**EDTA (Ethylenediaminetetraacetic Acid)**

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- **Name:** EDTA (Ethylenediaminetetraacetic Acid)
- **Chemical Abstracts Service Registry Number:** 60-00-4
- **Synonyms:** Ethylenedinitritetetraacetic acid; Celon A; Chelex; Edetic acid; Nullapon B Acid; Trilon BW; Versene
- **Molecular Formula:** C₁₀H₁₆N₂O₈
- **Chemical Structure:**

![Chemical Structure of EDTA](image)

**Background**

Ethylenediaminetetraacetic acid (EDTA) was developed by Franz Munz in Germany during the 1930s as an alternative to citric acid. About the same time, Frederick Bersworth synthesized EDTA in the United States using a different technique. He obtained a US patent for this technique in 1945. EDTA was approved by the US Food and Drug Administration (FDA) as a food additive in 1947. Since the early 1950s, EDTA has been used in chelation treatment for lead poisoning. EDTA is a white, odorless, and crystalline (sugar or sandlike) material. It has a molecular weight of 292.28 and its melting point is 2401 °C. It is water insoluble.

**Uses**

EDTA is used as a food additive, in herbicides, in pharmaceuticals, and in a variety of consumer products. EDTA is used as a blood preservative by complexing free calcium ion (which promotes blood clotting). EDTA’s ability to bind to lead ions makes it useful as an antidote for lead poisoning. Furthermore, EDTA is often used to treat various cardiovascular diseases.

**Environmental Fate and Behavior**

EDTA can be very persistent in water, including wastewater-treatment plants. EDTA is often found in the receiving waters of many industrial areas, thus being classified as one of the major organic pollutants discharged in waters. The available ecotoxicity data for EDTA indicate that these compounds are slow to degrade under typical environmental conditions but are not expected to bioconcentrate. EDTA compounds range from practically nontoxic to moderately toxic on an acute basis, depending on the salt. Algae and invertebrates are among the most sensitive species based on predictive modeling for acute and chronic endpoints for EDTA, depending on the compound. EDTA and its salts also do not appear to be very toxic for terrestrial wild mammals, and adverse effects from reasonably expected agricultural uses are not expected.

According to ChemIDPlus, EDTA has the following physicochemical properties: melting point = 245 °C, pKₐ dissociation constant = 0.26, log P (octanol–water) = -3.860, water solubility = 1000 mg l⁻¹, vapor pressure = 4.98E-13 mm Hg, Henry’s law constant = 1.17E-23 atm·m³ mol⁻¹, and atmospheric OH rate constant = 1.82E-10 cm³ molecule⁻¹·s⁻¹.

Based on its physicochemical properties, EDTA is not expected to volatilize from soil or water. When released to the atmosphere, EDTA should sorb to particulate matter, and appears to have the potential to photolyze.

**Exposure and Exposure Monitoring**

Exposure to EDTA may be through FDA-approved uses as food additives, in sanitizing solutions, in pharmaceutical products, or through their use in soaps, shampoos, or cosmetics. EDTA has also been administered safely under medical supervision as treatment for heavy metal poisoning.

The most probable routes of human exposure to EDTA would be ingestion and dermal contact. Workers involved in the manufacture or use of EDTA may be exposed by inhalation and dermal contact. In chelation therapy, EDTA is administered via intravenous infusion.

According to the US Environmental Protection Agency, EDTA is of low risk to humans, since absorption through ingestion is of lower toxicity, especially with sufficient trace minerals within the daily diet. There is no reason to expect that reasonable use will constitute any significant hazard.

**Toxicokinetics**

EDTA is essentially not metabolized by the human body, and it is rapidly excreted in the urine. About 50% of EDTA administered intravenously is excreted within 1 h and 90% within 7 h. EDTA and its metal chelates do not permeate the cellular membrane to a significant extent; thus, most of the EDTA remains in the extracellular fluid until excreted in the urine.

EDTA is eliminated from the body, 95% via the kidneys and 5% by the bile, along with the metals and free ionic calcium that was bound in transit through the circulatory system. The binding of divalent and trivalent cations by EDTA can cause mineral deficiencies, which seem to be responsible for all of the known pharmacological and toxicological effects. Sensitivity to the toxic effects of EDTA is, at least in part, related to the deficiency of zinc.
**Mechanism of Toxicity**

The principal toxicity of EDTA relates to the metal chelate, especially in lead poisoning. Lead may be released from the chelate in the kidneys, and then the lead may affect the tubules and glomeruli of the kidneys.

**Acute and Short-Term Toxicity (or Exposure)**

**Animal**

In rats, more live fetuses resulted when calcium disodium EDTA was used to treat lead poisoning. However, in rats that were not lead poisoned, increases in submucosal cysts, cleft palate, syndactyly, adactyly, abnormal ribs, and abnormal vertebrae occurred. Furthermore, the doses of EDTA in the study were comparable to those used in humans and without noticeable changes in the mother. Since zinc calcium EDTA did not cause teratogenicity at low levels in rats, zinc calcium EDTA should be available for use in pregnancy.

**Human**

Cases of anuria have been reported when EDTA was administered to treat lead poisoning. Such kidney injury is reversible and is probably not due to the chelate directly, but to the reabsorption of the metal in the tubules. Of 130 children that received dimercaprol and EDTA, 3% developed acute renal failure and 13% had biochemical evidence of nephrotoxicity. However, lead poisoning can cause kidney injury without EDTA therapy. In another study, 122 patients were given EDTA and none showed posttreatment increases in plasma creatinine.

Reversible mild increases in plasma hepatic aminotransferase activities are frequently reported after use of EDTA. Furthermore, extravasation may result in the development of painful calcinosis at the injection site.

In a workplace setting, the following acute health effects may occur immediately or shortly after exposure to EDTA: Contact may irritate the skin, causing a rash or burning feeling; contact with high concentrations may irritate the eyes; and inhalation of EDTA dust may irritate the nose and throat.

**Chronic Toxicity (or Exposure)**

**Animal**

Laboratory studies on various animal species as well as reports from veterinary practices have revealed that long-term therapy with EDTA may cause deficiencies in zinc and vitamin B6.

**Human**

Prolonged systemic therapy with EDTA has resulted in zinc and vitamin B6 deficiencies. Furthermore, febrile reactions with headache, myalgia, nausea, vomiting, lachrymation, nasal lesions, glycosuria, hypotension, and electrocardiographic (ECG or EKG) changes have been reported.

**In Vitro Toxicity Data**

All known pharmacological effects of EDTA result from formation of chelates with divalent and trivalent metal ions in the body. Also, the effects on rat liver glucocorticoid receptor *in vitro* have been studied. At 41 °C, 10 mmol EDTA had a stabilizing effect on unbound hepatic glucocorticoid receptors. Apparently, endogenous metal ions are involved in the processes of glucocorticoid–receptor complex stabilization and transformation. Furthermore, EDTA increases the absorption of a number of agents. This effect is nonspecific because EDTA increases the absorption of bases, acids, and neutral compounds. It appears that by chelating calcium, EDTA causes a general increase in membrane permeability.

**Clinical Management**

In case of contact with EDTA, the eyes should be flushed immediately with running water for at least 15 min. Affected skin should be washed with soap and water. Contaminated clothing and shoes should be removed and isolated at the site.

**Exposure Standards and Guidelines**

EDTA is designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance. This designation includes any isomers and hydrates, as well as any solutions and mixtures containing this substance.

The Food and Agriculture Organization/World Health Organization acceptable daily intake for calcium disodium edetate as a food additive is 2.5 mg kg−1 body weight.

**See also:** Lead.

**Further Reading**


**Relevant Websites**
