

Norethisterone 5 mg and Mestranol 0.05 mg Tablets

Dissolution <6.10> Perform the test with 1 tablet of Norethisterone 5 mg and Mestranol 0.05 mg Tablets at 100 revolutions per minute according to the Paddle method, using 900 mL of a solution, prepared by adding water to 1 g of polysorbate 80 to make 1000 mL, as the dissolution medium. Withdraw not less than 20 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 µm. Discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 28 mg of Norethisterone RS, previously dried in vacuum with silica gel for 4 hours, dissolve in methanol to make exactly 50 mL, and use this solution as the standard stock solution (1). Further, weigh accurately about 28 mg of Mestranol RS, previously dried at 105°C for 3 hours, and dissolve in methanol to make exactly 100 mL. Pipet 2 mL of this solution, add methanol to make exactly 100 mL, and use this solution as the standard stock solution (2). Pipet 2 mL each of the standard stock solution (1) and the standard stock solution (2), add a solution, prepared by adding water to 1 g of polysorbate 80 to make 1000 mL, to make exactly 200 mL, and use this solution as the standard solution. Perform the test with 100 µL each of the sample solution and standard solution as directed under Liquid Chromatography <2.01> according to the following conditions, and determine the peak areas, A_{T_a} and A_{S_a} , of norethisterone, and the peak areas, A_{T_b} and A_{S_b} , of mestranol in each solution.

The requirements are met if Norethisterone 5 mg and Mestranol 0.05 mg Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of norethisterone ($C_{20}H_{26}O_2$)

$$= M_{S_a} \times A_{T_a} / A_{S_a} \times 1 / C_a \times 18$$

Dissolution rate (%) with respect to the labeled amount of mestranol ($C_{21}H_{26}O_2$)

$$= M_{S_b} \times A_{T_b} / A_{S_b} \times 1 / C_b \times 9 / 50$$

M_{S_a} : Amount (mg) of Norethisterone RS

M_{S_b} : Amount (mg) of Mestranol RS

C_a : Labeled amount (mg) of norethisterone ($C_{20}H_{26}O_2$) in 1 tablet

C_b : Labeled amount (mg) of mestranol ($C_{21}H_{26}O_2$) in 1 tablet

Operating conditions —

Detector: Norethisterone — An ultraviolet absorption photometer (wavelength: 244 nm).

Mestranol — A fluorophotometer (wavelength: excitation wavelength 281 nm, fluorescence wavelength: 302 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 µm in particle diameter).

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

Mobile phase: A mixture of acetonitrile and water (3:2).

Flow rate: Adjust the flow rate so that the retention time of norethisterone is about 3 minutes.

System suitability —

System performance: When the procedure is run with 100 µL of the standard solution under the above operating conditions, the numbers of theoretical plates and the symmetry factors of the peaks of norethisterone and mestranol are not less than 3000 and not more than 2.0, and not less than 3000 and not more than 1.5, respectively.

System repeatability: When the test is repeated 6 times with 100 µL of the standard solution according to the above operating conditions, the relative standard deviations of the peak areas of norethisterone and mestranol are not more than 2.0% and not more than 3.0%, respectively.

Dissolution Requirements

	Labeled amount	Specified minute	Dissolution rate
Norethisterone	5 mg	45 minutes	Not less than 70%
Mestranol	0.05 mg	45 minutes	Not less than 70%

Norethisterone RS Norethisterone (JP). When dried, it contains not less than 99.0% of norethisterone (C₂₀H₂₆O₂).