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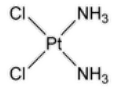
Cisplatin



$Cl_2H_6N_2Pt$ 300.05

Platinum, diamminedichloro-, (*SP*-4-2)-;

cis-Diamminedichloroplatinum CAS RN®: 15663-27-1; UNII: Q20Q21Q62J.

DEFINITION

Cisplatin contains NLT 98.0% and NMT 102.0% of cisplatin ($Cl_2H_6N_2Pt$), calculated on the anhydrous basis.

[**Caution—**Cisplatin is potentially cytotoxic. Great care should be taken to prevent inhaling particles and exposing the skin to it.]

IDENTIFICATION

Change to read:

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

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

ASSAY

• **Procedure**

Mobile phase: Ethyl acetate, methanol, dimethylformamide, and degassed water (25:16:5:5)

Standard solution: 1 mg/mL of USP Cisplatin RS in dimethylformamide. Use within 1 h.

Sample solution: 1 mg/mL of Cisplatin in dimethylformamide. Use within 1 h.

Chromatographic system

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

Mode: LC

Detector: UV 310 nm

Column: 4.0-mm × 30-cm; packing L8

Flow rate: 2.0 mL/min

Injection volume: 40 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cisplatin ($Cl_2H_6N_2Pt$) in the portion of Cisplatin taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• **Limit of Trichloroammineplatinate**

Mobile phase: 0.4 g/L of ammonium sulfate in water. Adjust with 6 N ammonium hydroxide to a pH of 5.9.

Standard solution: 6 µg/mL of USP Potassium Trichloroammineplatinate RS in saline TS. Protect the solution from light. Use the solution within 4 h.

Sample solution: 0.5 mg/mL of Cisplatin in saline TS. Completely dissolve by stirring by mechanical means for 30 min. Protect the solution from light. Use the solution within 4 h.

Chromatographic system

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

Mode: LC

Detector: UV 209 nm

Column: 4.6-mm × 25-cm; packing L14

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for saline and trichloroammineplatinate are about 0.4 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the saline and trichloroammineplatinate peaks

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of trichloroammineplatinate in the portion of Cisplatin taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak area of trichloroammineplatinate from the *Sample solution*

r_S = peak area of trichloroammineplatinate from the *Standard solution*

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

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

M_{r1} = molecular weight of trichloroammineplatinate, 318.48

M_{r2} = molecular weight of potassium trichloroammineplatinate, 357.58

Acceptance criteria: NMT 1.0%

• **Limit of Transplatin**

Mobile phase: 0.18 M monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.2.

Standard stock solution A: 0.05 mg/mL of USP Transplatin RS in saline TS. Dissolve by stirring by mechanical means for 30 min.

Standard stock solution B: Transfer 5 mL of *Standard stock solution A* to a 25-mL volumetric flask containing 12 mg of USP Cisplatin RS. Dilute with saline TS to volume, and stir by mechanical means for 30 min to dissolve.

System suitability stock solution: 0.05 mg/mL of USP Cisplatin RS in saline TS. Dissolve by stirring by mechanical means for 30 min.

System suitability solution: Transfer 10 mL each of *System suitability stock solution* and *Standard stock solution A* to a 50-mL volumetric flask. Add 5.0 mL of a solution (5 mg/mL) of thiourea (prepared fresh daily) and 5.0 mL of 1 N hydrochloric acid, and dilute with saline TS to volume. Place 10 mL of this solution in a suitable serum vial, seal with a polytef-lined closure, and heat in a heating block at 60 ± 0.5° for 60 min. Remove, and cool to room temperature.

Standard solution: Transfer 10 mL of *Standard stock solution B* to a 50-mL volumetric flask. Add 5.0 mL of a solution (5 mg/mL) of thiourea (prepared fresh daily) and 5.0 mL of 1 N hydrochloric acid, and dilute with saline TS to volume. Place 10 mL of this solution in a suitable serum vial, seal with a polytef-lined closure, and heat in a heating block at 60 ± 0.5° for 60 min. Remove, and cool to room temperature.

Sample stock solution: 0.5 mg/mL of Cisplatin in saline TS. Dissolve by stirring by mechanical means for 30 min.

Sample solution: Transfer 10 mL of *Sample stock solution* to a 50-mL volumetric flask. Add 5.0 mL of a solution (5 mg/mL) of thiourea (prepared fresh daily) and 5.0 mL of 1 N hydrochloric acid, and dilute with saline TS to volume. Place 10 mL of this solution in a suitable serum vial, seal with a polytef-lined closure, and heat in a heating block at 60 ± 0.5° for 60 min. Remove, and cool to room temperature.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L9

Column temperature: 45°

Flow rate: 2.0 mL/min

Injection volume: 20 µL

[NOTE—Condition the *Column* by pumping *Mobile phase* at a flow rate of 2.0 mL/min for 30 min, then at 0.5 mL/min for 30 min, and then again at 2.0 mL/min for 30 min.]

System suitability

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

[NOTE—The retention time for derivatized transplatin is between 5.0 and 9.0 min; or, if it is not, modify the *Mobile phase* as necessary, and recondition the *Column*. The relative retention times for derivatized cisplatin and derivatized transplatin are about 1.0 and 1.3, respectively.]

Suitability requirements

Resolution: NLT 1.7 between the derivatized cisplatin and derivatized transplatin peaks, *System suitability solution*

Relative standard deviation: NMT 4.0% for the derivatized transplatin peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of transplatin in the portion of Cisplatin taken:

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

r_U = peak area of derivatized transplatin from the *Sample solution*

r_S = peak area of derivatized transplatin from the *Standard solution*

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

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

Acceptance criteria: NMT 2.0%

• **UV PURITY RATIO**

Cleanse all glassware with a mixture of hydrochloric acid and nitric acid (3:1), rinse thoroughly with water, and dry before use. Do not use dichromate for cleaning. Do not use acetone or pressurized air for drying.

Sample: 98.5 ± 0.5 mg of ground Cisplatin

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: Maxima near 301 nm and minima near 246 nm

Cell: 2 cm

Blank: 0.1 N hydrochloric acid

Analysis: Transfer the *Sample* to a 100-mL volumetric flask, and add 0.1 N hydrochloric acid to volume. Using a clean magnetic stir bar, alternately stir at a high speed for 5 min and sonicate for 10 s until complete solution is effected, inverting the flask frequently to remove particles that may cling to the neck. Protect this solution from light, and use within 1 h of preparation. Obtain the absorption spectrum. Calculate the absorbance ratio as follows:

$$\text{Result} = A_{301}/A_{246}$$

A_{301} = absorbance at near 301 nm

A_{246} = absorbance at near 246 nm

Acceptance criteria: NLT 4.5

SPECIFIC TESTS

• **PLATINUM CONTENT**

Sample: 0.5 g of Cisplatin

Analysis: Ignite the *Sample* to constant weight at 800 ± 50°, and weigh the residue. The residue is platinum.

Calculate the platinum content in the portion of Cisplatin taken:

Result = $(W_U/W_S) \times 100$

W_U = weight of platinum

W_S = weight of the *Sample*

Acceptance criteria: 64.42%–65.22% on the anhydrous basis

- **Crystallinity** ⟨695⟩**:** Meets the requirements
- **Water Determination** ⟨921⟩, *Method I***:** NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Protect from light. Store at room temperature.
- **USP Reference Standards** ⟨11⟩

USP Cisplatin RS		
USP Potassium Trichloroammineplatinate RS	Cl_3H_3KNPt	357.58
USP Transplatin RS		

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

Topic/Question	Contact	Expert Committee
CISPLATIN	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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