

### Phenytoin 67 mg and Phenobarbital 33 mg Tablets

**Dissolution** <6.10> Perform the test with 1 tablet of Phenytoin 67 mg and Phenobarbital 33 mg Tablets at 100 revolutions per minute according to the Paddle method, using 900 mL of a solution, prepared by adding 1000 mL of water to 3 g of polysorbate 80, as the dissolution medium. Start the test, withdraw 20 mL of the medium at the specified minute after starting the test, and immediately fill up the dissolution medium with exactly 20 mL of a solution, prepared by adding 1000 mL of water to 3 g of polysorbate 80, previously warmed to  $37 \pm 0.5^\circ\text{C}$ , carefully. Filter the media withdrawn through a membrane filter with a pore size not exceeding  $0.45 \mu\text{m}$ . Discard the first 10 mL of the filtrate, pipet  $V$  mL of the subsequent filtrate, add a solution, prepared by adding 1000 mL of water to 1 g of polysorbate 80, to make exactly  $V'$  mL, so that each mL contains about  $70 \mu\text{g}$  of phenytoin ( $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2$ ) and about  $40 \mu\text{g}$  of phenobarbital ( $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_3$ ) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 19 mg of Phenytoin RS, previously dried at  $105^\circ\text{C}$  for 2 hours, dissolve in methanol to make exactly 50 mL, and use this solution as the standard stock solution (1). Weigh accurately about 19 mg of Phenobarbital RS, previously dried at  $105^\circ\text{C}$  for 2 hours, dissolve in methanol to make exactly 100 mL, and use this solution as the standard stock solution (2). Pipet 10 mL each of the standard stock solution (1) and the standard stock solution (2), add a solution, prepared by adding 1000 mL of water to 3 g of polysorbate 80, to make exactly 50 mL, and use this solution as the standard solution. Perform the test with exactly  $20 \mu\text{L}$  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,  $A_{\text{Ta}(n)}$  and  $A_{\text{Sa}}$ , of phenytoin and,  $A_{\text{Tb}(n)}$  and  $A_{\text{Sb}}$ , of phenobarbital of both solutions.

The requirements are met if Phenytoin 67 mg and Phenobarbital 33 mg Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of phenytoin ( $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2$ ) on the  $n$ th dissolution medium withdrawing ( $n=1,3$ )

$$= M_{\text{Sa}} \times \left\{ \frac{A_{\text{Ta}(n)}}{A_{\text{Sa}}} + \sum_{i=1}^{n-1} \left( \frac{A_{\text{Ta}(i)}}{A_{\text{Sa}}} \times \frac{1}{45} \right) \right\} \times \frac{V'}{V} \times \frac{1}{C_a} \times 360$$

Dissolution rate (%) with respect to the labeled amount of phenobarbital ( $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_3$ ) on the  $n$ th dissolution medium withdrawing ( $n=2$ )

$$= M_{\text{Sa}} \times \left\{ \frac{A_{\text{Tb}(n)}}{A_{\text{Sb}}} + \sum_{i=1}^{n-1} \left( \frac{A_{\text{Tb}(i)}}{A_{\text{Sb}}} \times \frac{1}{45} \right) \right\} \times \frac{V'}{V} \times \frac{1}{C_b} \times 180$$

$M_{\text{Sa}}$ : Amount (mg) of Phenytoin RS

$M_{\text{SB}}$ : Amount (mg) of Phenobarbital RS

$C_{\text{a}}$ : Labeled amount (mg) of phenytoin ( $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2$ ) in 1 tablet

$C_{\text{b}}$ : Labeled amount (mg) of phenobarbital ( $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_3$ ) in 1 tablet

*Operating conditions—*

Detector: An ultraviolet absorption photometer (wavelength: 258 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  $\mu\text{m}$  in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 3.58 g of disodium hydrogen phosphate dodecahydrate in 900 mL of water, adjust the pH to 3.0 with diluted phosphoric acid (1 in 5), and add water to make 1000 mL. To 450 mL of this solution add 550 mL of methanol.

Flow rate: Adjust the flow rate so that the retention time of phenytoin is about 5 minutes.

*System suitability—*

System performance: When the procedure is run with 20  $\mu\text{L}$  of the standard solution under the above operating conditions, phenobarbital and phenytoin are eluted in this order with the resolution between these peaks being not less than 2.0.

System repeatability: When the test is repeated 6 times with 20  $\mu\text{L}$  of the standard solution under the above operating conditions, the relative standard deviations of the peak areas of phenobarbital and phenytoin are not more than 2.0%, respectively.

Dissolution Requirements

		Labeled amount	Specified minute	Dissolution rate
Phenytoin	67 mg		10 minutes	Not more than 70%
			120 minutes	Not less than 70%
Phenobarbital	33 mg		15 minutes	Not less than 85%

**Phenytoin RS** Phenytoin (JP).

**Phenobarbital RS** Phenobarbital (JP).