Digoxin Tablets

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Digoxin Tablets contain not less than 90% and not more than 110% of the labeled amount of digoxin ($C_{41}H_{64}O_{14}$: 780.94).

Method of preparation Prepare as directed under Tablets, with Digoxin.

Identification Evaporate 2 mL of the sample solution obtained in Assay on a water bath to dryness. Cool, and dissolve the residue in 5 mL of alkaline 1,3-dinitrobenzene TS: a blue color develops within 10 minutes, then fades gradually.

Purity Related substances—Proceed as directed in the Purity (2) under Digoxin, using 10 mL of the sample solution obtained in Assay under Digoxin Tablets instead of 1 mL of the sample stock solution of Assay under Digoxin in (iii) procedure.

Dissolution test Take 1 tablet of Digoxin Tablets, and perform the test, using 500 mL of diluted hydrochloric acid (3 in 500), deaerated by a suitable method as the test solution at 100 revolutions per minute as directed in the Method 1 under the Dissolution Test. At 60 minutes after starting the test, take 30 mL or more of the dissolved solution, 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 0.025 g of Digoxin Reference Standard, previously dried in vacuum at 105°C for 1 hour, dissolve in a small portion of ethanol (95), and add diluted ethanol (95) (4 in 5) to make exactly 500 mL. Measure exactly 5 mL of this solution, add the test solution to make exactly 500 mL, and use this solution as the standard solution. Measure exactly 2 mL each of the sample solution, the standard solution and the test solution, and transfer to brown glass-stoppered test tubes T, S, and B, respectively. Add exactly 10 mL of 0.012 w/v% L-ascorbic acid-hydrochloric acid TS to these solutions, and shake. Immediately add exactly 1 mL of dilute hydrogen peroxide TS, shake well, and allow to stand at a constant temperature between 25°C and 30°C for 45 minutes. Determine the fluorescence intensities, F_T, F_S, and F_B, of these solutions at 360 nm of the excitation wavelength and at 485 nm of the fluorescence wavelength as directed under the Fluorometry, respectively.

The dissolution rate of Digoxin Tablets after 60 minutes should be not less than 65%.

No retest requirement is applied to Digoxin Tablets.

$$\text{Dissolution rate (\%) with respect to the labeled amount of digoxin } (C_{41}H_{64}O_{14}) = W_S \times \frac{F_T - F_B}{F_S - F_B} \times \frac{1}{C}$$

W_S: Amount (mg) of Digoxin Reference Standard.

C: The labeled amount (mg) of digoxin ($C_{41}H_{64}O_{14}$) in 1 tablet.

Content uniformity To 1 tablet of Digoxin Tablets add 0.5 mL of water to disintegrate, add 30 mL of ethanol (95), and shake for 15 minutes. Add ethanol (95) to make exactly V mL of a solution containing about 5 μg of digoxin ($C_{41}H_{64}O_{14}$) per ml. Filter, discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.01 g of Digoxin Reference Standard, previously dried in vacuum at 105°C for 1 hour, dissolve in 50 mL of warm ethanol (95), and after cooling add ethanol (95) to make exactly 100 mL. Pipet 5 mL of this solution, add 50 mL of ethanol (95) and 1 mL of water, then ethanol (95) to make exactly 100 mL, and use this solution as the standard solution. Pipet 2 mL each of the sample solution, the standard solution and diluted ethanol (95) (47 in 50) into brown glass-stoppered test tubes T, S, and B. To each tube add exactly 10 mL of 0.012 w/v% L-ascorbic acid-hydrochloric acid TS, shake, and add immediately 1 mL of dilute hydrogen peroxide TS. Shake well, and allow to stand at 30°C for 45 minutes. Determine the fluorescence intensities, F_T, F_S and F_B, of the solutions in test tubes T, S and B at 360 nm by the excitation wavelength and at 485 nm of the fluorescence wavelength as directed under the Fluorometry, respectively.

$$\text{Amount (mg) of digoxin } (C_{41}H_{64}O_{14}) = \text{amount (mg) of Digoxin Reference Standard} \times \frac{F_T - F_B}{F_S - F_B} \times \frac{V}{2000}$$

Assay Weigh accurately and powder not less than 20 Digoxin Tablets. Weigh accurately a portion of the powder, equivalent to about 2.5 mg of digoxin ($C_{41}H_{64}O_{14}$), add 5 mL of heated 1-propanol, stir vigorously, and allow the mixture to cool for 20 minutes, while stirring frequently. Transfer to a separator, add 20 mL of water, extract with two 30-mL portions of a mixture of chloroform and 1-propanol (5:1), and wash each extract with the same 5 mL of water. Filter the extracts through absorbent cotton moistened with chloroform into a 100-mL volumetric flask. Add ethanol (95) to make 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.025 g of Digoxin Reference Standard, previously dried in vacuum at 105°C for 1 hour, dissolve in 50 mL of warm ethanol (95), cool, and add ethanol (95) to make exactly 100 mL. Pipet 10 mL of the solution, add ethanol (95) to make exactly 100 mL, and use this solution as the standard solution. Pipet 10 mL each of the sample solution and the standard solution into separate conical flasks. Evaporate on a water bath with the aid of a current of air nearly to dryness, and allow to stand in a desiccator (in vacuum, phosphorus (V) oxide) for 15 minutes. Dissolve each residue in 5 mL of acidic iron (III) chloride TS with occasional stirring, allow to stand at a temperature not exceeding 30°C for 10 minutes, protected from light, and filter through a plug of glass wool, if necessary. Perform the test with these solutions, using acidic iron (III) chloride TS as the blank, as directed under the Ultraviolet-visible Spectrophotometry. Determine the maximum absorbances, A_T and A_S, of the subsequent solutions obtained from the sample solution and the standard solution by repeating the determination at 590 nm at 2-minute intervals, respectively.

$$\text{Amount (mg) of digoxin } (C_{41}H_{64}O_{14}) = \text{amount (mg) of Digoxin Reference Standard} \times \frac{A_T}{A_S} \times \frac{1}{10}$$

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