German Chemical Society
Gesellschaft Deutscher Chemiker

GDCh-Advisory Committee
on Existing Chemicals of
Environmental Relevance (BUA)

Ethylenediaminetetra-acetic acid / Tetrasodium ethylenediaminetetra-acetate (H_4EDTA/Na_4EDTA)

BUA Report 168
(May 1995)

S. Hirzel
Wissenschaftliche Verlagsgesellschaft 1997

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Ethylenediaminetetraacetic acid / Tetrasodium ethylene-diaminetetraacetate

(H_4EDTA/Na_4EDTA)

BUA Report 168

(May 1995)

edited by the GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance

Beratergremium für Umweltrelevante Altstoffe (BUA)

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Wissenschaftliche Verlagsgesellschaft 1997

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Die Deutsche Bibliothek — CIP-Einheitsaufnahme

Ethylenediaminetetraacetic acid, tetrasodium ethylenediaminetetraacetate / ed. by the GDCh Advisory Committee on Existing Chemicals of Environmental Relevance. — (May 1995). — Stuttgart: Hirzel ; Stuttgart : Wiss. Verl.-Ges., 1997

(BUA report; 168)
Dt. Ausg. u.d.T.: Ethylendiamintetraessigsäure, Tetranatriumethylendiamintetraacetat
ISBN 3-7776-0766-5

Printed in acid-free and low-chlorine paper.

Printing and binding: Druckhaus Beltz, Hemsbach
Printed in F.R. Germany

Foreword

The German Chemicals Act (Chemikaliengesetz — ChemG) of 1980 stipulates that certain existing chemicals must be reported to the competent authority, if they exhibit properties which indicate that they may be hazardous, either alone or in combination with other substances.
In the summer of 1982, an Advisory Committee on Existing Chemicals of Environmental Relevance (BUA) was set up by the German Chemical Society (Gesellschaft Deutscher Chemiker — GDCh). It brings together representatives from the scientific community, the chemical industry and the governmental authorities. This Advisory Committee is responsible for elaborating appropriate solutions for substances of relevance for health and the environment on the basis of voluntary measures. It selects and examines existing chemicals from the aforementioned angles. The testing and evaluation are based on scientific criteria alone.
It was, therefore, necessary to develop priority setting procedures. In a first phase reports were only prepared for priority chemicals. Within the framework of a first priority setting procedure, chemicals were complied from several priority lists and 135 chemicals were selected for detailed reports.
In a second priority setting procedure the survey of the German Chemical Industry Association (VCI) on all substances with a production volume of more than 10 tons per year was used as a starting list. Since this survey covered 4,600 chemicals, BUA decided to process the corresponding list in several stages. The first stage included approx. 1,050 substances with a production volume of more than 1,000 tons per year.
Detailed reports are drawn up on chemicals suspected of having a hazard potential and abridged reports on those presenting only a minor hazard potential, according to the current state of knowledge.
The detailed BUA reports take in both the published literature and data from industry. If data for the evaluation of the chemicals are not available, additional studies are recommended and the results are published as update to the reports. The reports serve as a basis for the instigation of administrative measures, when there are indications of risks to health or the environment.

Tübingen, May 1993

Ernst Bayer
Chairman of the Advisory Committee
on Existing Chemicals
of Environmental Relevance

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BUA Report on Ethylenediaminetetraacetic acid, H_4EDTA and Ethylenediaminetetraacetic acid tetrasodium salt, Na_4EDTA

Summary and conclusions

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In 1994, about 4,350 t of EDTA were sold in the Federal Republic of Germany, as were about 29, 822 t in Western Europe.

EDTA is used in many fields of application because of its ability to complex metals. In the Federal Republic of Germany, applications include:

Photographic chemicals	33 %
Washing and cleaning agents for the home and for industry	23 %
Desulfurization of flue gases	approx. 10 %
Textile processing chemicals	4 %
Drug and food industries, Construction industry, agriculture	4 %
Cosmetic industry	3 %
Water softening	0.7 %
Leather industry, paints and coatings industry, papermaking	*)
Metal industry	*)

*) Not published, in agreement with the statistical rules.

Less than 400 g/t of H_4EDTA and 2 kg/t of Na_4EDTA powder enter the atmosphere during manufacture.

It is estimated that in the Federal Republic of Germany about 170 t of EDTA enter the environment every year via trace nutrient fertilizers. To a smaller extent EDTA is used as a foliar nutrient in powder form: 0.3 - 1.5 kg of EDTA/ha. By far the largest proportion is used in the form of liquid foliar nutrients: 0.004 - 0.15 kg EDTA/ha.

If it is properly used, only about one third of the solution reaches the soil. The theoretical EDTA concentration in the upper horizon of the soil (the first 30 cm) is about 0.02 - 0.1 mg/kg after application.

Four of the seven EDTA producers in the EU have submitted data on discharges into the hydrosphere which were reported in an anonymous form. In 1993, 13.1 kg/t of H_4EDTA and Na_4EDTA were discharged, dropping to about 12 kg/t in 1994.

In 1994, EDTA production resulted in the discharge of 25 t of EDTA into the receiving water body with a further contribution of 33 t by the manufacturer as a result of its application.

After use, most of the EDTA is discharged into waste-water treatment plants in accordance with the regulations. No data are available on its subsequent discharge into surface waters.

The following data for the occurrence of EDTA in the environment are available:

- Surface waters

    - The Rhine at Bimmen, 1993: Mean value 15.2 µg/l
Maximum value 35 µg/l

    - The Main at Bischofsheim, 1993: Mean value 35.3 µg/l
Maximum value 62 µg/l

- Lake Constance

Middle of the lake between Fischbach and Uttwil (7 August 1990)	Mean value 2.5 µg/l Maximum value 3.5 µg/l

- Effluent from waste-water treatment plants in Hesse

Municipal:	1987	5 - 350 µg/l
	1988	66 - 1720 µg/l
Industrial:	1987	15 - 400 µg/l
	1988	35 - 6100 µg/l

- Munich raw waste water, range of values from 1988 to 1989: 5 - 100 µg/l

- Essen drinking water, Jan. 1992 to April 1993:

50 percentile	10 µg/l
Maximum value	27 µg/l

A joint declaration on the reduction of the EDTA burden in surface waters announced by the German Federal Minister for the Environment, Protection of Nature and Reactor Safety on 31 July 91 aims to halve the current EDTA burden in surface waters in the medium term (approx. 5 years). By 1992, a reduction of 20 % had been achieved in the Rhine at Duesseldorf, compared with the day the declaration took effect in 1991. From 1986 to 1992, a total reduction of 70 % was measured at the sampling point at Duesseldorf. These calculations are based on the 90 percentile burdens. While most of the measurements at other sampling points and rivers show a clear reduction in the EDTA burdens in surface waters, there are a few individual values that indicate unchanged or increased burdens.

Degradability

In the OECD degradation tests, EDTA was found to be “not readily biodegradable“ and in the tests for potential biological degradability, not “potentially degradable/eliminable“. In other tests, however, EDTA was biologically degraded under suitable test conditions with longer incubation times and adaptation of the microorganisms.

EDTA is resistant to hydrolysis and is attacked neither by strong acids nor by strong alkalis. No data are available on the hydrolysis of EDTA and its salts under the conditions encountered in the environment.

EDTA complexes with calcium, copper and zinc are stable to light. Fe(III)HEDTA is degraded by light similar to sunlight. EDTA is no longer detectable in solutions at pH 4.5 and pH 6.9 after 24, and at pH 8.5 after 32 hours‘ irradiation with a xenon lamp. The biodegradation of EDTA-containing waste waters is promoted by light.

Calculated half lives:

River Neckar, at a depth of 2 m	
March - September	5 - 24 hours
October - February	33 - 480 hours
River Glatt, at a depth of 70 cm	
Summer	2 hours
Winter	10 hours

Accumulation

Various bioaccumulation tests on fish have given BCF values from 0.8 to 1.9. Thus, the BCF value for EDTA is given as 1.

Tests on various animals and plants (e.g. rainbow trout, oysters, and sea pocks as well as sugar beet seedlings) showed a reduction in the uptake and accumulation of cadmium in the presence of EDTA.

Distribution and migration processes within and between compartments of the environment

The different tests to determine the adsorption behaviour of EDTA in soils indicate that it is adsorbed only in small quantities. In the neutral pH range, EDTA complexes are negatively charged ions that can therefore fundamentally be adsorbed by solids with a positive surface charge.
At pH 7, however, adsorption can vary quite considerably from one adsorbent to another.

Interaction with heavy metals

Because of the high complexation constants for heavy metals, EDTA is already in the form of a heavy-metal chelate when it is discharged into surface waters. It is therefore very unlikely that the heavy metals could be remobilized from sediments in surface waters. It would appear to be theoretically possible for free EDTA to hinder the adsorption of heavy metals to solids in waste-water treatment plants. Considering the actual conditions and the concentrations of heavy metals and EDTA-metal complexes and the variation in their concentration, EDTA is not expected to have significant influence on the levels of heavy metals in surface waters.

Ecotoxicological effect

In principle, the effect of EDTA is not a result of its own toxicity, but mainly of its ability to form complexes. Depending on the concentration of polyvalent ions, this chelating effect can deplete essential ions such as Fe(III) in aqueous media, which inhibits growth, e.g. in green algae. This mode of action must be carefully considered in assessing standard laboratory tests: Although the concentrations of certain individual ions are specified in the test methods in accordance with physiological requirements, the wide range of ions available for complexation in the environment is not taken into account. Thus limiting conditions for essential ions frequently occur in standardized laboratory tests, as the essential ions are “withdrawn“ from the test medium by EDTA. An effect achieved on this basis, however, has no ecological relevance with respect to the outdoor situation, as here is a molar excess of dissolved metals, compared with EDTA.

Towards bacteria, the toxic threshold concentration for Na_4EDTA after 8 days was 105 mg/l. The EC_{10} of Na_2H_2EDTA after 30 minutes was 55 mg/l.

The toxic threshold concentration of Na_4EDTA for three species of protozoa after 72 hours was 17,36 and 663 mg/l.

For algae, the EC_3 value of Na_4EDTA after 8 days was 11 mg/l. Because the substance under investigation, Na_4EDTA interferes with the test system, the tests for the “determination of growth inhibition in green algae“ are not suitable for determining the toxicity of EDTA towards algae. Investigations of ecosystems indicate that EDTA in concentrations around 100 µg/l has no eutrophic effect.

The growth of higher water plants is inhibited after 10 days by 292.2 mg/l of EDTA.

The EC_{50} (24 h) value of Na_4EDTA for small crustaceans was 625 - 1033 mg/l.

The effective concentration (96h LC_{50}) of H_4EDTA towards fish was 59.8 mg/l; when the tests were conducted in water of different hardness, 41 mg/l in soft water, 159 mg/l in medium hard water and 532 mg/l in hard water were found.

The effective concentration (96h LC_{50}) of Na_4EDTA in medium-hard water towards fish was found to be 486 mg/l.

There have been many investigations into the influence of EDTA on the effect of heavy metals on different aquatic and terrestrial organisms. With all the species investigated, EDTA reduced or even completely eliminated the toxicity of copper, cadmium, zinc, manganese and nickel. In one case, however, the effects of chromium and lead on the cyanobacterium, Nostoc muscorum, was increased by the addition of EDTA.

Toxicological aspect

The toxicological profile of EDTA is determined by its formation of chelates with metal ions, particularly zinc.

About 5 % is absorbed after oral administration and only 0.001 % after dermal application. It is eliminated via tubular secretion and glomerular filtration. After parenteral injection, 95 - 98 % of the EDTA is eliminated via the kidneys without any metabolic transformation. A very small proportion is retained by the kidneys.

The acute oral toxicity of EDTA, Na_4EDTA and EDTA disodium salt is low. The substances can cause convulsions, diarrhoea, exsiccosis and malfunctions in the central nervous system.

EDTA and its disodium salt do not irritate the skin, while Na_4EDTA is a mild irritant. In the eye, EDTA and Na_4EDTA caused slight to definite irritation effects. In animal trials, no sensitizing potential by the disodium or trisodium salts, or the magnesium salt could be detected. No data is available for EDTA. A few cases of dermal sensitization (contact eczema) and allergic conjunctivitis have been described in man.

Damage to the tubuli of the kidneys occurred after i.p. injection of high subacute, subchronic and chronic dosages. After oral uptake, diarrhoea, reductions in body weight and changes in the blood occurred.

There are differing results on the genetic toxicity of EDTA. No genetic mutation is induced in bacteria. By contrast, DNA damage and mutations were found in cultures of mammalian cells in the mouse lymphoma test, after exposure to high concentrations. Some of the papers published considered indications of genetic effects in vivo particularly with regard to the induction of aneuploidy. Thus, it cannot yet be determined with certainty whether EDTA has any genotoxic effect.

In a long-term feeding study with rats and mice conducted under conditions that do not meet standards today, Na_3HEDTA was found to have no carcinogenic effects. No studies have been carried out with EDTA or Na_4EDTA.

In high, maternally toxic dosages, EDTA is fetotoxic and teratogenic. It is assumed that this is due to zinc depletion.

Treatment with EDTA causes kidney damage, nausea, headaches, ventricular fibrillation, impaired repolarization and obstruction of the respiratory tract in man.

Recommendations

Ecological recommendations

The ecotoxicological results and the information on behaviour in the environment presented here are regarded as adequate for assessing the relevance to the environment.

Toxicological recommendations

The genotoxicity results for EDTA and its salts are contradictory so that it is not possible to assess the potential with certainty. Hypotheses on their mode of action include both a direct genotoxic effect and an interference with essential metal ions. As knowledge of the mode of action is important for assessing the risk with regard to an effect threshold, the following two-stage test plan should be considered:

(1) In vitro chromosome mutation test (chromosome tests on V79 cells) with Na_4EDTA and CaZnEDTA.

(2) In vivo micronucleus test on mouse bone marrow (oral administration) with Na_4EDTA and CaZnEDTA.

Depending on the test results, it should be decided whether it is necessary to conduct in vivo micronucleus tests on mouse bone marrow with i.p. administration and to determine possible induction of mutation in germ cells.