Edetate Disodium

1 Nonproprietary Names

BP: Disodium Edetate

JP: Disodium Edetate Hydrate

PhEur: Disodium Edetate

USP–NF: Edetate Disodium

2 Synonyms

Dinatrii edetas; disodium edetate; disodium EDTA; disodium ethylenediaminetetraacetate; edathamil disodium; edetic acid, disodium salt; *Versene*.

3 Chemical Name and CAS Registry Number

Ethylenediaminetetraacetic acid, disodium salt [139-33-3]

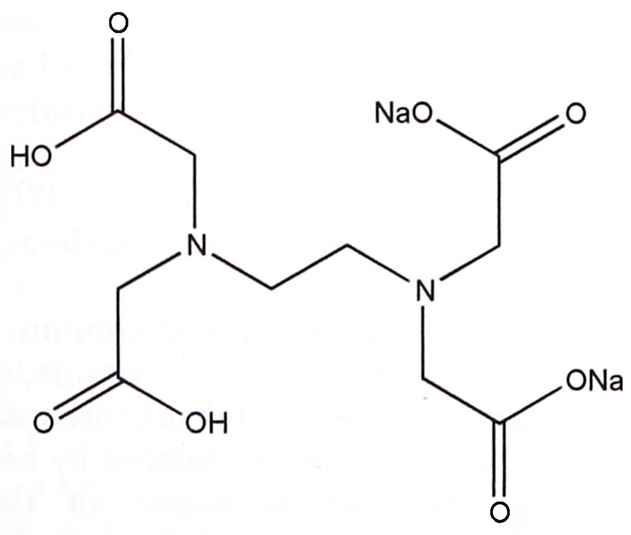
Disodium ethylenediaminetetraacetate dihydrate [6381-92-6]

4 Empirical Formula and Molecular Weight

$C_{10}H_{14}N_2Na_2O_8$ 336.2 (for anhydrous)

$C_{10}H_{18}N_2Na_2O_{10}$ 372.2 (for dihydrate)

5 Structural Formula



6 Functional Category

Complexing agent.

7 Applications in Pharmaceutical Formulation or Technology

Edetate disodium is used as a complexing agent in a wide range of pharmaceutical preparations, including mouthwashes, ophthalmic preparations, and topical preparations,[1–3] typically at concentrations between 0.005 and 0.1% w/v.

Edetate disodium forms stable water-soluble complexes (chelates) with alkaline earth and heavy-metal ions. The chelated form has few of the properties of the free ion, and for this reason chelating agents are often described as 'removing' ions from solution, a process known as sequestering. The stability of the metal–edetate complex is dependent on the metal ion involved and the pH.

Edetate disodium has been used experimentally to investigate the stability and skin penetration capacity of captopril gel, in which edetate disodium was shown to exert a potent stabilizing effect, and may be used in the development of a transdermal drug delivery system.[4] A chitosan–EDTA conjugate has been investigated as a novel polymer for use in topical gels. The conjugate was shown to be stable, colorless, and transparent, and it also demonstrated antimicrobial effects.[5] Studies have shown that edetate disodium may be effective in retarding microbial growth in propofol formulations[6] and for the prevention of biofilm formation in catheters.[7]

Research has also been done to prepare and characterize hot melt dispersion formulations of mini-pellets containing EDTA.[8] A salt complex of iron and EDTA has been used to develop chewable and orodispersible tablets in studies in humans and rats.[9]

See also Edetic Acid.

8 Description

Edetate disodium occurs as a white, crystalline, odorless powder with a slightly acidic taste.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for edetate disodium.

Test	JP XVII	PhEur 9.2	USP 40–NF 35 S1
Identification	+	+	+
Characters	+	+	–
Appearance of solution	+	+	–
pH	4.3–4.7	4.0–5.5	4.0–6.0
Iron	–	≤80 ppm	–
Calcium	–	–	+
Heavy metals	≤10 ppm	–	≤0.005%
Cyanide	+	–	–
Arsenic	≤2 ppm	–	–
Limit of nitrilotriacetic acid	–	≤0.1%	≤0.1%
Residue on ignition	37.0–39.0%	–	–
Loss on drying	–	–	8.7–11.4%
Assay	≥99.0%	98.5–101.0%	99.0–101.0%

10 Typical Properties

Acidity/alkalinity pH 4.3–4.7 (1% w/v solution in carbon dioxide-free water)

Density (bulk) 980 kg/m^3 (for *Versene*)

Freezing point depression 0.14°C (1% w/v aqueous solution)

Melting point Decomposition at 252°C for the dihydrate.

Refractive index 1.33 (1% w/v aqueous solution)

Solubility Practically insoluble in chloroform and ether; slightly soluble in ethanol (95%); soluble 1 part in 11 parts water.

Specific gravity 1.004 (1% w/v aqueous solution)

Spectroscopy

IR spectrum *see* Figure 1.

NIR spectrum *see* Figure 2.

Raman spectrum *see* Figure 3.

Viscosity (kinematic) 1.03 mm^2/s (1.03 cSt) (1% w/v aqueous solution).

11 Stability and Storage Conditions

Edetate salts are more stable than edetic acid (*see also* Edetic Acid). However, edetate disodium dihydrate loses its water of crystal-