USP monograph for Wheat Starch include the following: under *Identification* test *A*, "Between crossed nicol prisms" is changed to "Between orthogonally-oriented polarizing plates or prisms."

(EM2: K. Moore.) RTS—C50840

Add the following:

▲Wheat Starch

Attributes	EP	JP	USP
Definition	+	+	+
Identification A	+	+	+
Identification B	+	+	+
Identification C	+	+	+
pH	+	+	+
Loss on Drying	+	+	+
Residue on Ignition	+	+	+
Limit of Iron	+	+	+
Limit of Oxidizing Substances	+	+	+
Limit of Sulfur Dioxide	+	+	+
Total Protein	+	+	+

Legend: + will adopt and implement; - will not stipulate.
Nonharmonized attributes: Characters, *Microbial Enumeration Tests,* and *Tests for Specified Microorganisms*, and *Packing and Storage* (USP)
Specific local attributes: Foreign matter (EP)
Reagents and Reference materials: Each pharmacopeia will adapt the text to take account of local reference materials and reagent specifications.

DEFINITION

Wheat starch is obtained from the caryopsis of *Triticum aestivum L.* (*T. vulgare* Vill.).

IDENTIFICATION

- **A. PROCEDURE**

Analysis: Examine under a microscope using equal volumes of glycerol and water.

Acceptance criteria: It presents large and small granules, and, very rarely, intermediate sizes. The large granules, usually 10–60 µm in diameter, are discoid or, more rarely, reniform when seen face-on. The central hilum and striations are invisible or barely visible, and the granules sometimes show cracks on the edges. Seen in profile, the granules are elliptical and fusiform and the hilum appears as a slit along the main axis. The small granules, rounded or polyhedral, are 2–10 µm in diameter. Between orthogonally-oriented polarizing plates or prisms, the granules show a distinct black cross intersecting at the hilum.

- **B. PROCEDURE**

Sample solution: 20 mg/mL in water
Analysis: Boil for 1 min, and cool.
Acceptance criteria: A thin, cloudy mucilage is formed.

- **C. PROCEDURE**

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