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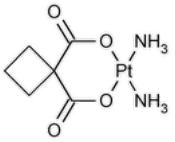
Carboplatin



$C_6H_{12}N_2O_4Pt$ 371.25

Platinum, diammine[1,1-cyclobutanedicarboxylato(2-)- *O,O′*]-, (*SP*-4-2);

cis-Diammine(1,1-cyclobutanedicarboxylato)platinum CAS RN®: 41575-94-4; UNII: BG3F62OND5.

DEFINITION

Carboplatin contains NLT 98.0% and NMT 102.0% of carboplatin ($C_6H_{12}N_2O_4Pt$), calculated on the dried basis.

[**Caution—**Great care should be taken in handling Carboplatin because it is a suspected carcinogen.]

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K
- **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: Acetonitrile and water (87:13)

Standard solution: 1 mg/mL of USP Carboplatin RS in water. Use it within 2 h.

Sample solution: 1 mg/mL of Carboplatin in water. Use it within 2 h.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L8

Flow rate: 2.0 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 1.2%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of carboplatin ($C_6H_{12}N_2O_4Pt$) in the portion of Carboplatin 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 Carboplatin RS in the *Standard solution* (mg/mL)

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

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

OTHER COMPONENTS

- **Platinum Content**

Sample: 0.2 g of Carboplatin, from *Loss on Drying*

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 Carboplatin taken:

$$\text{Result} = (W_U/W_S) \times 100$$

W_U = weight of platinum

W_S = weight of *Sample*

Acceptance criteria: 52.0%–53.0% on the dried basis

IMPURITIES

Change to read:

• **Limit of 1,1-Cyclobutanedicarboxylic Acid**

Solution A: Dissolve 8.5 g of tetrabutylammonium hydrogen sulfate in 80 mL of water. Add 3.4 mL of phosphoric acid, and adjust with 10 N sodium hydroxide to a pH of 7.55.

Mobile phase: Acetonitrile, *Solution A*, and water (100:20:880)

Standard solution: 5 µg/mL of 1,1-cyclobutanedicarboxylic acid in *Mobile phase*

System suitability solution: 2.5 µg/mL of 1,1-cyclobutanedicarboxylic acid and 0.5 mg/mL of Carboplatin in *Mobile phase* prepared as follows. Mix 1.0 mL of *Standard solution* with 1.0 mL of *Standard solution* in the *Assay*.

Sample solution: 1 mg/mL of Carboplatin in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: ▲3.9-mm▲ (ERR 1-Jan-2022) × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 100 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for carboplatin and 1,1-cyclobutanedicarboxylic acid are 0.65 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.5 between the carboplatin and 1,1-cyclobutanedicarboxylic acid peaks

Relative standard deviation: NMT 10%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of 1,1-cyclobutanedicarboxylic acid in the portion of Carboplatin taken:

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

r_U = peak response of 1,1-cyclobutanedicarboxylic acid from the *Sample solution*

r_S = peak response of 1,1-cyclobutanedicarboxylic acid from the *Standard solution*

C_S = concentration of 1,1-cyclobutanedicarboxylic acid in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 0.5%

• **Organic Impurities**

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

Diluted standard solution: 2.5 µg/mL of USP Carboplatin RS in water, from the *Standard solution*

Chromatographic system: Proceed as directed in the *Assay*, and the run time is at least 2.5 times the retention time of the carboplatin peak.

Analysis

Samples: *Sample solution* and *Diluted standard solution*

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

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

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

r_S = peak response of carboplatin from the *Diluted standard solution*

C_S = concentration of USP Carboplatin RS in the *Diluted standard solution* (mg/mL)

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

Acceptance criteria: See *Table 1*. Disregard any peak less than 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cisplatin[a]	0.3	0.25
Carboplatin	1.0	—
Any individual unspecified impurity	—	0.25
Total impurities	—	0.5

[a] *cis*-Diamminedichloroplatinum(II).

SPECIFIC TESTS

- **Crystallinity ⟨695⟩:** Meets the requirements
- **pH ⟨791⟩**
  Sample solution: 10 mg/mL in water
  Acceptance criteria: 5.0–7.0
- **Loss on Drying ⟨731⟩**
  Sample: 1 g
  Analysis: Dry the *Sample* at 105° to constant weight.
  Acceptance criteria: NMT 0.5%
- **Transmittance**
  Sample solution: 10 mg/mL of Carboplatin in water
  Analysis: Determine the percent transmittance in 1-cm cells at a wavelength of 440 nm, using water as the blank.
  Acceptance criteria: NLT 97%
- **Water-Insoluble Matter**
  Sample: 1 g
  Analysis: Transfer the *Sample* to a 150-mL beaker. Add 100 mL of water, and dissolve by stirring with a stirring bar for 30 min. With the aid of suction, pass through a tared filtering crucible. Rinse the beaker with water, and transfer the rinsings to the crucible. Dry the crucible at 130 ± 10° to constant weight.
  Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

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

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

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

Chromatographic Database Information: Chromatographic Database

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