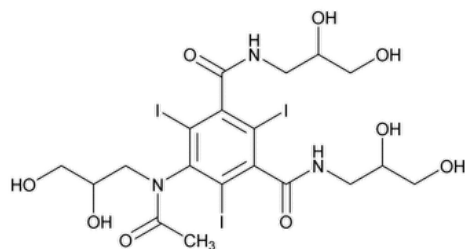


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Iohexol



$C_{19}H_{26}I_3N_3O_9$ 821.14

1,3-Benzenedicarboxamide, 5-[acetyl(2,3-dihydroxypropyl)amino]-*N,N'*-bis(2,3-dihydroxypropyl)-2,4,6-triiodo;

N,N'-Bis(2,3-dihydroxypropyl)-5-[*N*-(2,3-dihydroxypropyl)acetamido]-2,4,6-triiodoisophthalamide CAS RN®: 66108-95-0; UNII: 4419T9MX03.

DEFINITION

Iohexol contains NLT 98.0% and NMT 102.0% of iohexol ($C_{19}H_{26}I_3N_3O_9$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **B.** The retention times of the two principal peaks of the *Sample solution* correspond to those of the *System suitability solution*, as obtained in the test for *Organic Impurities*.

ASSAY

PROCEDURE

Sample: 500 mg of Iohexol

Sample solution: Transfer the *Sample* to a glass-stoppered, 125-mL conical flask. Add 25 mL of 1.25 N [sodium hydroxide](#) and 500 mg of powdered [zinc](#). Connect the flask to a reflux condenser, and reflux for 1 h. Cool the flask to room temperature, rinse the condenser with 20 mL of [water](#), disconnect the flask from the condenser, and pass the mixture through a filter. Rinse the flask and the filter thoroughly with small portions of [water](#), adding the rinsings to the filtrate. Add 5 mL of [glacial acetic acid](#).

Titrimetric system

(See [Titrimetry \(541\)](#).)

Mode: Direct titration

Titrant: [0.1 N silver nitrate VS](#)

Endpoint detection: Potentiometric

Analysis: Titrate the *Sample solution* with *Titrant*.

Calculate the percentage of iohexol ($C_{19}H_{26}I_3N_3O_9$) in the portion of Iohexol taken:

$$\text{Result} = [(V \times N \times F)/W] \times 100$$

V = *Titrant* volume consumed by the *Sample* (mL)

N = *Titrant* normality (mEq/mL)

F = equivalent weight of iohexol, 273.7 mg/mEq

W = *Sample* weight (mg)

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

IMPURITIES

- **LIMIT OF IONIC COMPOUNDS**

Rinse all glassware five times with distilled water.

Standard solution: 0.002 mg/mL of sodium chloride in [water](#)

Sample solution: 1 g of Iohexol in 50 mL of [water](#)

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The specific conductance of the *Sample solution* is NMT that of the *Standard solution* (equivalent to 0.01% ionic compounds as sodium chloride).

Change to read:

• LIMIT OF FREE IODIDE

Sample: 5 g of Iohexol

Sample solution: Dissolve the *Sample* in 20 mL of [water](#).

Titrimetric system

(See [Titrimetry \(541\)](#).)

Mode: Direct titration

Titrant: 0.001 N [silver nitrate](#) ▲ (USP 1-Dec-2021)

Endpoint detection: Potentiometric

Analysis: Calculate the percentage of free iodide in the portion of Iohexol taken:

$$\text{Result} = [(V \times N \times F)/W] \times 100$$

V = *Titrant* volume consumed by the *Sample* (mL)

N = *Titrant* normality (mEq/mL)

F = equivalent weight of iodide, 126.9 mg/mEq

W = *Sample* weight (mg)

Acceptance criteria: NMT 0.001%

• ORGANIC IMPURITIES

Solution A: [Acetonitrile](#)

Solution B: [Water](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	1	99
60	13	87

System suitability solution: 1.5 mg/mL of [USP Iohexol RS](#) and 0.0075 mg/mL of [USP Iohexol Related Compound A RS](#) in [water](#)

Sample solution: 1.5 mg/mL of Iohexol

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 10 μL

System suitability

Sample: *System suitability solution*

[NOTE—Iohexol may give two nonresolved peaks due to exo–endo isomerism. In addition, a small peak due to Iohexol usually appears at the leading edge of the first principal peak. This small peak has a retention time about 1.2 min less than the first principal peak. The relative retention times for the Iohexol related compound A, Iohexol endo-isomer, Iohexol exo-isomer, and O-alkylated compounds peaks are 0.85, 0.96, 1.0, and 1.1–1.4, respectively.]

Suitability requirements