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Edetate Disodium

$C_{10}H_{14}N_2Na_2O_8 \cdot 2H_2O$ 372.24
$C_{10}H_{14}N_2Na_2O_8$ 336.21
Glycine, *N*,*N*'-1,2-ethanediylbis[*N*-(carboxymethyl)-, disodium salt, dihydrate;
Disodium (ethylenedinitrilo)tetraacetate dihydrate CAS RN®: 6381-92-6.
Anhydrous CAS RN®: 139-33-3.

DEFINITION

Edetate Disodium contains NLT 99.0% and NMT 101.0% of edetate disodium ($C_{10}H_{14}N_2Na_2O_8$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)
- **B.**

Sample: 50 mg

Analysis: To 5 mL of water in a test tube add 2 drops of ammonium thiocyanate TS and 2 drops of ferric chloride TS. To the deep red solution add the *Sample*.

Acceptance criteria: The red color is discharged, leaving a yellowish solution.

- **C.** Identification Tests—General ⟨191⟩, *Sodium*: It meets the requirements of test *A*.

ASSAY

- **Procedure**

Sample solution: Dissolve 5 g of Edetate Disodium in about 100 mL of water contained in a 250-mL volumetric flask. Add water to volume.

Analysis: Place 200 mg of chelometric standard calcium carbonate, previously dried at 110° for 2 h and cooled in a desiccator, into a 400-mL beaker. Add 10 mL of water, and swirl to form a slurry. Cover the beaker with a watch glass, and without removing the latter, add 2 mL of 3 N hydrochloric acid from a pipet. Swirl the contents of the beaker, and dissolve the calcium carbonate. With water, wash down the sides of the beaker, the outer surface of the pipet, and the watch glass, and dilute with water to 100 mL. While stirring the solution, preferably with a magnetic stirrer, add 30 mL of the *Sample solution* from a 50-mL buret. Add 15 mL of 1 N sodium hydroxide and 0.30 g of hydroxy naphthol blue, and continue the titration with the *Sample solution* to a blue endpoint.

Calculate the weight of edetate disodium ($C_{10}H_{14}N_2Na_2O_8$) in the portion of Edetate Disodium taken:

$$\text{Result} = (V_T/V_U) \times W \times (M_{r1}/M_{r2})$$

V_T = total volume of the *Sample solution* (mL)

V_U = volume of the *Sample solution* consumed in the titration (mL)

W = weight of calcium carbonate (mg)

M_{r1} = molecular weight of edetate disodium, 336.21

M_{r2} = molecular weight of calcium carbonate, 100.09

Acceptance criteria: 99.0%–101.0% on the dried basis

IMPURITIES

- **Calcium**

Sample solution: 1 g of Edetate Disodium in 20 mL of water

Analysis: To the *Sample solution* add 2 drops of methyl red TS, and neutralize with 6 N ammonium hydroxide. Add 3 N hydrochloric acid dropwise until the solution is just acidic, and then add 1 mL of ammonium oxalate TS.

Acceptance criteria: No precipitate is formed.

- **Limit of Nitrilotriacetic Acid**

Mobile phase: Add 10 mL of 1.0 M tetrabutylammonium hydroxide in methanol to 200 mL of water, and adjust with 1 M phosphoric acid to a pH of 7.5 ± 0.1. Transfer the solution so obtained to a 1000-mL volumetric flask. Add 90 mL of methanol, and dilute with water to volume.

Pass through a filter of 0.5-µm or finer pore size, and degas.

Cupric nitrate solution: 10 mg/mL of cupric nitrate [$Cu(NO_3)_2$]

Standard stock solution: Transfer 100 mg of nitrilotriacetic acid to a 10-mL volumetric flask. Add 0.5 mL of ammonium hydroxide, mix, and dilute with water to volume.

Standard solution: Transfer 1.0 g of Edetate Disodium to a 100-mL volumetric flask. Add 100 µL of *Standard stock solution*, and dilute with *Cupric nitrate solution* to volume. If necessary, sonicate to dissolve.

System suitability solution: Transfer 10 mg of Edetate Disodium to a 100-mL volumetric flask. Add 100 µL of *Standard stock solution*, and dilute with *Cupric nitrate solution* to volume. If necessary, sonicate to dissolve.

Sample solution: 10 mg/mL of Edetate Disodium in *Cupric nitrate solution*. If necessary, sonicate to dissolve.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; packing L7

Flow rate: 2 mL/min

Injection volume: 50 µL

System suitability

Samples: *Standard solution* and *System suitability solution*

[Note—The relative retention times for nitrilotriacetic acid, copper, and edetate are about 0.35, 0.65, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3 between nitrilotriacetic acid and copper, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: NMT 0.1%; the response of the nitrilotriacetic acid peak of the *Sample solution* does not exceed the difference between the nitrilotriacetic acid peak responses from the *Standard solution* and the *Sample solution*.

SPECIFIC TESTS

- **pH ⟨791⟩**

Sample solution: 50 mg/mL

Acceptance criteria: 4.0–6.0

- **Loss on Drying ⟨731⟩**

Analysis: Dry at 150° for 6 h.

Acceptance criteria: 8.7%–11.4%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards ⟨11⟩**

USP Edetate Disodium RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
EDETATE DISODIUM	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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