

I U C L I D

D a t a s e t

Existing Chemical	Substance ID: 56-84-8
CAS No.	56-84-8
EINECS Name	aspartic acid
EINECS No.	200-291-6
Molecular Weight	133.1
Structural Formula	CH ₂ CH(NH ₂)COOH
Molecular Formula	C ₄ H ₇ N ₁ O ₄

Dataset created by: EUROPEAN COMMISSION - European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

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1.0.1 OECD and Company Information

Name: Chemie Linz Ges.m.b.H.
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Town: 4021 Linz
Country: Austria

Name: ORSAN
Street: Rue Ballu, 16
Town: 75009 PARIS
Country: France
Phone: (33) (1) 40 82 34 34
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Name: Rexim S.A. Produits Chimiques
Street: Avenue Marceau
Town: F-92400 Courbevoie
Country: France

Name: Welding GmbH & Co.
Street: Grosse Theaterstrasse 50
Town: 20354 Hamburg
Country: Germany
Phone: 0049 40 35908-0
Telefax: -250

1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: organic
Physical status: solid

1.1.1 Spectra

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1.2 Synonyms

(S)-Aminobutanedioic acid
Source: Rexim S.A. Produits Chimiques Courbevoie

L-Aminobernsteinsäure
Source: Rexim S.A. Produits Chimiques Courbevoie

L-Aminobernsteinsäure; L-Aspartinsäure

Source: Welding GmbH & Co. Hamburg

L-Aminosuccinic acid

Source: Rexim S.A. Produits Chimiques Courbevoie

L-aminosuccinic acid

Source: ORSAN PARIS
Chemie Linz Ges.m.b.H. Linz

L-asparagic acid

Source: ORSAN PARIS

L-asparaginic acid

Source: ORSAN PARIS

L-Asparaginsaeure

Source: Rexim S.A. Produits Chimiques Courbevoie

L-Aspartic acid

Source: Rexim S.A. Produits Chimiques Courbevoie

L-aspartic acid

Source: ORSAN PARIS
Chemie Linz Ges.m.b.H. Linz**1.3 Impurities**

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1.4 Additives

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1.5 Quantity**Quantity** 5 000 - 10 000 tonnes**1.6.1 Labelling**

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1.6.2 Classification

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1.7 Use Pattern**Type:** type
Category: Wide dispersive use**Type:** industrial
Category: Chemical industry: used in synthesis

Type: industrial
Category: other

Type: use
Category: Cosmetics

Type: use
Category: Food/foodstuff additives

Type: use
Category: Intermediates

Type: use
Category: Laboratory chemicals

Type: use
Category: Pharmaceuticals

1.7.1 Technology Production/Use

-

1.8 Occupational Exposure Limit Values

Type of limit:

Limit value:

Remark: L-Aspartic acid is a naturally occurring amino acid present in all living organisms. It is synthesized by the body.

To the best of our knowledge, no occupational limits have been established.

Source: ORSAN PARIS

1.9 Source of Exposure

Remark: The main (by far) exposure of Humans to L-Aspartic acid results from food intake.

A small exposure to the product may result from its handling during its production (packaging step) or its use through the dust generated (skin contact, inhalation). As for any dust generating activity in factories, workshops and workers have to be equipped accordingly and according to local regulations.

Safety data sheets provide the necessary information about precautionary measures.

Source: ORSAN PARIS

1.10.1 Recommendations/Precautionary Measures

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1.10.2 Emergency Measures

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1.11 Packaging

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1.12 Possib. of Rendering Subst. Harmless

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1.13 Statements Concerning Waste

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1.14.1 Water Pollution

Classified by: other: provisionally by manufacturer/importer
Labelled by:
Class of danger: 0 (generally not water polluting)
Country: Germany
Source: Rexim S.A. Produits Chimiques Courbevoie

1.14.2 Major Accident Hazards

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1.14.3 Air Pollution

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1.15 Additional Remarks

Remark: Measures after spills or leaks;

- * Product in aqueous solution

Wear rubber boots and rubber gloves.

- Take up with sand or other absorbent material and place into containers for waste disposal.
- It is also possible to swill down if cleaning water can be collected in draining off system and sent to a waste water treatment station (L-Aspartic acid is easily biodegradable).
- * Product in solid form
- Avoid raising dust. Wear self-contained breathing apparatus, rubber gloves and boots. Sweep up, place in a bag and hold for waste disposal.

May be swill down as when in solution.
Transport: no precautionary measures.

Source: ORSAN PARIS

1.16 Last Literature Search

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1.17 Reviews

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1.18 Listings e.g. Chemical Inventories

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2.1 Melting Point

Value: 269 - 271 degree C
Decomposition: ambiguous
Sublimation: no
Source: Welding GmbH & Co. Hamburg

Value: 270 - 271 degree C
Decomposition: no
Sublimation: no
Method: other
Remark: Crystallized amino acids have a fairly high melting or decomposition point.

L-Aspartic acid

* Melting point : 270 - 271 degree C. (sealed capillary, preheated bath)

Reference: The Merck Index, 11th edition, 1989.

* Decomposition point: more than 300 degree C.

* Stable under normal conditions.

* Hazardous polymerization has not been reported to occur under normal temperatures and pressures.

Source: ORSAN PARIS

2.2 Boiling Point

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2.3 Density

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2.3.1 Granulometry

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2.4 Vapour Pressure

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2.5 Partition Coefficient

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2.6.1 Water Solubility

Value: = 4 g/l at 20 degree C
Qualitative: of low solubility
pH: 2.5 - 3.5 at 4 g/l and 20 degree C
Source: Welding GmbH & Co. Hamburg

Value: 5 g/l at 25 degree C
pH: 2.5 - 3.5 at 5 g/l and 25 degree C
Method: other
Remark: Ionization constants of L-Aspartic acid in water at 25 degree C.

* Classical

pka1 : 3.86
pka2 : 9.82
pkb1 : 11.93

* Zwitterionic

pKA1 : 2.10
pKA2 : 3.86
pKB1 : 4.18

* Acidic

pK1 : 2.10
pK2 : 3.86
pK3 : 9.82

Reference:

Handbook of Chemistry and Physics, 53rd edition, 1972-1973
Solubility of L-aspartic acid:

* In water : sparingly soluble

- 2.10 g/l at 0 degree C.
- 5.00 g/l at 25 degree C.
- 12.00 g/l at 50 degree C.
- 28.75 g/l at 75 degree C.
- 68.90 g/l at 100 degree C.

Reference:

Dalton, J.B. and Schmidt, C.L.A., 1933
J. Biol. Chem., 103, 549

* In acid and alkaline solutions : soluble

* In alcohol and organic solvents : insoluble

Reference:

The Merck Index, 11th edition, 1989

Source: ORSAN PARIS

2.6.2 Surface Tension

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2.7 Flash Point

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2.8 Auto Flammability

Value: 580 degree C
Method: other
Source: ORSAN PARIS
Test condition: Test carried out according to:

International Electrotechnical Commission standard
(Sub-Committee 31H), Aug. 1984.

* Measure carried out on dust clouds.

* Device : oven of the Godbert - Greenwald type in which a certain quantity of dust (0.15 - 0.30 and 0.60 g) is injected through a compressed air jet (500 cm³) under various pressures (0.15 - 0.30 and 0.50 bar). The temperature is measured through a thermocouple placed in contact with the oven wall at a middle distance of the two ends of the oven. The maximal temperature reached by this device is 900 degree C.

* L-Aspartic acid : 580 degree C.

By comparison:

- Wheat meal : 420 degree C.

- Montrambert coal : 580 degree C.

(1)

2.9 Flammability

Result: non flammable
Method: other
Source: ORSAN PARIS
Test condition: Test carried out according to conditions classically used by INERIS (Institut National de l'Environnement Industriel et des Risques).

According to INERIS this method will become an international standard, in the future.

* Flammability (Minimal Ignition Energy = Energie Minimale d'Inflammation) was determined on dust clouds of the product (fraction of the product with a particle size of less than 0.100 mm).

* Device : oven of the Hartman type with an air or oxygen atmosphere.

- In air:

L-Aspartic acid can not be ignited by an electric spark

of 1200 mJ (highest energy used in the device).

- In oxygen:
E 5 % = 40 mJ (moderately flammable by an electric spark).

(1)

2.10 Explosive Properties

Result: no data
Source: Welding GmbH & Co. Hamburg

Result: not explosive
Method: other
Source: ORSAN PARIS
Test condition: Test conditions correspond to the ones defined in:

ISO standard 61841 (or French standard NF EN 261841 of June 1991).

* Test carried out on dust clouds of the product to determine which precautionary measures have to be implemented by the producer or the user during the handling of the product when dust may be generated.

* Trials were carried out in a closed spheric 20 l tank to characterize the violence of the explosion according to the dust cloud concentration.

The explosion maximum overpressure (P max) and the maximum speed in pressure rise (SPR) were measured. For the dust cloud concentration (in g/m³) producing the highest value for SPR (expressed in bar/s) the value of the coefficient Kst (expressed in bar*m/s), corrected for a volume of 1 m³ is determined according to the law:

$$K_{st} = \frac{SPR \cdot V}{1/3}$$

with V = 0.020 m³

Nota:

- * Coefficient Kst as defined in:
 - VDI 3673 recommendation of Oct. 1983,
 - ASTM E 1336-88 standard.

- * K max as defined in:
 - the experimental standard AFNOR U 54-540 of Dec. 1986,
 - the European standard NF EN 26 184-1 of June 1991.

Results:

- P max (bar) = 6.8
- SPR (bar/s) = 355
- K max or Kst (bar*m/s) = 96
- Explosion category = St1 (weak explosion)
(according to VDI 3673)

(2)

2.11 Oxidizing Properties

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2.12 Additional Remarks

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3.1.1 Photodegradation

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3.1.2 Stability in Water

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3.1.3 Stability in Soil

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3.2 Monitoring Data (Environment)

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3.3.1 Transport between Environmental Compartments

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3.3.2 Distribution

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3.4 Mode of Degradation in Actual Use

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3.5 Biodegradation

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3.6 BOD5, COD or BOD5/COD Ratio

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3.7 Bioaccumulation

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3.8 Additional Remarks

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AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

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4.2 Acute Toxicity to Aquatic Invertebrates

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4.3 Toxicity to Aquatic Plants e.g. Algae

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4.4 Toxicity to Microorganisms e.g. Bacteria

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4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

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4.6.2 Toxicity to Terrestrial Plants

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4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

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4.7 Biological Effects Monitoring

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4.8 Biotransformation and Kinetics

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4.9 Additional Remarks

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5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: = 9000 mg/kg bw
Method:
Year: **GLP:**
Test substance: no data
Remark: LD50 basiert auf den Angaben unseres Lieferanten für DL-Asparaginsäure.
Source: Welding GmbH & Co. Hamburg

5.1.2 Acute Inhalation Toxicity

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5.1.3 Acute Dermal Toxicity

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5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 6000 mg/kg bw
Method:
Year: **GLP:**
Test substance: as prescribed by 1.1 - 1.4
Source: ORSAN PARIS

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:

Result: not irritating
EC classificat.: not irritating
Method: other
Year: 1992 **GLP:** yes

Test substance: as prescribed by 1.1 - 1.4
Remark: According to HRC report (see reference), L-Aspartic acid does not require labelling with the risk phrase R 38 "Irritating to skin" in accordance with EEC Council Directive 79/831/EEC, Annex VI, Part II (D) as described in Commission Directive 93/21/EEC.

Source: ORSAN PARIS

(3)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:

Result: slightly irritating
EC classificat.: not irritating
Method: other
Year: 1992 **GLP:** yes

Test substance: as prescribed by 1.1 - 1.4
Remark: Remark:

Approximately 90 mg of the test substance, the weight occupying a volume of 0.1 ml, was placed into the lower everted lid of one eye of each animal.

The instillation of L-Aspartic acid into the rabbit eye elicited dulling of the normal lustre of the cornea and transient well-defined conjunctival irritation.

- one hour after instillation
 - * Cornea: dulling
 - * Conjunctiva:
 - . redness : grade 2
 - . chemosis : grade 2
- one day after instillation
 - * Cornea : return to normal
 - * Conjunctiva:

- . redness : grade 1
- . chemosis : grade 1 for 2 animals out of 3 (the 3rd one with grade 0)

- two days after instillation: return to normal

Considering the fact that L-Aspartic acid is marketed under a crystalline form, a part of the ocular reactions observed is likely attributable to mechanical effects.

According to HRC report (see reference), L-Aspartic acid does not require labelling with the risk phrase R 36 "Irritating to eyes" in accordance with Council Directive 79/831/EEC, Annex VI, Part II (D) as described in Commission Directive 93/21/EEC.

Source: ORSAN PARIS

(4)

5.3 Sensitization

Type: Guinea pig maximization test
Species: guinea pig
Number of Animals:
Vehicle:
Result: not sensitizing
Classification: not sensitizing
Method: other
Year: 1992 GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: According to HRC report (see reference), L-Aspartic acid does not require labelling with the risk phrase R 43 "May cause sensitization by skin contact" in accordance with Council Directive 79/831/EEC, Annex VI, Part II (D) as described in the Commission Directive 93/21/EEC.

Source: ORSAN PARIS

(5)

5.4 Repeated Dose Toxicity

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5.5 Genetic Toxicity 'in Vitro'

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5.6 Genetic Toxicity 'in Vivo'

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5.7 Carcinogenicity

-

5.8 Toxicity to Reproduction

-

5.9 Developmental Toxicity/Teratogenicity

-

5.10 Other Relevant Information

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5.11 Experience with Human Exposure**Remark:**

BACKGROUND

Aspartic acid, a dispensable dicarboxylic amino acid, is produced endogenously by the vitamin B6-dependent transamination of oxaloacetic acid. This reversible reaction also converts aspartate in the presence of alpha-ketoglutarate to oxaloacetate and glutamate. Consequent to the inextricable relationship between aspartate and glutamate, these dicarboxylic amino acids are generally considered together in discussions of absorption, transport, and intermediary metabolism.

The role of aspartic acid in intermediary metabolism is via oxaloacetate, which enters either the TCA cycle directly or is converted to phosphoenolpyruvate for gluconeogenesis or conversion to pyruvate and acetyl CoA. Another important role for aspartate is the malate shuttle system for the generation of reducing equivalents in mitochondria.

Aspartic acid also plays a role in the urea cycle where it combines with citrulline to form arginosuccinate. The arginosuccinate is subsequently converted to arginine and fumarate and eventually urea, ornithine (from arginine), and malate and oxaloacetate (from fumarate). The oxaloacetate may then be transaminated to regenerate aspartate; thereby replenishing the endogenous supply.

Baverel et al. (1990) investigated the role of aspartate in the production of glutamine in the kidney. These authors noted that aspartic acid is actively reabsorbed by the renal tubule. In investigating the fate of aspartic acid, Baverel et al. (1990) found that glutamine was the primary carbon and nitrogen product and that glutamate, ammonia, and alanine represented only minor products.

Source:

ORSAN PARIS

(6)

Remark:

ABSORPTION AND TRANSPORT

Both aspartate and glutamate are absorbed via a sodium-dependent active transport system. This a saturable process subject to inhibition and influenced by sodium concentration in the intestinal mucosa. While sodium is

necessary for transport of acidic amino acids such as aspartate and glutamate, the cation associated with these anionic amino acids in plasma or specific tissues is not known.

Aspartic acid may be absorbed as the free amino acid or as a constituent of a peptide. After a protein meal, it is primarily as the latter (Stegink, 1984). Aspartic acid, as the free amino acid, is absorbed via an active transport system whereas, the aspartic acid-containing peptides are directly absorbed and subsequently must be hydrolyzed by specific intracellular peptidases. A protein-bound aspartic acid load of 40 to 46 mg/kg body weight caused increased plasma aspartic acid concentrations (5.3 to 8.1 micromol/L over baseline) after 3 hours in humans (Stegink, 1984). Absorption of free aspartic acid has been found to be slower than other amino acids in humans (Adibi et al., 1967). Silk et al. (1973) reported that aspartic acid from peptides is absorbed more rapidly than the free form.

Source: ORSAN PARIS

(7) (8) (9)

Remark: METABOLISM

The fate of absorbed aspartic acid has been assumed to be related to its transamination to oxaloacetate. The amount of ingested aspartic acid or glutamate appearing in portal blood as alanine, glutamate, or aspartate is a function of the amount given and the availability of glucose as a pyruvate precursor (Stegink, 1976). Neame and Wiseman (1957) reported that alanine was the major amino acid product of aspartic acid absorption and gut metabolism. This finding was supported by the work of Pearsons and Voltman-Mitchell (1974) who estimated that 85 percent of the intestinal metabolism of aspartate is through the transamination pathway and the eventual evolution of CO₂.

Another possible fate for ingested aspartic acid is related to the rapid interconversion of aspartate and glutamate. Blood concentrations of both aspartate and glutamate are significantly elevated following administration of a bolus of aspartic acid (Finkelstein et al., 1983).

Several other factors can influence the amount of aspartic acid that enters the circulation. It has been suggested that the composition of the meal, specifically carbohydrate content, can influence the mucosal intracellular metabolism of aspartic acid and subsequent release into the portal circulation through several possible mechanisms as outlined by Stegink (1984). The basis for these suggestions was a series of studies of glutamate absorption. Daabes et al. (1985) found that, in contrast to glutamate, metabolizable carbohydrates had no significant effect on plasma aspartic acid concentrations.

Source: ORSAN PARIS

(10) (11) (12) (13) (14)

Remark: HUMAN STUDIES

Studies on animals have been carried out using routes of administration (I.V., I.P., S.C.) of aspartic acid that are not related to the actual main exposure route: i.e. through the food intake.

Only a few studies have specifically examined the safety of aspartic acid supplementation in Humans.

Doses of up to 8 g/ day of the sodium salt of L-aspartic acid (Koyuncuoglu, 1983) or 10 g of L-aspartic acid - oral bolus in gel capsule given with 500 ml saline - (Carlson et al., 1989) have been given to humans with no reported side effects.

For perspective, a person consuming 100 g protein per day would consume about 3.2 g aspartic acid.

Source: ORSAN PARIS

(15) (16)

Remark: L-Asparaginsäure ist eine für den Menschen nicht essentielle Aminosäure. Die Substanz wird in Arzneimitteln verwendet

z.B. in Infusionslösungen zur parenteralen Ernährung.

Source: Welding GmbH & Co. Hamburg

(17) (18)

(1) Reference:

INERIS (Institut National de l'Environnement Industriel et des Risques - formerly CERCHAR -) report to ORSAN.
Report on 30 November 1984, (unpublished).

(2) Reference:

INERIS (Institut National de l'Environnement Industriel et des Risques - formerly CERCHAR -) report to ORSAN.
Report on 14 June 1990, (unpublished).

(3) Reference:

L-Aspartic acid: skin irritation to the rabbit.
Report by Huntingdon Research Centre Ltd (HRC) to ORSAN,
3 March 1994, (unpublished).

The method followed was that described in:
EEC Methods for the detection of toxicity,
Annex to Directive 92/69/EEC, Part B, Method B.4. Acute
toxicity (skin irritation).
(OJ Nr. L383A, 29-12-1992).

(4) Reference:

L-Aspartic acid: eye irritation to the rabbit.
Report by Huntingdon Research Centre Ltd (HRC) to ORSAN,
7 April 1994, (unpublished).

The method followed was that described in:
EEC Methods for the detection of toxicity,
Annex to Directive 92/69/EEC, Part B, Method B.5. Acute
toxicity (eye irritation).
(OJ Nr L383A, 29-12-1992).

(5) Reference:

L-Aspartic acid: skin sensitization in the guinea-pig.
Huntingdon Research Centre Ltd (HRC) report to ORSAN,
22 February 1994, (unpublished).

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Glutamine synthesis from aspartate in guinea-pig renal
cortex.
Biochem. J., 268: 437-442.

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The kinetics of amino acid absorption and alteration of
plasma composition of free amino acids after intestinal
perfusion of amino acid mixtures.
Am. J. Clin. Nutr., 20: 24-33.

- (8) Silk, D.B.A., Marrs, T.C., Addison, J.M., Burston, D., Clark, M.L., and Matthews, D.M., 1973.
Absorption of amino acids from an amino acid mixture simulating casein and a tryptic hydrolysate of casein in man.
Clin. Sci. Mol. Med., 45: 715-719.
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Aspartate and glutamate metabolism.
In: Stegink, L., and Filer, L.J., Jr., eds.
Aspartame: physiology and biochemistry.
New York, Marcel Dekker, P.47-76
- (10) Daabes, T.T., Finkelstein, M.W., Applebaum, A.E., and Stegink, L.D., 1985.
Effect of carbohydrate ingestion on plasma aspartate concentrations in infant mice administered sodium L-aspartate.
J. Nutr., 115: 226-232.
- (11) Finkelstein, M.W., Daabes, T.T., Stegink, L.D., and Applebaum, A.E., 1983.
Correlation of aspartate dose, plasma dicarboxylic amino acid concentration, and neuronal necrosis in infant mice.
Toxicology, 29: 109-119.
- (12) Neame, K.D., and Wiseman, G., 1957.
The transamination of glutamic acid aspartic acids during absorption by the small intestine of the dog in vivo.
J. Physiol., 135: 442-450.
- (13) Parsons, D.S., and Voltman-Mitchell, H., 1974.
The transamination of glutamate and aspartate during absorption in vitro by small intestine of chicken, guinea-pig and rat.
J. Physiol., 239: 677-694.
- (14) Stegink, L.D., 1976.
Absorption, utilization, and safety of aspartic acid.
J. Toxicol. Environ. Health, 2: 215-242.
- (15) Carlson, H.E., Miglietta, J.T., Roginsky, M.S., and Stegink, L.D., 1989.
Stimulation of pituitary hormone secretion by neurotransmitter amino acids in humans.
Metabolism, 38: 1179-1182.
- (16) Koyuncuoglu, H., 1983.
The treatment with L-aspartic acid of persons addicted to opiates.
Bull. Narc., 35: 11-15.

- (17) Merck Index 12th Ed., monograph no.: 875
- (18) Römpp Chemie Lexikon, 9. Auflage. Seite 267.

7.1 Risk Assessment

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