

Edetic Acid

1 Nonproprietary Names

BP: Edetic Acid

PhEur: Edetic Acid

USP–NF: Edetic Acid

2 Synonyms

Acidum edeticum; 3,6-bis(carboxymethyl)-3,5-diazoctanedioic acid; ethylenebis(iminodiacetic acid); *Dissolvine*; edathamil; EDTA; ethylenediaminetetraacetic acid; (ethylenedinitrilo)tetraacetic acid; *Sequestrene AA*; tetracemic acid; *Versene Acid*.

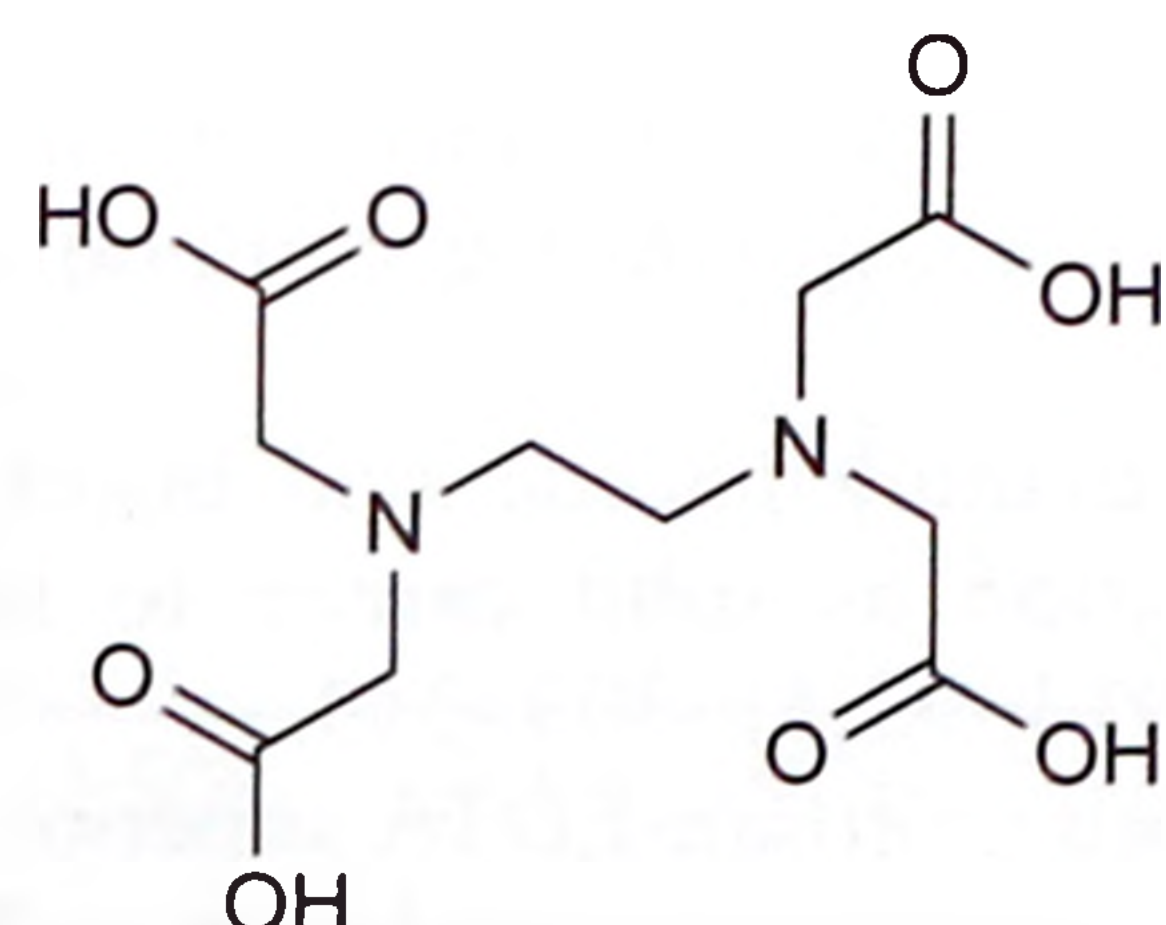
3 Chemical Name and CAS Registry Number

N,N-1,2-Ethanediyldis[*N*-(carboxymethyl)glycine] [60-00-4]

4 Empirical Formula and Molecular Weight

$C_{10}H_{16}N_2O_8$ 292.24

5 Structural Formula



6 Functional Category

Antimicrobial preservative; complexing agent.

7 Applications in Pharmaceutical Formulation or Technology

Edetic acid and edetate salts are used in pharmaceutical formulations as complexing agents. They form stable water-soluble complexes (chelates) with alkaline earth and heavy metal ions. The complexed form has few of the properties of the free ion, and for this reason complexing agents are often described as 'removing' ions from solution; this process is also called sequestering. The stability of the metal–edetate complex depends on the metal ion involved and also on the pH. The calcium complex is relatively weak and will preferentially exchange calcium for heavy metals, such as iron, copper, and lead, with the release of calcium ions.

Edetic acid and edetates are primarily used as antioxidant synergists, sequestering trace amounts of metal ions (particularly copper, iron, and manganese) that might otherwise catalyze autoxidation reactions. Edetic acid and edetates may be used alone or in combination with true antioxidants, the usual concentration employed being in the range 0.005–0.1% w/v. Edetates have been used to stabilize ascorbic acid, corticosteroids, epinephrine, folic acid, formaldehyde, gums and resins, hyaluronidase, hydrogen peroxide, oxytetracycline, penicillin, salicylic acid, and unsaturated fatty acids. Essential oils may be washed with a 2% w/v solution of edetate to remove trace metal impurities.

Edetic acid and edetates possess some antimicrobial activity but are most frequently used in combination with other antimicrobial preservatives owing to their synergistic effects. Typically, edetic acid

and edetates are used in concentrations of 0.01–0.1% w/v as antimicrobial preservative synergists; see Section 10.

Edetates, particularly edetate disodium and edetate calcium disodium, are used in a greater number and variety of pharmaceutical formulations than the free acid.

See Edetate Disodium and Edetate Calcium Disodium.

8 Description

Edetic acid occurs as an odorless white or almost white crystalline powder or colorless crystals.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for edetic acid.

Test	PhEur 9.2	USP 40–NF 35 S1
Identification	+	+
Characters	+	–
Appearance of solution	+	–
Residue on ignition	–	≤0.2%
Sulfated ash	≤0.2%	–
Heavy metals	–	≤30 μg/g
Nitritotriacetic acid	≤0.1%	≤0.3%
Iron	≤80 ppm	≤0.005%
Chloride	≤200 ppm	–
Assay	98.0–101.0%	98.0–100.5%

10 Typical Properties

Acidity/alkalinity pH = 2.2 for a 0.2% w/v aqueous solution.

Antimicrobial activity Edetic acid has some antimicrobial activity against Gram-negative microorganisms, *Pseudomonas aeruginosa*, some yeasts, and fungi although this activity is insufficient for edetic acid to be used effectively as an antimicrobial preservative on its own.^(1,2) However, when used with other antimicrobial preservatives, edetic acid demonstrates a marked synergistic effect in its antimicrobial activity. Edetic acid and edetates are therefore frequently used in combination with such preservatives as benzalkonium chloride; bronopol; cetrimide; imidurea; parabens; and phenols, especially chloroxylenol. Typically, edetic acid is used at a concentration of 0.1–0.15% w/v. In the presence of some divalent metal ions, such as Ca^{2+} or Mg^{2+} , the synergistic effect may be reduced or lost altogether. Edetic acid and iodine form a colorless addition compound that is bactericidal.

See also Edetate Disodium.

Dissociation constant

$pK_{a1} = 2.00$;

$pK_{a2} = 2.67$;

$pK_{a3} = 6.16$;

$pK_{a4} = 10.26$.

Melting point 240–241°C, with decomposition.

Solubility Soluble in solutions of alkali hydroxides; practically insoluble in water (1 in 500) and ethanol (96%); insoluble in common organic solvents.

Specific gravity 0.721

Spectroscopy

NIR spectrum see Figure 1.