Calcium Disodium Edetate Enteric-coated Tablets

Dissolution *<6.10>*

[pH 1.2] Perform the test with 1 tablet of Calcium Disodium Edetate Enteric-coated Tablets at 100 revolutions per minute according to the Paddle method, using 900 mL of 1st fluid for dissolution test 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, pipet *V* mL of the subsequent filtrate, add 0.1 mol/L hydrochloric acid TS to make exactly *V′* mL so that each mL contains about 11.1 μg of calcium disodium edetate ($C_{10}H_{12}CaN_2Na_2O_8$) according to the labeled amount. Pipet 20 mL of this solution, add exactly 1 mL of 0.01 mol/L iron (III) chloride TS, and use this solution as the sample solution. Separately, weigh accurately about 22 mg of Calcium Disodium Edetate RS (previously determine the water with 0.2 g by direct titration in volumetric titration), and dissolve in 1st fluid for dissolution test to make exactly 200 mL. To exactly 10 mL of this solution add 0.1 mol/L hydrochloric acid TS to make exactly 100 mL. Further, pipet 20 mL of this solution, add exactly 1 mL of 0.01 mol/L iron (III) chloride TS, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and the standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and determine the peak areas, A_T and A_S, of edetic acid in each solution.

The requirements are met if Calcium Disodium Edetate Enteric-coated Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of calcium disodium edetate ($C_{10}H_{12}CaN_2Na_2O_8$)

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 45$

M_S: Amount (mg) of Calcium Disodium Edetate RS, calculated on the anhydrous basis

C: Labeled amount (mg) of calcium disodium edetate ($C_{10}H_{12}CaN_2Na_2O_8$) in 1 tablet

[pH 6.8] Perform the test with 1 tablet of Calcium Disodium Edetate Enteric-coated Tablets at 100 revolutions per minute according to the Paddle method, using 900 mL of 2nd fluid for dissolution test 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, pipet *V* mL of the subsequent filtrate, add 0.1 mol/L hydrochloric acid TS to make exactly *V′* mL so that each mL contains about 11.1 μg of calcium disodium edetate ($C_{10}H_{12}CaN_2Na_2O_8$) according to the labeled amount. Pipet 20 mL of this solution, add exactly 1 mL of 0.01 mol/L iron (III) chloride TS, and use this solution

as the sample solution. Separately, weigh accurately about 22 mg of Calcium Disodium Edetate RS (previously determine the water <2.48> with 0.2 g by direct titration in volumetric titration), and dissolve in 2nd fluid for dissolution test to make exactly 200 mL. To exactly 10 mL of this solution add 0.1 mol/L hydrochloric acid TS to make exactly 100 mL. Further, pipet 20 mL of this solution, add exactly 1 mL of 0.01 mol/L iron (III) chloride TS, and use this solution as the standard solution. Perform the test with exactly 10 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 and A_S, of edetic acid in each solution.

The requirements are met if Calcium Disodium Edetate Enteric-coated Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of calcium disodium edetate ($C_{10}H_{12}CaN_2Na_2O_8$)

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 45$

M_S: Amount (mg) of Calcium Disodium Edetate RS, calculated on the anhydrous basis

C: Labeled amount (mg) of calcium disodium edetate ($C_{10}H_{12}CaN_2Na_2O_8$) (mg) in 1 tablet

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 255 nm).

Column: A stainless column 4 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of around 40ºC.

Mobile phase: Dissolve 3.2 g of tetra-*n*-butylammonium bromide in water to make 1000 mL, and adjust to pH 2.5 with phosphoric acid. To 960 mL of this solution add 40 mL of acetonitrile.

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

System suitability —

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of edetic acid are not less than 5000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of edetic acid is not more than 2.0%.

Dissolution Requirements

Labeled amount	pH	Specified minute	Dissolution rate
500 mg	1.2	120 minutes	Not more than 5%
	6.8	120 minutes	Not less than 80%

Calcium Disodium Edetate RS $C_{10}H_{12}CaN_2Na_2O_8$: 374.27 ({*N,N'*-1,2-ethanediylbis[*N*-(carboxymethyl)glycinato]}(4-)-*N,N',O,O',O*^{N},-*O*$^{N'}$)calciate(2-)disodium. It meets the following requirements.

Description —Calcium Disodium Edetate RS occurs as a white powder or granules.

pH <*2.54*> —The pH of a solution obtained by dissolving 2.0 g of Calcium Disodium Edetate RS in water to make 10 mL is between 6.5 to 8.0.

Purity —

Disodium Edetate Hydrate—Take 1.00 g of Calcium Disodium Edetate RS, dissolve in 50 mL of water, add 5 mL of ammonia-ammonium buffer solution, pH 10.7, and titrate <*2.50*> with 0.01 mol/L magnesium chloride VS: the consumed volume is not more than 3.0 mL (not more than 1.2% as disodium edetate hydrate) (indicator: 40 mg of eriochrome black T-sodium chloride indicator), until the color of the solution changes from blue to red.

Water <*2.48*>: not less than 13.0% (0.2 g, volumetric titration, direct titration).

Content: not less than 99.0%, calculated on the dehydrated basis. Assay—Weigh accurately about 0.5 g of Calcium Disodium Edetate RS, add water to dissolve to make exactly 200 mL. Pipet 20 mL of this solution, add 80 mL of water, then adjust to pH 2 to 3 with dilute nitric acid, and titrate <*2.50*> with 0.01 mo1/L bismuth nitrate VS (indicator: 2 drops of xylenol orange TS), until the color of the solution changes from yellow to red. Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.01 mo1/L bismuth nitrate VS
= 3.743 mg of $C_{10}H_{12}CaN_2Na_2O_8$

0.01 mol/L iron (III) chloride TS Dissolve 0.27 g of iron (III) chloride hexahydrate in 0.01 mol/L hydrochloric acid TS to make 100 mL.