Indometacin Capsules

インドメタシンカプセル

Indometacin Capsules contain not less than 90% and not more than 110% of the labeled amount of indometacin ($C_{19}H_{16}ClNO_4$: 357.79).

Method of preparation Prepare as directed under Capsules, with Indometacin.

Identification Powder the contents of Indometacin Capsules. To a quantity of the powder, equivalent to 0.1 g of Indometacin according to the labeled amount, add 20 mL of chloroform, shake well, and centrifuge. Filter the supernatant liquid, and evaporate the filtrate to dryness. After cooling, dissolve the residue in 20 mL of methanol. To 10 mL of this solution add methanol to make 50 mL, then to 2 mL of this solution add methanol to make 100 mL, and use this solution as the sample solution. Determine the absorption spectrum of the sample solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 317 nm and 321 nm.

Purity Related substances—Powder the content of Indometacin Capsules. To a quantity of the powder, equivalent to 0.10 g of Indometacin according to the labeled amount, add exactly 10 mL of methanol, shake well, filter, and use the filtrate as the sample solution. Dissolve 0.025 g of Indometacin Reference Standard in methanol to make exactly 50 mL. Pipet 1 mL of the solution, add methanol to make exactly 10 mL, and use this solution as the standard solution. Proceed as directed in the Purity (4) under Indometacin.

Dissolution test Take 1 capsule of Indometacin Capsules, and perform the test using 900 mL of a mixture of water and phosphate buffer solution, pH 7.2, (4:1) as the test solution at 100 revolutions per minute as directed in Method 1 under the Dissolution Test. Take 20 mL or more of the dissolved solution at 20 minutes after starting the test, and filter through a membrane filter (less than 0.8 μm in pore size). Discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.03 g of Indometacin Reference Standard, previously dried at 105°C for 4 hours, dissolve in a mixture of water and phosphate buffer solution, pH 7.2, (4:1) to make exactly 1000 mL, and use this as the standard solution. Determine the absorbances, A_T and A_S, of the sample solution and the standard solution at 320 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Indometacin Capsules in 20 minutes should be not less than 75%.

Dissolution rate (%) with respect to the labeled amount of indometacin ($C_{19}H_{16}ClNO_4$)

$$= W_S \times \frac{A_T}{A_S} \times \frac{90}{C}$$

W_S: Amount (mg) of Indometacin Reference Standard.
C: Labeled amount (mg) of indometacin ($C_{19}H_{16}ClNO_4$) in 1 capsule.

Assay Weigh accurately the contents of not less than 20 Indometacin Capsules. Powder the combined contents, and weigh accurately a portion of the powder, equivalent to about 0.05 g of indometacin ($C_{19}H_{16}ClNO_4$). Dissolve in 40 mL of methanol, and add methanol to make exactly 50 mL. Filter this solution, discarding the first 10-mL portion of the filtrate. Pipet the subsequent 5 mL of the filtrate, add exactly 3 mL of the internal standard solution, add the mobile phase to make 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of Indometacin Reference Standard, previously dried at 105°C for 4 hours, and dissolve in methanol to make exactly 50 mL. Pipet 5 mL of the solution, add exactly 3 mL of the internal standard solution, add the mobile phase to make 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of indometacin to that of the internal standard, respectively.

Amount (mg) of indometacin ($C_{19}H_{16}ClNO_4$)

$$= \text{amount (mg) of Indometacin Reference Standard} \times \frac{Q_T}{Q_S}$$

Internal standard solution—A solution of butyl parahydroxybenzoate in methanol (1 in 1000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (7 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: A mixture of methanol and diluted phosphoric acid (1 in 1000) (7:3).

Flow rate: Adjust the flow rate so that the retention time of indometacin is about 8 minutes.

System suitability—

System performance: Dissolve 0.050 g of 4-chlorobenzoic acid, 0.030 g of butyl parahydroxybenzoate and 0.050 g of indometacin in 50 mL of methanol. To 5 mL of this solution add the mobile phase to make 100 mL. When the procedure is run with 20 μL of this solution under the above operating conditions, 4-chlorobenzoic acid, butyl parahydroxybenzoate and indometacin are eluted in this order, with the resolution between the peaks of 4-chlorobenzoic acid and butyl parahydroxybenzoate being not less than 2.0, and between the peaks of butyl parahydroxybenzoate and indometacin being not less than 5.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of indometacin to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.