Amendment to the Enforcement Ordinance of the Food Sanitation Law and the Standards and Specifications for Foods and Food Additives.

The government of Japan will designate Polyvinylpyrrolidone as an authorized food additive.

Summary

Under Article 10 of the Food Sanitation Law, food additives shall not be used marketed without authorization by the Minister of Health, Labour and Welfare (hereinafter referred as "the Minister"). In addition, when specifications or standards are established for food additives based on Article 11 of the act and stipulated in the Ministry of Health, Labour and Welfare Notification (Ministry of Health and Welfare Notification No. 370, 1959), those additives shall not be used or marketed unless they meet the standards or specifications.

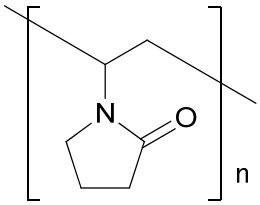
In response to a request from the Minister, the Committee on Food Additives of the Food Sanitation Council that is established under the Pharmaceutical Affairs and Food Sanitation Council has discussed the adequacy of the designation of Polyvinylpyrrolidone as food additives. The conclusion of the committee is outlined below.

Outline of conclusion

The Minister, based on Article 10 of the Food Sanitation Law, should designate Polyvinylpyrrolidone, as food additives unlikely to harm human health, and establish standard for use and compositional specifications, based on Article 11 of the law (see Attachment).

Attachment

Polyvinylpyrrolidone
Povidone
ポリビニルピロリドン



Standards for use

Permitted for use only in foods not in conventional food form, like those in capsule or tablet form.

Compositional specifications

Substance name Polyvinylpyrrolidone

Molecular formula $(C_6H_9NO)_n$

Chemical name [CAS number] Poly[1-(2-oxopyrrolidin-1-yl)ethylene] [9003-39-8]

Content Polyvinylpyrrolidone , when calculated on the anhydrous basis, contains 11.5–12.8% of nitrogen (N=14.01).

Description Polyvinylpyrrolidone is a white to pale yellow powder.

Identification Determine the infrared absorption spectrum of Polyvinylpyrrolidone , previously dried at 105°C for 6 hours, as directed in the Potassium Bromide Disk Method under Infrared Spectrophotometry, and compare with the Reference Spectrum. Both spectra exhibit absorptions having about the same intensity at the same wavenumbers.

Purity

(1) pH 3.0–7.0 (1.0 g, water 20 ml).

(2) Viscosity

Test Solution Weigh accurately an amount, equivalent to 1.00 g of Polyvinylpyrrolidone on the anhydrous basis, add water to dissolve, and make exactly

100 ml. Allow the solution to stand for 60 minutes.

Procedure Measure the kinematic viscosity of the test solution and water at 25°C as directed under Method 1 in Viscosity, and determine K value by the following fomu1a. The K value is 90–108% of the labeled value.

$$K = \frac{1.5 log v_{rel} - 1}{0.15 + 0.003c} + \frac{\sqrt{300c\ log v_{rel} + (c + 1.5 log v_{rel})^2}}{0.15c + +0.003c^2}$$

c= the amount (g) of the sample, on the anhydrous basis, in 100 ml of the test solution

v_{rel} = ratio of the kinematic viscosity of the test solution to the kinematic viscosity of water

(3) Lead Not more than 2.0 μg/g as Pb.

Test Solution Weigh 2.0 g of Polyvinylpyrrolidone in a platinum, quartz, or porcelain crucible or a quartz beaker. Moisten the sample entirely with sulfuric acid, heat on a hot plate by increasing the temperature gradually until the sample is carbonized and white fumes are no longer evolved. Place it in an electric furnace, heat by increasing the temperature gradually, and incinerate at 500–600°C. To the residue, add 10 ml of diluted hydrochloric acid (1 in 4), and evaporate on a water bath to dryness. To the residue, add a little amount of diluted nitric acid (1 in 100), and dissolve while heating. After cooling, add diluted nitric acid (1 in 100) to make exactly 10 ml.

Control Solution Measure exactly 1 ml of the Lead Standard Stock Solution, and add water to make exactly 100 ml. Measure exactly 4 ml of this solution, and add diluted nitric acid (1 in 100) to make exactly 10 ml.

Procedure Proceed as directed under Method 1 in the Lead Limit Test.

(4) Aldehyde Not more than 500 μg/g as acetaldehyde.

Test Solution Weigh accurately about 1 g of Polyvinylpyrrolidone , and dissolve in potassium pyrophosphate–hydrochloric acid buffer (0.05 mol/L, pH9.0) to make exactly 100 ml. Stopper tightly, heat at 60°C for 60 minutes, and cool to room temperature.

Standard Solution Weigh 0.100 g of freshly distilled acetaldehyde, and dissolve in 4°C water to make exactly 100 ml. Allow to stand at 4°C for about 20 hours. Take exactly 1 ml of this solution, add potassium pyrophosphate–hydrochloric acid buffer (0.05 mol/L, pH 9.0) to make exactly 100 ml.

Procedure Place 0.5 ml each of the test solution, standard solution, and water in separate cells, and add exactly 2.5 ml of potassium pyrophosphate–hydrochloric acid buffer (0.05 mol/L, pH9.0) and 0.2 ml β-nicotinamide adenine dinucleotide TS in each cell. Stir them well, stopper tightly, and allow to stand at 22 ± 2°C for 2–3 minutes. Measure the absorbances (A_{T1}, A_{S1}, and A_{B1}) of these solutions at 340 nm against water

as reference. To each solution, add 0.05 ml of aldehyde dehydrogenase TS, stir, stopper, and allow to stand at 22 ± 2°C for 5 minutes. Measure the absorbances (A_{T2}, A_{S2}, and A_{B2}) of these solutions in the same manner. Determine the amount of aldehyde by formula:

$$\text{Amount of aldehyde (μg/g)} = \frac{1000}{\text{Anhydrous basis weight (g) of the sample}} \times \frac{(A_{T2} - A_{T1}) - (A_{B2} - A_{B1})}{(A_{S2} - A_{S1}) - (A_{B2} - A_{B1})}$$

(5) 1-Vinyl-2-pyrrolidone Not more than 10 μg/g as 1-vinyl-2-pyrrolidone.

Test Solution Weigh accurately about 0.25 g of Polyvinylpyrrolidone , and dissolve in methanol (1 in 5) to make exactly 10 ml.

Standard Solution Weigh exactly 0.050 g of 1-vinyl-2-pyrrolidone, add methanol to dissolve, and make exactly 100 ml. Measure exactly 1 ml of this solution, add methanol to make exactly 100 ml. Measure exactly 5 ml of the second solution, and add methanol (1 in 5) to make exactly 100 ml.

Procedure Analyze 50 μl-potions of the test solution and the standard solution by liquid chromatography using the operating conditions given below. Measure the peak areas (A_T and A_S) of 1-vinyl-2-pyrrolidone for the test solution and the standard solution, and determine its amount by the formula:

$$\text{Amount (μg/g) of } 1-\text{vinyl}-2-\text{pyrrolidone} = \frac{2.5}{\text{Anhydrous basis weight (g) of the sample}} \times \frac{A_T}{A_S}$$

Operating Conditions

Detector: Ultraviolet spectrophotometer (wavelength 254 nm).

Column: A stainless steel tube of about 4 mm internal diameter and about 25 cm length.

Column packing material: 5-μm octylsilanized silica gel for liquid chromatography.

Guard column: A column with the same internal diameter as the main column, packed with the same material as the main column.

Column temperature: A constant temperature around 40°C.

Mobile phase: A 4:1 mixture of water/methanol.

Flow rate: Adjust so that the retention time of 1-vinyl-2-pyrrolidone is about 10 minutes.

Column selection: Use a column that is capable of eluting 1-vinyl-2-pyrrolidone and vinyl acetate in that order and whose separation rate is not less than 2.0 when 50 μl of the solution prepared as directed below is chromatographed

according to the above operating conditions. When the test is repeated 6 times according to the above operating conditions, the relative standard deviation of the peak areas of 1-vinyl-2-pyrrolidone is not more than 2%.

Preparation of the solution Dissolving 0.010 g of Polyvinylpyrrolidone and 0.5 g of vinyl acetate in 100 ml of methanol. To 1 mL of this solution, add methanol (1 in 5) to make 100 ml.

Rinse of guard column: After testing , run the mobile phase through the guard column in reverse direction to testing operation at the above flow rate for 30 minute.

(6) Hydrazine Not more than 1 μg/g as hydrazine.

Test Solution Transfer about 2.5 g of Polyvinylpyrrolidone, weighed accurately, into a 50-ml centrifuge tube, add 25 ml of water, and dissolve by stirring. Add 500 μl of a solution (1 in 20) of salicylaldehyde in methanol, shake, and heat in a water bath at 60°C for 15 minutes. After cooling, add 2.0 ml of toluene, stopper, and shake vigorously for 2 minutes. Centrifuge, and use the upper layer as the test solution.

Standard Solution Weigh 0.090 g of salicylaldazine, and dissolve in toluene to make exactly 100 ml. To exactly measured 1 ml of this solution, add toluene to make exactly 100 ml.

Procedure Analyze 10-μL portions of the test solution and the standard solution by thin-layer chromatography, using methanol solution (2 in 3) as the developing solvent. Use a thin-layer plate coated with fluorescent dimethylsilanized silica gel for thin-layer chromatography as the solid support and then dried at 110ºC for 1 hour. Stop the development when the solvent front has ascended to a point about 15 cm above the original line, and air-dry the plate. Examine under ultraviolet light (around 365 nm). A spot from the test solution appears at the position corresponding to the spot from the standard solution. The fluorescence of the spot from the test solution is not more intense than that produced by the spot from the standard solution.

Water Not more than 5.0% (0.5g, Direct Titration).

Residue on Ignition Not more than 0.1% (1 g, 600 ± 50°C)

Assay (1) Apparatus Use hard-glass apparatus, as illustrated below. Ground-glass may be used for joint parts. Before use, all rubber parts used for the apparatus should be boiled in sodium hydroxide solution (1 in 25) for 10–30 minutes and then in water for 30–60 minutes, and finally rinsed thoroughly with water.

A: Kjeldahl flask.

B: Steam generator (filled with water containing 2 to 3 drops of sulfuric acid, and boiling chips to prevent bumping).

C: Spray trap.

D: Water supply funnel.

E: Steam generator.

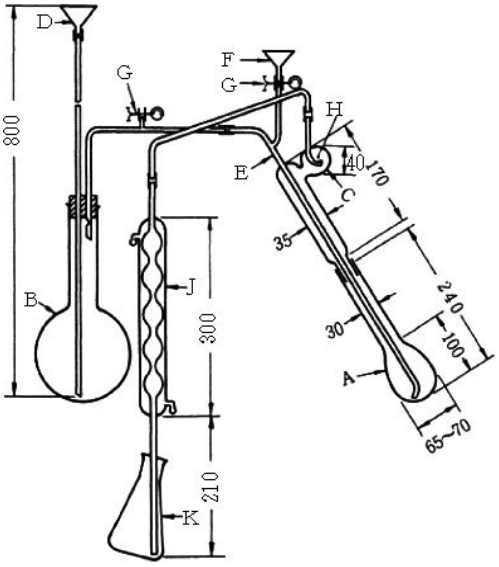
F: Injection funnel for alkali solution.

G: Rubber tube with pinch cock.

H: Small hole (the diameter is almost the same as the internal diameter of the tube).

J: Condenser (with the lower end cut diagonally).

K: Absorption flask.



(Unit: mm)

(2) Procedure

Transfer about 0.1 g of Polyvinylpyrrolidone, accurately weighed, in Kjeldahl flask A, and add 5 g of a powdered mixture of 33 g of potassium sulfate, 1 g of cupper(II) sulfate pentahydrate, and 1 g of titanium(IV) oxide. Wash down the sample adhering to the neck of A with a small amount of f water, and then pour 7 ml of sulfuric acid down the inside wall of A. Heat A gradually until the solution in the flask exhibits a clear yellow-green color and the inside walls of flask A are free from carbonized material, and heat for another 45 minute. After cooling, add 20 ml of water carefully, and cool. Connect A to the distillation apparatus, washed by passing steam through it. To absorption flask K, add 30 ml of boric acid solution (1 in 25) and 3 drops of bromocresol green–methyl red mixture TS, and add an adequate amount of water to immerse the lower end of condenser J in the solution. Add 30 ml of sodium hydroxide solution (2 in 5) through funnel F, carefully wash down with 10 ml of water, and immediately close the pinch cock attached to rubber tube G. Distill with steam until 80–100 ml of distillate is obtained. Lower absorption K so that the lower end of J comes above the solution, and rinse the end of J with a small amount of water. Titrate with 0.025 mol/L sulfuric acid. The endpoint is when the color of the solution changes from green through slightly grayish blue to slightly grayish red-violet. Separately, perform a blank test to make necessary correction.

Each ml of 0.025 mol/L sulfuric acid =0.7003 mg of N

Reagents

Aldehyde Dehydrogenase A white powder. Enzyme activity equivalent to not less than 2 units per milligram.

Enzyme activity determination

(i) Sample solution Dissolve about 20 mg of Aldehyde Dehydrogenase, accurately weighed, in 1 ml of water, add an ice-cold solution of bovine serum albumin (1 in 100) to make exactly 200 ml.

(ii) Procedure Dissolve 20.0 mg of β-nicotinamido adenine dinucleotide in water to exactly 1 ml. Add 0.20 ml of this solution, 0.10 ml of pyrazole solution (17 in 2500), and 0.10 ml of the sample solution to 2.50 ml of pyrophosphate buffer (pH9.0), stir, stopper tightly, and allow to stand at 25 ± 1°C for 2 minutes. To this solution, add 0.10 ml of acetaldehyde solution (3 in 1000), stir, and stopper. Every 30 seconds, measure the absorbance at 340 nm as directed under Ultraviolet-visible Spectrophotometry, and calculate a change (ΔA) in absorbance per minute from the straight line region of the absorbance-straight curve, and determine the enzyme activity by the formula given below. One unit is an amount of enzyme that oxidizes 1μmol of acetaldehyde per minute when enzyme activity measurement is done using the operating conditions given in the procedure.

Enzyme activity unit $(unit/mg)$of aldehyde dehydrogenase

$$= \frac{2.91 \times \Delta A \times 200}{6.3 \times amount\ (g) of\ the\ sample \times 0.10 \times 1000}$$

Aldehyde Dehydrogenase TS Dissolve an amount equivalent to 70 units of aldehyde dehydrogenase in 10 ml of water. Prepare fresh before use.

Bovine Serum Albumin A substance obtained from cattle serum. It contains not less than 95% of albumin.

Dimethylsilanized Silica Gel for Thin-layer Chromatography (fluorescent) Use dimethylsilanized silica gel that has been produced exclusively for thin-layer chromatography and to which a fluorescent agent is added.

Dithiothreitol $C_4H_{10}O_2S_2$ Crystals.

Melting point 42–43°C

β-Nicotinamido Adenine Dinucleotide $C_{21}H_{27}N_7O_{14}P_2$ [β-NAD^+ , K9802.]

β-Nicotinamido Adenine Dinucleotide TS Dissolve 0.04 g of β-Nicotinamido Adenine Dinucleotide in 10 ml of water. Prepare fresh before use.

Potassium Pyrophosphate $K_4O_7P_2$ A white crystalline powder. Very soluble in water.

Melting point 1109°C.

Potassium Pyrophosphate–Hydrochloric Acid Buffer (0.05 mol/L, pH9.0) Dissolve 0.83 g of potassium pyrophosphate in 40 ml of water. To this solution, add 1 mol/L hydrochloric acid to adjust its pH to 9.0, and add water to make 50 ml. Adjust the temperature to 22 ± 2°C before use.

Pyrazole $C_3H_4N_2$ White to pale yellow crystals or crystalline powder.

Melting point 67–71°C.

Pyrophosphate buffer (pH9.0) Weigh 3.3 g of potassium pyrophosphate, 15 mg of dithiothreitol, and 40 mg of disodium ethylenediaminetetraacetate dehydrate, add water to dissolve them, and make 70 ml. Adjust the pH to 9.0 with citric acid monohydrate (21 in 100), and add water to make exactly 100 ml. Prepare fresh before use.

Salicylaldazine $C_{14}H_{12}N_2O_2$

Melting point 213–219°C.

Purity Dissolve 0.09 g of Salicylaldazine in toluene to make 100 ml. To exactly measured 1 ml of this solution, add toluene to make exactly 100 ml. When the resulting solution is analyzed as directed under Purity (6) for Polyvinylpyrrolidone, any spot other than the main spot does not appear.

Titanium(IV) Oxide TiO_2 [K8703]

1-Vinyl-2-pyrrolidone C_6H_9NO A clear liquid.

Purity Analyze 0.5-μl portions of 1-Vinyl-2-pyrrolidone by gas chromatography using the operating conditions given below. Measure the peak areas of the components contained, and determine 1-vinyl-2-pyrrolidone as directed under the Peak Area Percentage Method in the Flavoring Substances Tests. Its concentration shall be not

less than 99.0%. The detection sensitivity must be adjusted so that the peak height of 1-vinyl-2-pyrrolidone obtained from a 0.5-µl portion of the sample is about 70% of its full scale.

Operating conditions

Detector: Flame-ionization detector

Column: A silicate glass capillary tube (0.53 mm internal diameter and 30 m length) coated with a 1.0 µm thick layer of polyethylene glycol for gas chromatography.

Column temperature: Maintain the temperature at 80°C for 1 minute, raise it to 190°C at a rate of 10°C/minute, and maintain for 20 minutes.

Inlet temperature: 190°C.

Carrier gas: Helium.

Flow rate: Adjust so that the peak of 1-vinyl-2-pyrrolidoe appears about 15 minutes after injection.

Infrared Reference Spectrum

Polyvinylpyrrolidone