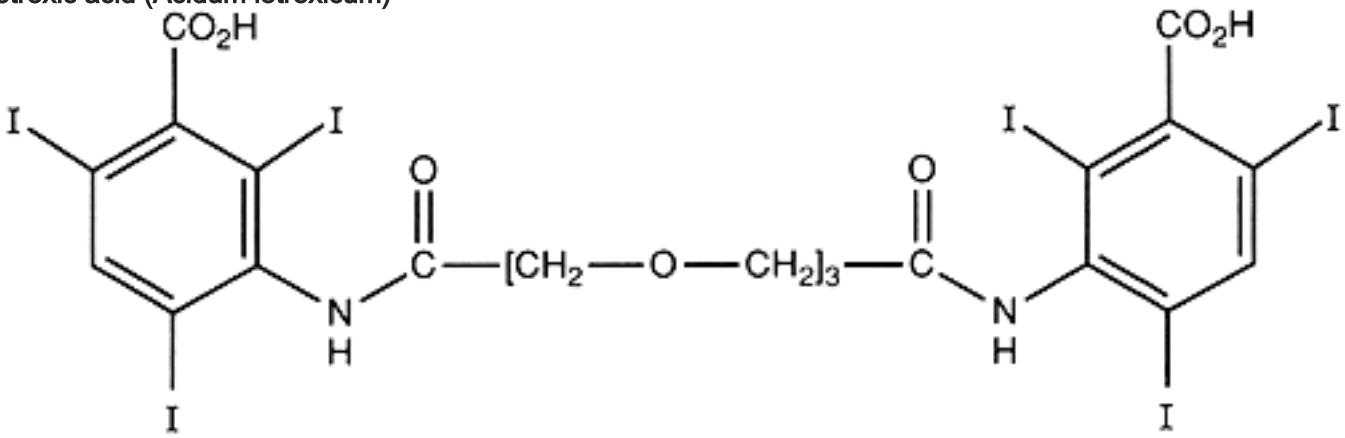
Iotroxic acid (Acidum iotroxicum)



$C_{22}H_{18}I_6N_2O_9$

Relative molecular mass. 1215.8

Chemical name. 3,3'-[Oxybis(ethyleneoxymethylenecarbonylimino)]bis[2,4,6-triiodobenzoic acid]; 3,3'-[oxybis[2,1-ethanediyloxy(1-oxo-2,1-ethanediyl)imino]]-bis[2,4,6,-triiodobenzoic acid]; CAS Reg. No. 51022-74-3.

Description. An almost white powder.

Solubility. Practically insoluble in water, benzene R, and ether R; freely soluble in methanol R and dimethylformamide R; dissolves in solutions of alkali hydroxides.

Category. Used in the preparation of meglumine iotroxate as a radiocontrast medium.

Storage. Iotroxic acid should be kept in a well-closed container, protected from light.

Requirements

Iotroxic acid contains not less than **98.0%** and not more than the equivalent of **102.0%** of $C_{22}H_{18}I_6N_2O_9$, calculated with reference to the anhydrous substance.

Identity tests

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from iotroxic acid RS or with the *reference spectrum* of iotroxic acid.

B. Heat 0.05 g with 2 mL of sulfuric acid (~1760 g/l) TS in a suitable crucible; violet vapours are evolved.

Heavy metals. For the preparation of the test solution use 1.0 g, add 3 mL of meglumine (100 g/l) TS, and proceed as described under 2.2.3 Limit test for heavy metals, Procedure 1; determine the heavy metals content according to Method A; not more than 10 µg/g.

Halides. Dissolve 10 g in 30 mL of meglumine (100 g/l) TS and titrate potentiometrically with silver nitrate (0.001 mol/l) VS. Each mL of silver nitrate (0.001 mol/l) VS is equivalent to 0.1269 mg of I; the content of halides, expressed as iodides, does not exceed 40 µg/g.

Solution in alkali. Dissolve 5 g in 5 mL of sodium hydroxide (~80 g/l) TS and add 2 mL of water; the solution is not more intensely coloured than standard colour solution Yw2 when compared as described under 1.11 Colour of liquids.

Sulfated ash. Not more than 1.0 mg/g.

Water. Determine as described under 2.8 Determination of water by the Karl Fischer method, Method A, using 0.4 g; the water content is not less than 10 mg/g and not more than 30 mg/g.

Foreign substances. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R6 as the coating substance and a mixture of 62 volumes of chloroform R, 32 volumes of methanol R, 2 volumes of anhydrous formic acid R, and 6 volumes of water as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in methanol R containing (A) 0.1 g of Iotroxic acid per mL and (B) 0.5 mg of Iotroxic acid per mL. After removing the plate from the chromatographic chamber, allow it to dry in a current of air at room temperature, and examine the chromatogram in ultraviolet light (254 nm).

Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B.

Primary aromatic amines. Transfer about 1 g, accurately weighed, to a 50-mL volumetric flask, dissolve in 2.5 mL of sodium hydroxide (1 mol/l) VS, and add 12.5 mL of water (= *solution A*). Dissolve 5 mg of 3-amino-2,4,6-triiodobenzoic acid RS in 0.2 mL of sodium hydroxide (0.1 mol/l) VS and dilute with sufficient water to produce 10 mL. Introduce 2 mL of this solution to a 50-mL volumetric flask and add 3 mL of water and 10 mL of sodium hydroxide (0.1 mol/l) VS (= *solution B*). For the blank solution, transfer 5 mL of water to a 50-mL volumetric flask and add 10 mL of sodium hydroxide (0.1 mol/l) VS.

Note: Strictly observe the instructions and proceed without delay using the three solutions concurrently.

Add 25 mL of dimethyl sulfoxide R to each solution, close the flasks, and swirl to mix. Place them in the dark in an ice-bath and allow to stand for 5 minutes. Continue the procedure in the dark. Add while shaking 2 mL of hydrochloric acid (~420 g/l) TS and allow to stand again in the ice-bath for 5 minutes. Add while shaking 2 mL of freshly prepared sodium nitrite (20 g/l) TS. Using a stopwatch readable to 1 second, start the timing and allow to stand in the ice-bath for exactly 5 minutes. Add 1 mL of freshly prepared sulfamic acid (80 g/l) TS, start the timing again, shake until no more gas evolves, and allow to stand in the ice-bath for exactly 5 minutes. Continue to add 2 mL of freshly prepared *N*-(1-naphthyl)ethylenediamine hydrochloride/propylene glycol TS, allow to stand in a water-bath at 22-25 °C for exactly 10 minutes, and dilute to volume with water.

Proceed immediately with the measurement of the absorbances of solutions A and B against the blank solution at a wavelength of about 465 nm. The absorbance of solution A does not exceed that of solution B.

Assay. Carry out the combustion as described under 2.4 Oxygen flask method, but using about 4 mg of Iotroxic acid, accurately weighed, and allowing the absorbing liquid after rinsing to stand for 20-30 minutes. Titrate the liberated iodine with sodium thiosulfate (0.02 mol/l) VS.

Each mL of sodium thiosulfate (0.02 mol/l) VS is equivalent to 0.6754 mg of $C_{22}H_{18}I_6N_2O_9$.

Additional requirement for Iotroxic acid for parenteral use

Complies with the monograph for "Parenteral preparations".

Pyrogens. Carry out the test as described under 3.5 Test for pyrogens, injecting, per kg of the rabbit's mass, a solution in sterile water R containing 0.6 g of Iotroxic acid in not more than 5 mL.

Additional requirement for Iotroxic acid for sterile use

Complies with 3.2 Test for sterility.