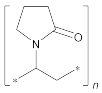
Povidone

Portions of the monograph text that are national *USP* text, and are not part of the harmonized text, are marked with symbols (✦✦) to specify this fact.



$(C_6H_9NO)_n$
2-Pyrrolidinone, 1-ethenyl-, homopolymer;
1-Vinyl-2-pyrrolidinone polymer [9003-39-8].

DEFINITION

Change to read:

Povidone is a synthetic polymer consisting essentially of linear 1-vinyl-2-pyrrolidinone groups, the degree of polymerization of which results in polymers of various molecular weights. The different types of Povidone are characterized by their viscosity in aqueous solution, relative to that of water, expressed as a K-value (see *Specific Tests*, *K-value*). The K-value of Povidone having a stated (nominal) K-value of 15 or less is NLT 85.0% and NMT 115.0% of the stated values. The K-value of Povidone having a stated K-value or a stated K-value range with an average of more than 15 is NLT 90.0% and NMT 108.0% of the stated value or of the average of the stated range. ■It contains NLT 11.5% and NMT 12.8% of nitrogen (N: 14.01), calculated on the anhydrous basis. It has the nominal K-value of NLT 10 and NMT 120. The nominal K-value is shown on the label.■2S *(USP34)*

IDENTIFICATION

- **✦A.**
  Sample solution: 20 mg/mL of Povidone
  Analysis: To 10 mL of the *Sample solution* add 20 mL of 1 N hydrochloric acid and 5 mL of potassium dichromate TS.
  Acceptance criteria: An orange-yellow precipitate is formed.✦
- **✦B.**
  Solution A: Dissolve 75 mg of cobalt nitrate and 300 mg of ammonium thiocyanate in 2 mL of water.
  Sample solution: 20 mg/mL of Povidone
  Analysis: Combine *Solution A* and 5 mL of the *Sample solution*, and render the resulting solution acid by the addition of 3 N hydrochloric acid.
  Acceptance criteria: A pale blue precipitate is formed.✦
- **✦C.**
  Sample solution: 5 mg/mL of Povidone
  Analysis: To 5 mL of the *Sample solution* add a few drops of iodine TS.
  Acceptance criteria: A deep red color is produced.✦

Add the following:

- **■D.**
  Sample solution: 50 mg/mL of Povidone in water
  Acceptance criteria: The substance dissolves.■2S *(USP34)*

ASSAY

- **NITROGEN DETERMINATION,** *Method II* ⟨**461**⟩
  Sample: 0.1 g of Povidone
  Analysis: Proceed as directed, using the *Sample*. In the *Procedure*, omit the use of hydrogen peroxide, and use 5 g of a powdered mixture of potassium sulfate, cupric sulfate, and titanium dioxide (33:1:1) instead of potassium sulfate and cupric sulfate (10:1). Heat until a clear, light-green solution is obtained. Heat for an additional 45 min and proceed as directed for *Procedure*, beginning with "Cautiously add to the digestion mixture 70 mL of water".
  Acceptance criteria: 11.5%–12.8% on the anhydrous basis

IMPURITIES

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%
- **LEAD** ⟨**251**⟩
  Sample solution: 1.0 g in 25 mL of water
  Acceptance criteria: NMT 10 ppm

Change to read:

- **LIMIT OF ALDEHYDES**
  Solution A: Transfer 8.3 g of potassium pyrophosphate to a 500-mL volumetric flask, and dissolve in 400 mL of water. Adjust, if necessary, with 1 N hydrochloric acid to a pH of 9.0, and dilute with water to volume.
  Solution B: Transfer a quantity of lyophilized aldehyde dehydrogenase equivalent to 70 units to a glass vial, and dissolve in 10.0 mL of water. [NOTE—This solution is stable for 8 h at 4°.]
  Solution C: Transfer 40 mg of nicotinamide adenine dinucleotide to a glass vial, and dissolve in 10.0 mL of *Solution A*. [NOTE—This solution is stable for 4 weeks at 4°.]
  Standard solution: Add 2 mL of water to a glass weighing bottle, and weigh. Add 100 mg (0.13 mL) of freshly distilled acetaldehyde and weigh. Transfer this solution to a 100-mL volumetric flask. Rinse the weighing bottle with several portions of water, transferring each rinsing to the 100-mL volumetric flask. Dilute the solution in the 100-mL volumetric flask with water to volume. Store at 4° for about 20 h. Pipet 1 mL of this solution into a 100-mL volumetric flask, and dilute with water to volume.
  Sample solution: 20 mg/mL of Povidone in *Solution A*. ■■2S *(USP34)* Insert a stopper into the flask, heat at 60° for 1 h, and cool to room temperature.
  Blank: Water
  Instrumental conditions
  (See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
  Mode: UV
  Analytical wavelength: 340 nm
  Cell: 1 cm
  Analysis
  Samples: *Standard solution*, *Sample solution*, and *Blank*
  Pipet 0.5 mL each of the *Standard solution*, *Sample solution*, and *Blank* into separate cells. Add 2.5 mL of *Solution A* and 0.2 mL of *Solution C* to each cell. Cover the cells to exclude oxygen. Mix by inversion, and allow to stand for 2–3 min at 22 ± 2°. Determine the absorbances of the solutions using the *Blank* as the reference. Add 0.05 mL of *Solution B* to each cell. Cover the cells to exclude oxygen. Mix by inversion, and allow to stand for 5 min at 22 ± 2°. Determine the absorbances of the solutions, using the *Blank* as the reference.
  Calculate the percentage of aldehydes, expressed as acetaldehyde, in the portion of Povidone taken:

$$\text{Result} = 10 \times (C/W) \times [\{(A_{U2} - A_{U1}) - (A_{B2} - A_{B1})\}/\{(A_{S2} - A_{S1}) - (A_{B2} - A_{B1})\}]$$

C = concentration of acetaldehyde in the *Standard solution* (mg/mL)
W = weight of Povidone taken (g)
A_{U2} = absorbance of the solution from the *Sample solution*, after addition of *Solution B*

A_{U1} = absorbance of the solution from the *Sample solution*, before addition of *Solution B*
A_{B2} = absorbance of the solution from the *Blank*, after addition of *Solution B*
A_{B1} = absorbance of the solution from the *Blank*, before addition of *Solution B*
A_{S2} = absorbance of the solution from the *Standard solution*, after addition of *Solution B*
A_{S1} = absorbance of the solution from the *Standard solution*, before addition of *Solution B*

Acceptance criteria: NMT 0.05%

- **LIMIT OF HYDRAZINE**

Standard solution: 9.38 µg/mL of salicylaldazine in toluene
Sample solution: Transfer 2.5 g to a 50-mL centrifuge tube, add 25 mL of water, and mix to dissolve. Add 500 µL of a solution (1 in 20) of salicylaldehyde in methanol, swirl, and heat in a water bath at 60° for 15 min. Allow to cool, add 2.0 mL of toluene, insert a stopper in the tube, shake vigorously for 2 min, and centrifuge. Use the clear upper toluene layer in the centrifuge tube as the *Sample solution*.
Chromatographic system
(See *Chromatography* ⟨621⟩, *Thin-Layer Chromatography*.)
Mode: TLC
Adsorbent: 0.25-mm layer of dimethylsilanized chromatographic silica gel mixture
Application volume: 10 µL
Developing solvent system: Methanol and water (2:1)
Analytical wavelength: UV 365 nm
Analysis
Samples: *Standard solution* and *Sample solution*
Proceed as directed in the chapter. Allow the spots to dry, and develop the chromatogram with the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Locate the spots on the plate by examination under UV light. Remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate.
Acceptance criteria: Salicylaldazine appears as a fluorescent spot having an R_F value of 0.3; and the fluorescence of any salicylaldazine spot from the *Sample solution* is not more intense than that produced by the spot from the *Standard solution* (NMT 1 ppm of hydrazine).

Change to read:

- **VINYLPYRROLIDINONE**

Mobile phase: Methanol and water (1:4)
System suitability solution: Transfer 10 mg of vinylpyrrolidinone and 500 mg of vinyl acetate to a 100-mL volumetric flask, and dissolve in and dilute with methanol to volume. Transfer 1.0 mL of this solution to a 100-mL volumetric flask, and dilute with *Mobile phase* to volume.
Standard stock solution: 5 µg/mL of vinylpyrrolidinone in methanol
Standard solution: 0.25 µg/mL from vinylpyrrolidinone *Standard stock solution* in *Mobile phase*
Sample solution: 25 mg/mL of Povidone in *Mobile phase*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 235 nm
Column
Guard: 4.0-mm × 2.5-cm; packing ■L1■ *(USP34)*
Analytical: 4.0-mm × 25-cm; 5-µm packing ■L1■ *(USP34)*
[NOTE—The analysis can also be performed with a 4.0- × 30-mm or a 4.6- × 30-mm guard column containing packing L7 and with a 4.6- × 25-cm analytical column containing 5-µm packing L7.]
Column temperature: 40°
[NOTE—Adjust the flow rate so that the retention time of vinylpyrrolidinone is about 10 min.]
Injection size: 50 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 2.0 between vinylpyrrolidinone and vinyl acetate, *System suitability solution*
Relative standard deviation: NMT 2.0% of vinylpyrrolidinone, for ■6■ *(USP34)* injections, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Record the chromatograms, and measure the responses for the vinylpyrrolidinone peak. [NOTE—If necessary, after each injection of the *Sample solution* wash the polymeric material of Povidone from the guard column by passing the *Mobile phase* through the column backwards for 30 min at the same flow rate.]
Calculate the percentage of vinylpyrrolidinone in the sample taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = vinylpyrrolidinone peak response from the *Sample solution*
r_S = vinylpyrrolidinone peak response from the *Standard solution*
C_S = concentration of vinylpyrrolidinone in the *Standard solution* (mg/mL)
C_U = concentration of Povidone in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.001%

Add the following:

- **2-PYRROLIDONE**

Mobile phase: Water adjusted with phosphoric acid to a pH of 2.4
Standard solution: 30 µg/mL of 2-pyrrolidinone in water
Sample solution: 5 mg/mL of Povidone in water
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 205 nm
Column
Guard: 4.0-mm × 2.5-cm; packing L1
Analytical: 4.0-mm × 25-cm; 5-µm packing L1
Column temperature: 30°
[NOTE—Adjust the flow rate so that the retention time of 2-pyrrolidinone is about 11 min.]
Injection size: 50 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 2.0% of 2-pyrrolidinone for 6 injections, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Record the chromatograms, and measure the responses for the 2-pyrrolidinone peak. [NOTE—After each injection of the *Sample solution* wash the polymeric material of Povidone from the guard column by passing the *Mobile phase* through the column backwards for 30 min at the same flow rate.]
Calculate the percentage of 2-pyrrolidinone in the sample taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = 2-pyrrolidinone peak response from the *Sample solution*
r_S = 2-pyrrolidinone peak response from the *Standard solution*
C_S = concentration of 2-pyrrolidinone in the *Standard solution* (mg/mL)
C_U = concentration of Povidone in the *Sample solution* (mg/mL), calculated on the anhydrous basis

Acceptance criteria: NMT 3.0%■2S (*USP34*)

Add the following:

■• **PEROXIDES**

Sample solution: 40 mg/mL of Povidone in water, calculated on the anhydrous basis
Blank: To 25 mL of the *Sample solution* add 2 mL of 13% sulfuric acid.
Instrumental conditions
(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
Mode: UV-Vis
Analytical wavelength: 405 nm
Cell: 1 cm
Analysis
Sample: *Sample solution*
To 25 mL of the *Sample solution* add 2 mL of titanium trichloride–sulfuric acid TS, and allow to stand for 30 min. Measure the absorbance of a portion of this solution against the *Blank*.
Acceptance criteria: NMT 0.35, corresponding to NMT 400 ppm, expressed as H_2O_2■2S (*USP34*)

Add the following:

■• **FORMIC ACID**

Mobile phase: Diluted perchloric acid (5 in 1000)
Standard solution: 10 µg/mL of formic acid in water
Sample stock solution: 20 mg/mL of Povidone in water
Sample solution: Transfer a suspension of strongly acidic ion exchange resin (use the hydrogen form of ion-exchange resin) in water to a column of about 0.8 cm in inside diameter to give a packing depth of about 20 mm in length, and keep the strongly acidic ion-exchange resin layer constantly immersed in water. Pour 5 mL of water and adjust the flow rate so that water drops at a rate of about 20 drops per min. When the level of the water is near the top of the strongly acidic ion-exchange resin layer, add 100 mL of the *Sample stock solution* into the column. After dropping 2 mL of the solution, collect 1.5 mL of the solution, and use this as the *Sample solution*.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 210 nm
Column 4- to 8-mm × 25- to 30-cm; 5- to 10-µm packing L17
Column temperature: 30°
[NOTE—Adjust the flow rate so that the retention time of formic acid is about 11 min.]
Injection size: 50 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 2.0% of formic acid for 6 injections, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Record the chromatograms, and measure the responses for the formic acid peak.

Calculate the percentage of formic acid in the sample taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of formic acid from the *Sample solution*
r_S = peak response of formic acid from the *Standard solution*
C_S = concentration of formic acid in the *Standard solution* (mg/mL)
C_U = concentration of Povidone in the *Sample solution* (mg/mL), calculated on the anhydrous basis

Acceptance criteria: NMT 0.5%■2S (*USP34*)

SPECIFIC TESTS

Change to read:

• **PH** ⟨**791**⟩
■**Sample solution:** 50 mg/mL in water
Acceptance criteria: 3.0–5.0 for Povidone having the nominal K-value of 30 or less; 4.0–7.0 for Povidone having the nominal K-value greater than 30■2S (*USP34*)
• **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 5.0%
• **K-VALUE**
Sample solution: Weigh a quantity of undried Povidone equivalent on the anhydrous basis to the amount specified in *Table 1*.

Table 1

Nominal K-value	Quantity (g)
≤18	5.00
>18 to ≤95	1.00
>95	0.10

Dissolve it in 50 mL of water in a 100-mL volumetric flask, and dilute to volume. Allow to stand for 1 h.
Analysis
Sample: *Sample solution*
Determine the viscosity of the *Sample solution*, using a capillary-tube viscosimeter (see *Viscosity* ⟨911⟩), at 25 ± 0.2°. Calculate the K-value of Povidone:

$$\text{Result} = \left[\sqrt{300c\log z + (c + 1.5c\log z)^2} + 1.5c\log z - c\right] \Big/ \left(0.15c + 0.003c^2\right)$$

c = weight, on the anhydrous basis, of the specimen tested in each 100.0 mL of solution (g)
z = viscosity of the *Sample solution* relative to that of water

Acceptance criteria
K-value of Povidone having a stated (nominal) K-value NMT 15: 85.0%–115.0% of the stated values
K-value of Povidone having a stated K-value or a stated K-value range with an average of more than 15: 90.0%–108.0% of the stated value or of the average of the stated range

ADDITIONAL REQUIREMENTS

• ✦**PACKAGING AND STORAGE:** Preserve in tight containers.✦
• ✦**LABELING:** Label it to state, as part of the official title, the K-value or K-value range of Povidone.✦