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TOXICOLOGICAL EVALUATIONS

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TOXICOLOGICAL EVALUATION

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7-Amino-4-hydroxy-2-naphthalene-sulfonic acid

No. 226

CAS No. 87-02-5

BG Chemie
Berufsgenossenschaft der chemischen Industrie

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7-Amino-4-hydroxy-2-naphthalenesulfonic acid

This Toxicological Evaluation replaces the previously published version in volume 10.

1 Summary and assessment

On single oral administration, 7-amino-4-hydroxy-2-naphthalenesulfonic acid causes no clinical signs of toxicity in rats (LD_{50} rat oral > 5000 mg/kg body weight).

In rabbits, 7-amino-4-hydroxy-2-naphthalenesulfonic acid is not irritating to the intact skin or the eye.

7-Amino-4-hydroxy-2-naphthalenesulfonic acid of unspecified purity and of 91-percent purity has given a positive result in the Salmonella/microsome assay with metabolic activation. In contrast, 7-amino-4-hydroxy-2-naphthalenesulfonic acid of higher purity (96.1%, 4.4% water) has not proved to be mutagenic in the Salmonella/microsome assay. In the chromosome aberration test in vitro, the test substance (purity not specified) has caused an increased aberration rate in the presence of metabolic activation. The available in-vitro studies thus indicate that technical-grade product possibly has a genotoxic potential.

2 Name of substance

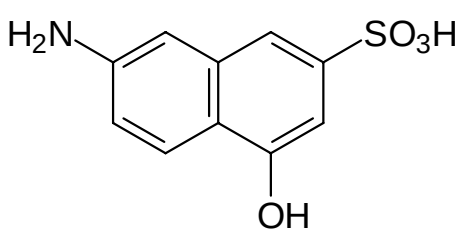
2.1	Usual name	7-Amino-4-hydroxy-2-naphthalenesulfonic acid
2.2	IUPAC name	7-Amino-4-hydroxynaphthalene-2-sulfonic acid
2.3	CAS No.	87-02-5
2.4	EINECS No.	201-718-9

3 Synonyms, common and trade names

2-Amino-5-hydroxynaphthalene-7-sulfonic acid
7-Amino-4-hydroxynaphthalene-2-sulfonic acid
7-Amino-4-hydroxy-2-naphthalinsulfonsäure
2-Amino-5-hydroxynaphthalin-7-sulfonsäure
6-Amino-1-hydroxy-3-sulfonaphthalin
Aminonaphthol sulfonic acid J
2-Amino-5-naphthol-7-sulfonsäure
6-Amino-1-naphthol-3-sulfonsäure
Aminonaphtholsulfonsäure J
I acid
I-Säure
Isogamma acid
J acid
2-Naphthalenesulfonic acid, 7-amino-4-hydroxy-

4 Structural and molecular formulae

4.1 Structural formula



4.2 Molecular formula $C_{10}H_9NO_4S$

5 Physical and chemical properties

5.1	Molecular mass, g/mol	239.25
5.2	Melting point, °C	180–200 (decomposition) (Bayer, 1990)
5.3	Boiling point, °C	No information available

5.4	Vapour pressure, hPa	No information available	
5.5	Density, g/cm³	Ca. 0.7 (bulk density)	(Bayer, 1990)
5.6	Solubility in water	Ca. 0.5 g/l (at 20 °C) Ca. 1.5 g/l (at 60 °C) 1 g/l (in cold water) Dissolves well (at 100 °C)	(Bayer, 1990) (Bayer, 1989) (Booth, 1991)
5.7	Solubility in organic solvents	No information available	
5.8	Solubility in fat	No information available	
5.9	pH value	Ca. 3 (at 0.5 g/l water)	(Bayer, 1989)
5.10	Conversion factor	1 ml/m³ (ppm) $\triangleq$ 9.77 mg/m³ 1 mg/m³ $\triangleq$ 0.10 ml/m³ (ppm) (at 1013 hPa and 25 °C)	

6 Uses

Coupling component for numerous azo dyes (Booth, 1991).

7 Experimental results

7.1 Toxicokinetics and metabolism

No information available.

7.2 Acute and subacute toxicity

Ten male Wistar rats (weighing 160 to 180 g) survived a single oral dose of 5000 mg 7-amino-4-hydroxy-2-naphthalenesulfonic acid (I acid, solution in water)/kg body weight without clinical signs of toxicity. The observation period was 14 days. Thus the LD_{50} was > 5000 mg/kg body weight (no further details; Bayer, 1978).

A further LD_{50} value for rats was reported as 11500 mg/kg body weight following oral administration (no further details; Marhold, 1986).

7.3 Skin and mucous membrane effects

In a skin irritation study, approx. 500 mg 7-amino-4-hydroxy-2-naphthalenesulfonic acid (I acid) were applied to the inner surface of the ears of 2 New Zealand white rabbits of both sexes (weighing 3 to 4 kg) under an adhesive dressing for 24 hours. At the end of the exposure period, the test substance was washed off with water and soap/vegetable oil. The observation period was 7 days. No skin irritation was observed (Bayer, 1979).

In an eye irritation study in rabbits, 50 mg 7-amino-4-hydroxy-2-naphthalenesulfonic acid (I acid) were instilled into the conjunctival sac of 2 animals. The observation period was 7 days. No skin irritation was observed (Bayer, 1979).

In a standard Draize test, instillation of 500 mg 7-amino-4-hydroxy-2-naphthalenesulfonic acid into the conjunctival sac of the rabbit eye caused mild ocular irritation following a 24-hour exposure (no further details; Marhold, 1986).

7.4 Sensitisation

No information available.

7.5 Subchronic and chronic toxicity

No information available.

7.6 Genotoxicity

7.6.1 In vitro

7-Amino-4-hydroxy-2-naphthalenesulfonic acid was tested for mutagenicity in the Salmonella/microsome assay using the *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538. The study was carried out as a standard-plate incorporation test with and without metabolic activation (S-9 mix from Aroclor 1254-induced rat liver) and in a preincubation test with metabolic activation in accordance with the method of Prival and Mitchell (1982). In the presence of metabolic activation, 5.2 and 41 re-

vertants/µmol test substance were recorded in the direct plate test and in the Prival modification, respectively (no data on control values given). The mutagenic effect was evaluated as weak and was attributed by the authors to possible contaminants in the product used. Details of the concentrations employed and the strains in which increased revertant counts were seen were not provided in the publication. (Freeman et al., 1987).

7-Amino-4-hydroxy-2-naphthalenesulfonic acid (purity: 91%, solvent: DMSO) was tested in a Salmonella/microsome assay , carried out as a standard-plate incorporation test (in accordance with OECD guideline No. 471), in the *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 both with and without metabolic activation (S-9 mix from Aroclor 1254-induced rat liver) in two series of experiments conducted independently of one another. Concentrations ranging from 100 to 5000 µg/plate were used. Up to the highest test concentration of 5000 µg/plate, there was no bacteriotoxicity. In the presence of metabolic activation, strains TA 98, TA 1537 and TA 1538 exhibited concentration-dependent increases in revertant counts by maximum factors of 26.9 and 35.5, 10.5 and 11.9 as well as 114 and 141, respectively. The substances used in this study as positive control chemicals with a clear mutagenic effect were 2-aminoanthracene, 2-nitrofluorene, 9-aminoacridine and 2-naphthylamine (Microbiological Associates, 1991). The test substance thus exhibited mutagenic activity under the testing conditions described above.

In a further Salmonella/microsome assay (standard-plate incorporation test; in accordance with OECD guideline No. 471), 7-amino-4-hydroxy-2-naphthalenesulfonic acid (I acid) of 96.1-percent purity (4.4% water) was tested in the *Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537 at concentrations ranging from 8 to 5000 µg/plate, with and without metabolic activation (S-9 mix from Aroclor 1254-induced livers of male Sprague-Dawley rats). Concentrations up to and including 40 µg/plate were not toxic to the bacteria. At the higher concentrations (from 200 µg/plate), the substance had a weak, strain-specific bacteriotoxic effect. No biologically relevant increase in the revertant count was observed either with or without metabolic activation. 7-Amino-4-hydroxy-2-naphthalenesulfonic acid was therefore not mutagenic in this study (Bayer, 1992).

7-Amino-4-hydroxy-2-naphthalenesulfonic acid (purity not specified) was also investigated in the chromosome aberration test in CHL cells. In a preli-

minary experiment without metabolic activation, the cells were incubated with the test substance, added as a solution in physiological saline, at concentrations ranging from 1.0 to 2.5 mg/ml for 24 and 48 hours (2 parallel cultures). Negative controls were treated with the solvent. Mitomycin C (0.04 µg/ml) served as the positive control chemical. Colcemid was added to the cells 2 hours prior to preparation. Per culture, 100 metaphases were counted. After 24 hours, a slight, but not concentration-dependent increase in aberration rate (gaps not included) was seen at concentrations of 2.0 mg/ml and above. After 48 hours, the aberration rate was slightly increased only at the 2.0 mg/ml level. In a second experiment, 7-amino-4-hydroxy-2-naphthalenesulfonic acid was tested, as a solution in carboxymethylcellulose, at concentrations ranging from 0.5 to 8.0 mg/ml in the absence and presence of metabolic activation (S-9 mix from rat liver induced with phenobarbital and 5,6-benzoflavone). The cells were incubated with the test substance for 6 hours (2 parallel cultures). Preparation was carried out 24 hours after the start of incubation. Negative and positive controls were treated with the solvent and with benzo(a)pyrene (10 µg/ml), respectively. Colcemid was added to the cells 2 hours prior to preparation. Per culture, 100 metaphases were counted. Evaluation of the highest test concentration (8.0 mg/ml) was not carried out. No increase in aberration rate was seen in the absence of metabolic activation. With metabolic activation, increase in aberration rates (gaps not included) was observed to be concentration-dependent at 2.0 mg/ml and above, and at the highest evaluated concentration of 4.0 mg/ml a significant increase was seen. According to the report, 7-amino-4-hydroxy-2-naphthalenesulfonic acid was tested for cytotoxicity. However, the publication fails to provide any further details. Based on these results, 7-amino-4-hydroxy-2-naphthalenesulfonic acid was evaluated as positive in this test system (JETOC, 1996).

7.6.2 In vivo

No information available.

7.7 Carcinogenicity

No information available.

7.8 Reproductive toxicity

No information available.

7.9 Effects on the immune system

No information available.

7.10 Neurotoxicity

No information available.

7.11 Other effects

No information available.

8 Experience in humans

No information available.

9 Classifications and threshold limit values

No information available.

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