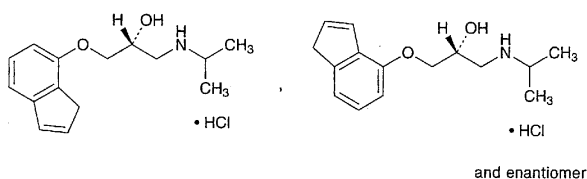


Indenolol Hydrochloride

塩酸インデノロール



$C_{15}H_{21}NO_2 \cdot HCl$: 283.79

(*RS*)-1-(3*H*-Inden-4-yloxy)-3-isopropylaminopropan-2-ol monohydrochloride

(*RS*)-1-(3*H*-Inden-7-yloxy)-3-isopropylaminopropan-2-ol monohydrochloride [68906-88-7]

Indenolol Hydrochloride is a mixture of 1-(7-indenyloxy)-3-isopropylamino-2-propanol monohydrochloride and 1-(4-indenyloxy)-3-isopropylamino-2-propanol monohydrochloride.

When dried, it contains not less than 98.5% of $C_{15}H_{21}NO_2 \cdot HCl$.

Description Indenolol Hydrochloride occurs as white to pale yellow crystals or crystalline powder.

It is freely soluble in water and in acetic acid (100), soluble in ethanol (95) and in chloroform, slightly soluble in acetic anhydride, very slightly soluble in ethyl acetate, and practically insoluble in diethyl ether.

The pH of a solution of Indenolol Hydrochloride (1 in 10) is between 3.5 and 5.5.

It is colored by light.

Identification (1) Dissolve 0.1 g of Indenolol Hydrochloride in 1 to 2 drops of dilute hydrochloric acid and 5 mL of water, and add 1 mL of Reinecke salt TS: a red-purple precipitate is formed.

(2) Determine the absorption spectrum of a solution of Indenolol Hydrochloride (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, determine the absorption spectrum of a solution of Indenolol Hydrochloride (1 in 10,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 2: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Determine the infrared absorption spectrum of Indenolol Hydrochloride, previously dried, as directed in the potassium chloride disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(4) A solution of Indenolol Hydrochloride (1 in 10) responds to the Qualitative Tests for chloride.

Absorbance $E_{1cm}^{1\%}$ (250 nm): 330 – 340 (after drying, 0.01 g, water, 1000 mL).

Melting point 140 – 143°C

Purity (1) Clarity and color of solution—Dissolve 1.0 g

of Indenolol Hydrochloride in 10 mL of water: the solution is clear and colorless to pale yellow.

(2) Heavy metals—Proceed with 1.0 g of Indenolol Hydrochloride according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(3) Arsenic—Prepare the test solution with 1.0 g of Indenolol Hydrochloride according to Method 1, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.20 g of Indenolol Hydrochloride in 10 mL of chloroform, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add chloroform to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of 1,2-dichloroethane, ethanol (99.5) and ammonia solution (28) (70:15:2) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying Not more than 0.5% (1 g, in vacuum, phosphorus (V) oxide, 4 hours).

Residue on ignition Not more than 0.10% (1 g).

Isomer ratio Dissolve 5 mg of Indenolol Hydrochloride in 1.0 mL of a mixture of ethyl acetate and dehydrated trifluoroacetic acid (9:1), and use this solution as the sample solution. Perform the test with 2 μ L of the sample solution as directed under the Gas Chromatography according to the following conditions. Determine the areas of two adjacent peaks, A_a and A_b , having the retention times of about 16 minutes, where A_a is the peak area of shorter retention time and A_b is the peak area of longer retention time: the ratio $A_a/(A_a + A_b)$ is between 0.6 and 0.7.

Operating conditions—

Detector: A hydrogen flame-ionization detector.

Column: A glass column about 2 mm in inside diameter and about 2 m in length, packed with siliceous earth for gas chromatography (150 to 180 μ m in particle diameter) coated with 65% phenyl-methyl silicon polymer for gas chromatography at the ratio of 2%.

Column temperature: A constant temperature between 150°C and 170°C.

Carrier gas: Helium.

Flow rate: Adjust the flow rate so that the retention time of the peak showing earlier elution of the two peaks of indenolol hydrochloride is about 16 minutes.

Selection of column: Proceed with 2 μ L of the sample solution under the above operating conditions, and calculate the resolution. Use a column with the resolution between the two peaks being not less than 1.1.

Assay Weigh accurately about 0.5 g of Indenolol Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (4:1), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue to green (indicator: 3 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

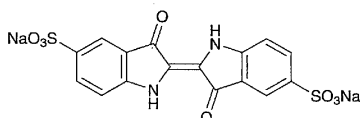
Each mL of 0.1 mol/L perchloric acid VS
= 28.380 mg of $C_{15}H_{21}NO_2 \cdot HCl$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Indigocarmine

インジゴカルミン



$C_{16}H_8N_2Na_2O_8S_2$: 466.35

Disodium 3,3'-dioxo-[4^{2,2'}-biindoline]-5,5'-disulfonate
[860-22-0]

Indigocarmine, when dried, contains not less than 95.0% of $C_{16}H_8N_2Na_2O_8S_2$.

Description Indigocarmine occurs as blue to dark blue powder or granules. It is odorless.

It is sparingly soluble in water, and practically insoluble in ethanol (95) and in diethyl ether.

It is hygroscopic.

When compressed, it has a coppery luster.

Identification (1) A solution of Indigocarmine (1 in 100) is dark blue in color. Perform the following tests with this solution as the sample solution: the dark blue color of each solution disappears.

(i) Add 1 mL of nitric acid to 2 mL of the sample solution;

(ii) Add 1 mL of bromine TS to 2 mL of the sample solution;

(iii) Add 1 mL of chlorine TS to 2 mL of the sample solution;

(iv) Add 2 mL of sodium hydroxide TS and 0.2 g of zinc powder to 2 mL of the sample solution, and warm.

(2) Dissolve 0.1 g of Indigocarmine in 100 mL of a solution of ammonium acetate (1 in 650). To 1 mL of the solution add a solution of ammonium acetate (1 in 650) to make 100 mL. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Ignite 1 g of Indigocarmine to carbonize. After cooling, add 20 mL of water to the residue, shake, and filter the mixture: the filtrate responds to the Qualitative Tests for sodium salt and for sulfate.

pH Dissolve 0.10 g of Indigocarmine in 20 mL of water: the pH of the solution is between 5.0 and 6.0.

Purity (1) Water-insoluble substances—To 1.00 g of Indigocarmine add 200 mL of water, shake, and filter through a tared glass filter (G4). Wash the residue with water until the blue color of the filtrate becomes practically colorless, and dry the residue at 105°C for 4 hours: the mass of the

residue does not exceed 5.0 mg.

(2) Arsenic—Place 0.8 g of Indigocarmine in a Kjeldahl flask, add 5 mL of sulfuric acid and 5 mL of nitric acid, and ignite gently. Repeat the addition of 2 to 3 mL of nitric acid occasionally, and continue to heat until a colorless to light yellow solution is obtained. After cooling, add 15 mL of a saturated ammonium oxalate solution, heat the solution until dense white fumes are evolved, and concentrate to 2 to 3 mL. After cooling, dilute with water to 10 mL, and perform the test using Apparatus B with 5 mL of this solution as the test solution (not more than 5 ppm).

Loss on drying Not more than 10.0% (1 g, 105°C, 2 hours).

Residue on ignition Not less than 28.0% and not more than 38.0% (after drying, 1 g).

Assay Weigh accurately about 0.5 g of Indigocarmine, previously dried, add 15 g of sodium hydrogen tartrate monohydrate, and dissolve in 200 mL of water, boil with bubbling of a stream of carbon dioxide, and titrate, while being hot, with 0.1 mol/L titanium (III) chloride VS until the color of the solution changes from blue through yellow to orange.

Each mL of 0.1 mol/L titanium (III) chloride VS
= 23.318 mg of $C_{16}H_8N_2Na_2O_8S_2$

Containers and storage Containers—Tight containers.
Storage—Light-resistant.

Indigocarmine Injection

インジゴカルミン注射液

Indigocarmine Injection is an aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of indigocarmine ($C_{16}H_8N_2Na_2O_8S_2$: 466.35).

Method of preparation Prepare as directed under Injection, with Indigocarmine.

Description Indigocarmine Injection is a dark blue liquid.
pH: 3.0 – 5.0

Identification (1) To a volume of Indigocarmine Injection, equivalent to 0.02 g of Indigocarmine according to the labeled amount, add 1 mL of nitric acid: the dark blue color of the liquid disappears, and a yellow-brown color develops.

(2) To a volume of Indigocarmine Injection, equivalent to 0.02 g of Indigocarmine according to the labeled amount, add 1 mL of bromine TS: the dark blue color disappears, and a yellow-brown color develops.

(3) To a volume of Indigocarmine Injection, equivalent to 0.02 g of Indigocarmine according to the labeled amount, add 1 mL of chlorine TS: the dark blue color disappears, and a yellow-brown color develops.

(4) To a volume of Indigocarmine Injection, equivalent to 0.01 g of Indigocarmine according to the labeled amount, add ammonium acetate solution (1 in 650) to make 1000 mL, and determine the absorbance of the solution as directed under the Ultraviolet-visible Spectrophotometry: it ex-