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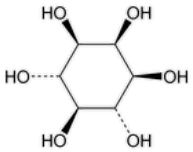
Inositol



$C_6H_{12}O_6$ 180.16

cis-1,2,3,5-*trans*-4,6-Cyclohexanehexol;

myo-Inositol CAS RN®: 87-89-8.

DEFINITION

Inositol contains NLT 97.0% and NMT 102.0% of Inositol ($C_6H_{12}O_6$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Mobile phase: Water

System suitability solution: 0.05 mg/mL of USP Inositol RS and 0.05 mg/mL of USP Mannitol RS

Standard solution: 50 mg/mL of USP Inositol RS

Sample solution: 50 mg/mL of Inositol

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: Refractive index

Column: 7.8-mm × 30-cm or equivalent; packing L19

Temperature

Column: 85°

Detector: Constant temperature of 30°–35°

Flow rate: 0.5 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for inositol and mannitol are 1.0 and 1.3, respectively.]

Suitability requirements

Resolution: NLT 4.0 between inositol and mannitol, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

[Note—Record the chromatograms over a period of two times the retention time of inositol, and measure the peak responses.]

Calculate the percentage of Inositol ($C_6H_{12}O_6$) in the portion of sample taken:

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

r_U = peak response of inositol from the *Sample solution*

r_S = peak response of inositol from the *Standard solution*

C_S = concentration of USP Inositol RS in the *Standard solution* (mg/mL)

C_U = concentration of Inositol in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–102.0% on the anhydrous basis

IMPURITIES

• **Barium**

Sample solution: Use the *Sample solution* prepared in the test for *Clarity of Solution*. To 10 mL of the *Sample solution* add 1 mL of diluted sulfuric acid.

Acceptance criteria: When examined immediately and after 1 h, any opalescence in the solution is not more intense than that in a mixture of 1 mL of water and 10 mL of the *Sample solution* from the test for *Clarity of Solution*.

Change to read:

• **Limit of Lead**

Lead nitrate stock solution: Dissolve 159.8 mg of lead nitrate in 100 mL of water to which has been added 1 mL of nitric acid, then dilute with water to 1000 mL. Prepare and store this solution in glass containers free from soluble lead salts.

Standard lead solution: On the day of use, dilute 10.0 mL of the *Lead nitrate stock solution* with water to 100.0 mL. Each mL of the *Standard lead solution* contains the equivalent of 10 µg of lead. ▲▲ (ERR 1-May-2019)

Sample solution: Dissolve 20.0 g of Inositol in diluted acetic acid, and dilute with diluted acetic acid to 100 mL. Add 2.0 mL of a saturated ammonium pyrrolidinedithiocarbamate solution (containing about 10 g of ammonium pyrrolidinedithiocarbamate per L) and 10.0 mL of methyl isobutyl ketone, and shake for 30 s. Protect from bright light. Allow the two layers to separate, and use the methyl isobutyl ketone layer.

Blank solution: Prepare as directed for the *Sample solution*, except omit the use of Inositol.

Standard solutions: Prepare as directed for the *Sample solution*, except prepare three *Standard solutions* by adding 0.5, 1.0, and 1.5 mL, respectively, of the *Standard lead solution* in addition to the 20.0 g of Inositol to be examined.

Instrumental conditions

(See *Atomic Absorption Spectroscopy ⟨852⟩*.)

Mode: Atomic absorption

Analytical wavelength: 283.3 nm

Lamp: Lead hollow-cathode

Flame: Air–acetylene

Analysis: Set the atomic absorption spectrometer to zero, using the *Blank solution*. Introduce the *Sample solution* and each of the three *Standard solutions* into the instrument, and record the steady absorbance reading. Plot the absorbance readings against the known concentrations of added lead (in µg), and draw a straight line. Extrapolate the line until it meets the concentration axis to obtain the concentration, in mg/kg, of lead in the sample.

Acceptance criteria: NMT 0.5 mg/kg

• **Organic Impurities**

Mobile phase, System suitability solution, and **Sample solution:** Proceed as directed in the *Assay*.

Standard solution: Transfer 2.0 mL of the *Standard solution*, prepared as directed in the *Assay*, to a 100-mL volumetric flask, and dilute with water to volume.

[Note—This solution contains 1 mg/mL of inositol.]

Chromatographic system: Proceed as directed in the *Assay*, except use an injection volume of 20 µL.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Inositol taken:

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

r_U = peak response of any impurity from the *Sample solution*

r_S = peak response of inositol from the *Standard solution*

C_S = concentration of USP Inositol RS in the *Standard solution* (mg/mL)

C_U = concentration of Inositol in the *Sample solution* (mg/mL)

Acceptance criteria

Individual impurities: NMT 0.3%

Total impurities: NMT 1.0%. [NOTE—Disregard any impurity peak that is less than 0.05%.]

SPECIFIC TESTS

Change to read:

• **CLARITY OF SOLUTION**

[NOTE—The *Sample solution* is to be compared to *Reference suspension A* in diffused daylight 5 min after preparation of *Reference suspension A*.]

Solution A: 10 mg/mL of hydrazine sulfate. Allow to stand for 4–6 h before use.

Solution B: 100 mg/mL of methenamine prepared in a glass-stoppered flask.

Primary opalescent suspension: [NOTE—This suspension is stable for 2 months, provided it is stored in a glass container free from surface defects. The suspension must not adhere to the glass and must be well mixed before use.]*Solution A* and *Solution B* (1:1). Allow to stand for 24 h.

Opalescence standard: Transfer 15.0 mL of the *Primary opalescent suspension* to a 1000-mL volumetric flask, dilute with water to volume. [NOTE—This suspension should not be used beyond 24 h after preparation.]

Reference suspensions

Reference suspension A: Transfer 5.0 mL of the *Opalescence standard* to a 100-mL volumetric flask, and dilute with water to volume.

Reference suspension B: Transfer 10.0 mL of the *Opalescence standard* to a 100-mL volumetric flask, and dilute with water to volume.

Sample solution: 100 mg/mL of Inositol

Analysis: Transfer a sufficient portion of the *Sample solution* to a sample tube of colorless, transparent, neutral glass, with a flat base and an internal diameter of 15–25 mm, to obtain a depth of 40 mm. Similarly transfer portions of *Reference suspension A*, *Reference suspension B*, and water to separate matching sample tubes. Compare the *Sample solution*, *Reference suspension A*, *Reference suspension B*, and water in diffused daylight, viewing vertically against a black background (see ▲*Visual Comparison ⟨630⟩*▲ (CN 1-May-2019)). [NOTE—The diffusion of light must be such that *Reference suspension A* can readily be distinguished from water, and that *Reference suspension B* can readily be distinguished from *Reference suspension A*.]

Acceptance criteria: The *Sample solution* shows the same clarity as that of water.

Change to read:

• **COLOR OF SOLUTION**

Standard stock solutions: Prepare three solutions, *A*, *B*, and *C*, containing, respectively, the following parts of ferric chloride CS, cobaltous chloride CS, cupric sulfate CS, and diluted hydrochloric acid.

Standard stock solution A: 2.4:0.6:0:7.0

Standard stock solution B: 2.4:1.0:0.4:6.2

Standard stock solution C: 9.6:0.2:0.2:0

Standard solutions: [NOTE—Prepare the *Standard solutions* immediately before use.]

Standard solution A: Transfer 2.5 mL of *Standard stock solution A* to a 100-mL volumetric flask, dilute with diluted hydrochloric acid to volume, and mix.

Standard solution B: Transfer 2.5 mL of *Standard stock solution B* to a 100-mL volumetric flask, dilute with diluted hydrochloric acid to volume, and mix.

Standard solution C: Transfer 0.75 mL of *Standard stock solution C* to a 100-mL volumetric flask, dilute with diluted hydrochloric acid to volume, and mix.

Sample solution: Use the *Sample solution* prepared in *Clarity of Solution*.

Analysis: Transfer a sufficient portion of the *Sample solution* to a sample tube of colorless, transparent, neutral glass, with a flat base and an internal diameter of 15–25 mm, to obtain a depth of 40 mm. Similarly transfer portions of *Standard solution A*, *Standard solution B*, *Standard solution C*, and water to separate matching sample tubes. Compare the *Sample solution*, *Standard solution A*, *Standard solution B*, *Standard solution C*, and water in diffused daylight, viewing vertically against a white background (see ▲*Visual Comparison ⟨630⟩*▲ (CN 1-May-2019)).

Acceptance criteria: The *Sample solution* is not more intensely colored than *Standard solution A*, *Standard solution B*, *Standard solution C*, or water.

• **CONDUCTIVITY**

Sample solution: 0.2 g/mL of Inositol in water (previously boiled and cooled to room temperature).

Apparatus: Use a conductivity meter or a resistivity meter that measures the resistance of the column of liquid between the electrodes of the immersed measuring device. The apparatus is supplied with alternating current to avoid the effects of electrode polarization. It is equipped with a temperature compensation device or a precision thermometer.

Reagents: Prepare three *Standard solutions* of potassium chloride containing 0.7455, 0.0746, and 0.0149 g, respectively, of potassium chloride per 1000.0 g of solution. These solutions should be prepared with water that has been previously boiled and cooled to room temperature and whose conductivity does not exceed 2 µS/cm. The conductivity and resistivity of these three solutions at 20° are provided in *Table 1*.

Table 1

Concentration of Solution (g/1000.0 g)	Conductivity (µS/cm)	Resistivity (Ω-cm)
0.7455	1330	752
0.0746	133.0	7519
0.0149	26.6	37,594

Calibration: Choose a conductivity cell that is appropriate for the conductivity of the solution to be examined. The higher the expected conductivity, the higher the cell constant that must be chosen. Commonly used conductivity cells have cell constants of the order 0.1, 1, and 10 cm^{-1}. Use a standard solution of potassium chloride that is appropriate for the measurement. The conductivity value of the standard solution of potassium chloride should be near the expected conductivity value of the *Sample solution*. Rinse the cell several times with water that has been previously boiled and cooled to room temperature, and rinse at least twice with the potassium chloride solution used for the determination of the cell constant of the conductivity cell. Measure the resistance of the conductivity cell, using the potassium chloride solution at 20 ± 0.1°.

Calculate the constant, in cm^{-1}, of the conductivity cell:

$$\text{Result} = R_{KCl} \times K_{KCl}$$

R_{KCl} = measured resistance, expressed in mega-ohms

K_{KCl} = conductivity of the standard solution of potassium chloride used, expressed in µS/cm. The measured constant of the conductivity cell must be within 5% of the given value.

Analysis: Rinse the conductivity cell several times with water that has been previously boiled and cooled to room temperature, and rinse at least twice with the *Sample solution*. Measure the conductivity of the *Sample solution*, while gently stirring with a magnetic stirrer.

Acceptance criteria: NMT 20 µS/cm

- **Water Determination, *Method I* ⟨921⟩:** NMT 0.5% determined on a 1.0-g sample

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers, and store at room temperature.
- **USP Reference Standards ⟨11⟩**
  USP Inositol RS
  USP Mannitol RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
INOSITOL	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 33(4)
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