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Information Profiles on Potential Occupational Hazards: Adipic Acid

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16. Abstract (Limit: 200 words)

Information on potential occupational hazards from exposure to adipic-acid (124049) was reviewed. Topics discussed included chemical and physical properties, production, use, manufacturers and distributors, manufacturing processes, occupational exposure, and biological effects. Production of adipic-acid was 1.8 million pounds in 1979; most of this was used in the production of nylon-66 fibers. Other uses included the production of nylon-66 resins, nylon-66 plastics, as a hexamethylenediamine precursor, in polyurethane resins and plasticizers, and as a food additive. To a much smaller extent adipic-acid was used in insecticides, adhesives, tanning and leather dyes, textile printing, and textile softening. Administration of adipic acid to experimental animals has produced patchy livers, irritation of organs directly exposed, hemorrhagic lungs and symptoms of acidosis. An median lethal dose of 940mg/kg was established for adult male rats. Subchronic exposures in rats produced symptoms of toxicity including depression, dyspnea, ataxia, and convulsions. No significant evidence for carcinogenicity has been reported nor has there been any finding of mutagenicity or teratogenicity or any reproductive effects. No evidence of toxicity was found on oral administration of 100mg/kg adipic-acid per day to human subjects.

17. Document Analysis a. Descriptors

b. Identifiers/Open-Ended Terms

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SUMMARY

In 1979, 1.8 billion pounds of adipic acid were produced. Roughly 90% of the adipic acid production is used captively by the manufacturers to make nylon 66 fibers and plastics. It is also used to make polyurethane resins, plasticizers, and synthetic lubricants and for a variety of miscellaneous applications including use as a food additive. Adipic acid is industrially manufactured by oxidizing cyclohexane to cyclohexanone-cyclohexanol with air and oxidizing this product to adipic acid with nitric acid.

Adipic acid, a GRAS food additive, appears to have a fairly low order of acute toxicity. Although the results of LD50 determinations with rats and mice were inconsistent, the lowest oral LD50 reported was approximately 1 g/kg.

When administered orally or by injection to experimental animals in very high doses, adipic acid produced depression of the central nervous system, convulsions, patchy livers, hemorrhagic lungs, mild impairment of renal function, and severe irritation of tissues directly exposed to the acid. Rats that inhaled powdered adipic acid (126 mg/m^3, 6 hours a day for 15 days), however, suffered no ill effects.

Human subjects who ingested adipic acid at a level of 100 mg/kg/day showed no signs of toxicity. When fed to rats at up to 5% in the diet for 2 years, adipic acid produced little evidence of adverse effects and no evidence of carcinogenicity. Adipic acid does not appear to be teratogenic for experimental animals. A battery of tests provided no clear evidence of mutagenicity.

1. Chemical Name: Adipic Acid

2. Chemical Structure: $HO_2C(CH_2)_4CO_2H$

3. Synonyms:

Adipinic acid	Acifloctin
1,4-Butanedicarboxylic acid	Acinetten
1,6-Hexanedioic acid	Adilactetten

4. Chemical Abstracts Service (CAS) Number: 124-04-9

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number: AU8400000

6. Chemical and Physical Properties

Description:	white crystalline solid that is odorless and has a slight acid taste
Molecular Weight:	146.14
Boiling Point:	330.5°C (with decomposition)
Melting Point:	153.0-153.1°C
Vapor Pressure:	0.073 mm Hg at 18.5°C
Solubility:	1.44 g/100 g water (15°C) 3.08 g/100 g water (34.1°C) 0.633/100 parts ether w/w (19°C) 16.1 g/100 ml ethanol (25°C) 0.92 g/100 ml ether (25°C) 30 g/100 g methanol (25°C) below 0.01 g/100 ml chloroform (25°C) freely soluble in methanol soluble in acetone slightly soluble in cyclohexane practically insoluble in benzene, petroleum ether, and acetic acid
Specific Gravity:	1.36
Stability:	combustible; flash point (closed cup): 385°F

7. Production

Production volumes for adipic acid for 1974 to 1979 are as follows (USITC, 1976, 1977a, 1977b, 1978, 1979; Storck, 1980).

Year	Production in Millions of Pounds
1979	1800
1978	1621
1977	1536
1976	1281
1975	1343
1974	1478

The historical (1969 to 1979) growth rate of adipic acid was 3.8% per year; the future growth is projected to be 0.6% per year through 1984 (CMR, 1980).

In 1978, 7.2 million pounds of adipic acid were exported (USDC, 1979); import figures were not available separately for 1978. Import and export figures, however, represent only a small fraction of domestic production.

8. Use

The following tabulation presents the percentage of the total amount of adipic acid produced that is used in each of the applications listed:

	Percentage of Total	
	CMR (1980)	Lawler (1979)
Nylon 66 fibers	74.0	86.0
Nylon 66 resins	8.7	5.0
Nylon 66 plastics	--	--
Hexamethylenediamine precursor	8.5	--
Polyurethane resins	3.6	4.0
Plasticizers	3.4	4.0 (includes lubricants)
Additives for food	--	0.5
Miscellaneous	1.8	0.5

Most of the adipic acid manufactured is captively used by the producers to make nylon 66 (CMR, 1978). The acid is used directly in the production of nylon 66 or, to a lesser extent, indirectly, to produce 1,6-hexamethylenediamine (Danly and Campbell, 1978).

Large volumes of adipic acid are used to produce esters that are utilized as plasticizers; in 1978, 67.7 million pounds of these adipates were made (USITC, 1979). The adipates most important commercially include di(2-ethylhexyl) adipate, dioctyl adipates, n-octyl and n-decyl adipate, and di[2-(2-

butoxyethoxy) ethyl]adipate. Isooctyl and isodecyl adipates are important lubricants in jet aircraft (O'Leary, 1974).

As a food additive, adipic acid is used in gelatin desserts, powdered concentrates for fruit-flavored beverages, bottled beverages, non-standardized jams and jellies, canned vegetables, candies, flavoring extracts, and baking powder (Danly and Campbell, 1978).

Miscellaneous uses include applications in insecticides, adhesives, tanning and leather dyeing (sodium salt), textile printing (ammonium salt), and textile softening (adipoyl chloride) (O'Leary, 1974).

9. Manufacturers and Distributors

The manufacturers of adipic acid are listed in Tables 1 and 2. A very high percentage of the adipic acid made is used captively by the manufacturers. Adipic acid is distributed (sold) by many companies, including the following (1980-81 OPD Chemical Buyers Directory, 1980; Chemical Week: 1981 Chemical Buyers Guide, 1980; Chem Sources--USA, 1980):

Aldrich Chem.	ICC Industries
Alfa Prod.	ICN/K and K
Alpha International Chem.	Intsel Corp.
Anachemia Chem.	Ishihara Corp.
Analabs	LaChat Chem.
Balfour-Maclaine Chem.	LaPine Sci.
BASF Wyandotte	Lux Chem.
Bentley Chem.	Mallinckrodt
Bio-Clinical Labs	MCB Reagents
Chemical Dynamics	Milijac Inc.
Chemical Procurement Labs	Montedison USA
Chemsampo Inc.	Pfaltz and Bauer
Chem. Serv.	Pioneer Salt and Chem.
Columbia Organics	Regis Chem.
Eastern Chem.	Reliable Chem.
Eastman Kodak	Rhone-Poulenc
EM Labs	Stinnes Oil and Chem.
Fallek Chem.	Thorson Chem.
Fehr	TR America
Fisher Sci.	Trans World Chem.

Table 1. Manufactuers of Adipic Acid (SRC International 1980; CMR, 1978)

Manufacturer	Location	Annual Capacity (Millions of Pounds)	Raw Material and Remarks
Allied Chemical Corp.	Hopewell, VA	30	Phenol; merchant
Celanese Corp.	Bay City, TX	140	Cyclohexane; mostly captive
DuPont	Orange, TX	400	Cyclohexane; mostly captive
	Victoria, TX	700	Cyclohexane; mostly captive
Monsanto Co.	Pensacola, FL	640	Cyclohexane; mostly captive
	TOTAL	1,190	

Table 2. Producers of Adipic Acid and Production Ranges (U.S. EPA, 1980)

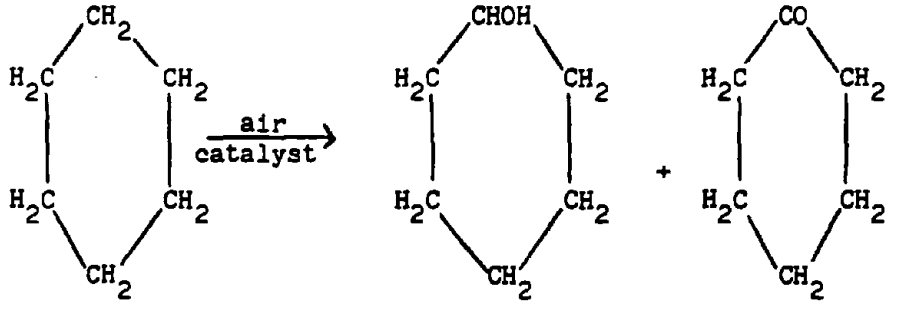
Producer and Location	Type of Production	1977 Production Range
Allied Chemical Hopewell, VA	Manufacturer	confidential
Celanese Chemical Co. Bay City, TX	Manufacturer	50 to 100 million lb
E.I. DuPont Victoria, TX Orange, TX	Manufacturer Manufacturer	100 to 500 million lb 100 to 500 million lb
Monsanto Pensacola, Fl	Manufacturer/ Produced Site Limited	100 to 500 million lb
Unnamed Co. Plant site not on file	Small Manufacturer	10 to 100 thousand lb
El Paso Products Co. Odessa, TX	Manufacturer	50 to 100 million lb
Haven Chemical Philadelphia, PA	Manufacturer	1 to 10 thousand lb
Norton Chemical Ringwood, IL	Manufacturer	1 to 10 thousand lb
Belding Chemical Industries Grosvenor, CT	Manufacturer/ Produced Site Limited	10 to 100 thousand lb
Cemco Inc. New Canaan, CT	Importer	zero
Miljac Inc. New Canaan, CT	Importer	zero
BASF Wyandotte Parsippany, NJ	Importer	zero
Union Camp Corp. Wayne, NJ	Importer	0.1 to 1 million lb
Thorson Chemial NYC, NY	Importer	0.1 to 1 million lb
Sakai Trading Co. NYC, NY	Importer	zero
Montedison USA NYC, NY	Importer	zero
ICC Industries NYC, NY	Importer	confidential
ICI Americas Wilmington, DE	Importer	0.1 to 1 million lb

Gallard-Schlesinger Chem.	Tridom Chem.
Gill and Duffus Chem.	United States Biochemical
M.W. Hardy and Co.	Var-Lac-Oid Chem.
Helm Chem.	Vega Biochemicals
Holtrachem	Velco Enterprises
	Van Waters and Rogers

10. Manufacturing Process

As can be seen from Table 1, approximately 98% of the domestic capacity to make adipic acid is based upon a cyclohexane feedstock. Although there are slight variations among the manufacturers, the general manufacturing operations are outlined in Figure 1.

Manufacture of adipic acid is accomplished in a two-stage process (Danly and Campbell, 1978; Lowenheim and Moran, 1975; Pervier et al., 1974). In the first stage, liquid cyclohexane is catalytically air oxidized to a mixture of cyclohexanone-cyclohexanol, which is also known as KA (ketone-alcohol) oil. The reaction may be represented as:



By-products formed in this reaction include acetic, formic, valeric, oxalic, succinic, and glutaric acids as well as cyclohexyl esters (O'Leary, 1974). In the second stage of manufacture, the KA oil is catalytically oxidized to adipic acid with nitric acid. This reaction may be represented as:

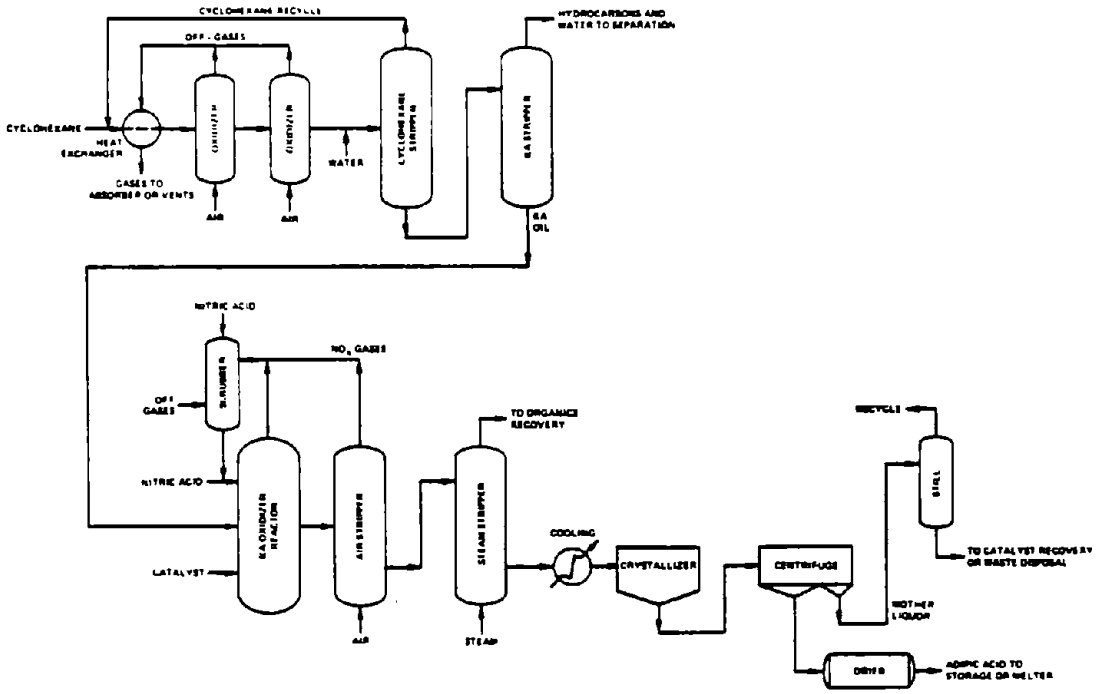
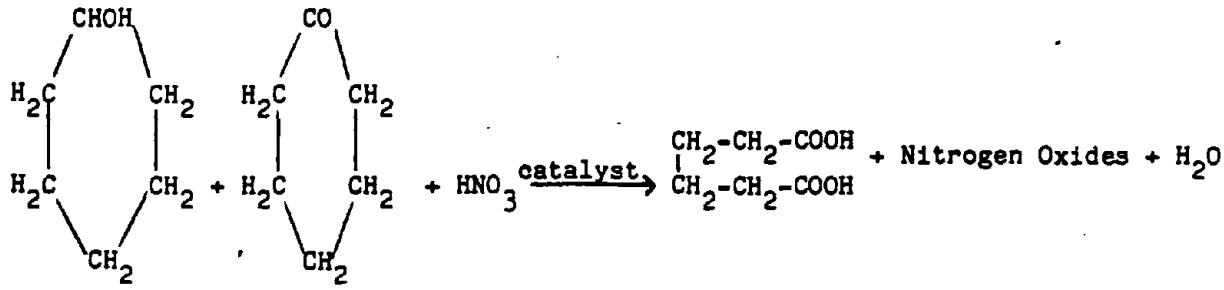


Figure 1. Manufacture of Adipic Acid (Adapted from Danly and Campbell, 1978; Lowenheim and Moran, 1975; Pervier et al., 1974)



The nitrogen oxides produced are predominantly NO, NO_2, and N_2O. Additionally, various organic acid by-products are formed; chief among these are acetic acid, glutaric acid, and succinic acid. In the larger plants, some of these by-products may be recovered and sold (Pervier et al., 1974).

The process operations begin with the oxidization of cyclohexane to KA oil with air as the oxidant. Typical commercial practice involves the use of undiluted air at 150 to 160°C and 8 to 10 atmospheres of pressure with a catalyst (cobalt) concentration of 0.3 to 3 ppm (Danly and Campbell, 1978). The oxidation may be a series of sparged reactors or in a multistage column contractor because cyclohexane conversion must be held at low levels to prevent overoxidation of the KA oil. Due to the low conversion levels, substanial quantities of cyclohexane must be separated by distillation from the oxidizer effluent for recycle to the feedstock.

The liquid product from the cyclohexane oxidation is mixed with water and delivered to a distillation column (stripper) or a series of columns and extractors. The unreacted cyclohexane is recycled. The by-product hydrocarbons distill overhead (Lowenheim and Moran, 1975) and may contain considerable benzene (depending on the grade of cyclohexane used as feedstock), which is separated by azeotropic distillation in another unit. Because this benzene is sulfur-free, it may readily be hydrogenated to cyclohexane and recycled. The product KA oil is delivered from the distillation units to a reactor for oxidation with nitric acid to make the adipic acid.

In commercial practice, the KA mixture is oxidized in a series (generally two) of stirred tank reactors (Pervier et al., 1974). Typical reaction conditions involve 50% to 60% HNO_3 at 60° to 80°C and a pressure of 1 to 4 atmospheres containing a copper-vanadium catalyst (Danly and Campbell, 1978). The liquid reactor product is a solution of adipic acid, nitric acid, and organic by-products. The organic by-products are separated via air and steam strippers; glutaric and succinic acid are the major by-products. The adipic acid is then recovered by crystallization at 30° to 70°C and the mother liquor is concentrated under pressure for recycle to the oxidizers. Centrifuging and drying complete the operations for adipic acid as product. The oxidation gases, primarily NO and NO_2, are recovered by absorption for reuse; then N_2O and N_2 must be vented from the reaction system. Yields from the process operations are 90% to 95% of the theoretical yield.

Allied Chemical uses phenol instead of cyclohexane as a feedstock material. The phenol is hydrogenated to cyclohexanol, which is then oxidized with nitric acid as described above.

Specifications for typical food-grade adipic acid are as follows (Danly and Campbell, 1978):

	Food-grade	Resin-grade
assay	99.7%	99.7%
residue on ignition, max.	0.002%	0.0012%
water	0.20%	---
iron, max.	---	2 ppm
heavy metal, max. as Pb	10 ppm	---
arsenic	3 ppm	---
hydrocarbon oil	10 ppm	---
caproic acid	10 ppm	---
succinic acid	50 ppm	---

Adipic acid is commonly sold in drums, paper bags, or hopper cars.

11. Impurities or Additives

As detailed in Section 10 (Manufacturing Process), nitrogen oxides and various organic acid by-products are formed during production; the major organic by-products are acetic acid, glutaric acid, and succinic acid.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 14,464 workers are exposed to adipic acid.

13. Control Technology

Specific factors that may contribute to or prevent employee exposure to adipic acid were not found in the literature searched.

14. Biological Effects

Adipic acid is a Generally Recognized as Safe (GRAS) food substance (21 CFR 182.1009) and a permitted synthetic flavoring substance or adjuvant (21 CFR 172.515). The use of adipic acid in foods has prompted much of the following research on its health effects.

A. Animal Studies

1. Acute Exposures

The acute effects of adipic acid are described in Table 3. Administration of adipic acid to experimental animals produced patchy livers (Litton Bionetics, 1974), irritation of organs directly exposed to the acid (Litton Bionetics, 1974; Horn et al., 1957; Enders, 1941), hemorrhagic lungs (Horn et al., 1957), and, after intravenous injection, symptoms of acidosis (Horn et al., 1957; Enders, 1941).

Litton Bionetics (1974) performed two series of tests of acute toxicity. In both, adipic acid was administered by intubation to adult male rats weighing 250 g (Test 1) or 267 g (Test 2). In the first test, a dose of 5000 mg/kg killed all 10 rats tested. An LD50 of 940 mg/kg was determined. In

Table 3. Acute Effects of Adipic Acid

Route	Species	Dose (mg/kg)	Response	Reference
oral	rats	940	LD50; death within 4 days; patchy livers, blood in intestinal mucosa (Test 1)	Litton Bionetics, 1974
oral	rats	5000	No deaths; no overt signs of toxicity or abnormal behavior within 7 days; no gross pathological changes (Test 2)	Litton Bionetics, 1974
oral	mice	1900	LD50; death within 1 week; distention of stomach and small intestine; spastic contraction of caecum, irritation and hemorrhage of intestines	Horn et al., 1957
oral	rabbits	2430	No deaths; inactivity; distended stomach, diarrhea	Enders, 1941,
oral	rabbits	4860	Lethal dose; death in 10 to 30 hours; swollen intestines, venous obstruction in liver and kidneys	Enders, 1941
i.p.	rats	275	LD50; death within 5 days; hemorrhagic lungs, irritation of intestines; survivors had extensive irritation and adhesion of viscera at 7 days	Horn et al., 1957

Table 3. Acute Effects of Adipic Acid (Cont'd)

Route	Species	Dose (mg/kg)	Response	Reference
i.p.	mice	600	Lethal dose; immediate depression, hemorrhagic lungs, irritation of intestines	Horn et al., 1957
i.v.	mice	680 (0.1 ml/sec of 2% soln.)	LD50; immediate convulsive death; hemorrhagic lungs	Horn et al., 1957
i.v.	rabbits	2430	No deaths; polyuria with loss of up to 20% body weight within 8 hours	Enders, 1941

Abbreviations: i.p. = intraperitoneal; i.v. = intravenous; sec = second; soln. = solution.

the second test, a dose of 5000 mg/kg appeared to have no effect on any of the 10 rats tested. The authors offered no explanation for this discrepancy.

Rose et al. (1925) reported that adipic acid (1 to 2 g/kg), administered to rabbits subcutaneously in the form of its sodium salt, was mildly nephropathic as indicated by changes in blood chemistry and decreased output of phenosulphonephthalein. Renal function appeared to return to normal within 48 hours. Larger doses produced more prolonged effects. Harding and Nicholson (1931) found that intramuscular injection of sodium adipate (dose not specified) into rabbits produced mild renal irritation (albumin and casts in urine) in only 2 out of 13 rabbits. Because sodium adipate caused slight local swelling with marked necrosis at the site of injection, the authors suggested that it may have been poorly absorbed as had been noted for higher homologues of the dicarboxylic acid series.

2. Subchronic Exposures

Adipic acid was administered by intubation to male rats (average body weight 248 grams, 6 rats/dose level) at doses of 3600, 4000, 5000, and 5600 mg/kg/day for 5 days. Symptoms of toxicity, which appeared on the second day and persisted throughout the treatment period, were depression, dyspnea, ataxia, and convulsions. Fourteen days after the start of treatment, the surviving animals were killed and gross necropsies performed. No abnormalities were noted. The LD50 was 3615 mg/kg/day (Litton Bionetics, 1974).

A dose of 243 mg adipic acid/day, given by intubation to five young rats for 4 weeks, was reported by Enders (1941) to have no significant effect on weight gain. This amount of adipic acid corresponded to a dose of 3471 mg/kg/day at the beginning of the experiment when the animals weighed 60 to 80 g. Three 300-g adult rats that received 730 mg adipic acid daily (2433 mg/kg/day) for 4 weeks appeared healthy throughout the test period;

weights remained constant. No evidence of adverse effects was found at autopsy at the end of the 4 weeks.

In a series of experiments conducted by Lang and Barstch (1953) male and female rats of 44 to 74 g initial body weight were fed up to 800 mg adipic acid a day (10 to 20 rats/dose level) for up to 33 weeks. Animals receiving 200 or 400 mg/day had weight gains similar to those of controls over a period of 5 weeks. Animals receiving 800 mg/day (corresponding to an average initial dose of 1356 mg/kg/day) appeared unkempt and apathetic and suffered from heavy diarrhea during the first 3 weeks. They recovered by the fifth week, although their weight gains were still significantly lower than controls. After 33 weeks, weights of the high-dose rats were the same as controls.

When fed a protein-deficient diet (11% protein), rats receiving 400 mg adipic acid/day had a significant inhibition of growth lasting through 19 weeks (Lang and Barstch, 1953). Blood tests revealed mild anemia in all treated groups.

Lang and Barstch (1953) found nothing remarkable during histological examination of rats fed less than 400 mg adipic acid a day. Levels of 400 and 800 mg/day produced slight histological changes in liver and kidneys and marked alterations, indicative of chronic inflammation, in the intestinal mucosa. These effects occurred regardless of whether the diet had been normal or deficient in protein.

Alderley Park specific-pathogen-free rats (2 males, 2 females; 200 g) inhaled powdered adipic acid (126 mg/m^3) in a dynamic chamber for 6 hours a day, 5 days a week for 3 weeks (Gage, 1978). No signs of toxicity were observed during this period. Blood tests, performed on samples taken the day after the last exposure, gave normal results. Gross and histological examination of the organs at autopsy, the day after the last exposure, revealed no evidence of abnormalities attributable to the treatment.

3. Chronic Exposures

Chronic feeding studies with male and female rats of the Carworth Farms strain were performed by Horn et al. (1957). Male rats, 20 per group, were fed 0, 0.1, 1, 3, and 5% adipic acid in the diet for 2 years. Ten female rats were fed no adipic acid and 19 females were fed 1% adipic acid. Results showed that male rats that were fed 3 and 5% adipic acid in the diet gained weight more slowly during the period of rapid growth than did controls. Throughout the second half of the 2-year study, body weights of the males receiving 5% adipic acid were lower than those of control and other treated males; food consumption decreased slightly at this dose level.

Percent survival of all treated males was higher than percent survival of control males (Horn et al., 1957). The incidence of respiratory infection and body sores in the males given 5% adipic acid was lower than the incidence in control males. There were no differences in survival between treated (1% adipic acid) and control females. When the surviving animals were killed after 2 years, no significant gross or microscopic pathological differences were observed between control and treated groups.

4. Carcinogenicity

In the previously described chronic feeding study of Horn et al. (1957), autopsy data for the animals that died during the study were combined with data for those killed at the end of the study. The incidence of tumors in any of the treated groups was not statistically different from the incidence in controls. It should be noted, however, that because the sizes of the groups in this experiment were small, this study may not be an adequate basis for discounting carcinogenicity.

5. Mutagenicity

Litton Bionetics (1974) tested the mutagenicity of adipic acid in the following assays:

(1) Microorganisms: Salmonella typhimurium TA1530 and G46 and Saccharomyces cerevisiae D3 (yeast)
   (a) In vitro (without microsomal activation)
   (b) Host-Mediated Assay with mice

(2) Mammals:
   (a) Cytogenetics
      in vivo - bone marrow of rats
      in vitro - human embryonic lung cultures (WI-38)
   (b) Dominant lethal assay - rats

Both positive and negative controls were included in each assay, but no clear indications of mutagenicity were detected in any of the tests.

6. Teratogenicity

The Food and Drug Research Laboratories (1973) have evaluated the teratogenicity of adipic acid in mice, rats, and hamsters. Adipic acid was administered by intubation according to the following schedule:

Species	Dose levels (mg/kg/day)	No. pregnant animals/dose level	Days gestation on which doses given
mice	0, 2.6, 12.0, 56.0, 263.0	20-24	6 through 15
rats	0, 2.9, 13.0, 62.0, 288.0	20-24	6 through 15
hamsters	0, 2.0, 9.5, 44.0, 205.0	21-24	6 through 10

In all three species, adipic acid had no apparent effect on nidation, maternal survival, or fetal survival. The incidence of abnormalities of soft and skeletal tissues of fetuses from treated dams did not differ from the incidence observed in fetuses from control dams.

7. Reproductive Effects

Among the rats that were fed 400 mg adipic acid/day in the previously described subchronic experiments of Lang and Bartsch (1953) were several pregnant females. Adipic acid appeared to have no effect on their ability to bear and suckle their litters.

8. Other Relevant Information

As reviewed by FASEB (1976) adipic acid administered orally or subcutaneously was readily absorbed by experimental animals. Much of the dose was excreted unchanged in the urine or metabolized to carbon dioxide and exhaled. Analysis of urinary metabolites indicated that adipic acid is metabolized by the same pathway as are fatty acids. Other urinary metabolites may have been derived from adipic acid indirectly via carbon dioxide.

B. Human Studies

1. Pharmacokinetics

Weitzel (1942) concluded that adipic acid, given in doses of 1.46 to 7.30 g/day (about 29 to 104 mg/kg/day), was metabolized to a greater extent when given in small doses than when given in large doses. Individual variations were considerable; 3 subjects excreted 66, 56, and 15% of the same dose as adipic acid in the urine. Weitzel (1947) subsequently reported that 54 to 75% of orally administered adipic acid (100 mg/kg/day for up to 8 days) was recovered in the urine.

2. Health Effects

Weitzel (1947) observed no evidence of toxicity from the oral administration of 100 mg adipic acid/kg/day to human subjects.

3. Target Organ Toxicity

No information was found in the literature searched.

4. Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No current toxicological or environmental studies of adipic acid were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for adipic acid were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

18. Other Pertinent Data

Small but detectible amounts of adipic acid are normally excreted in human urine (Witten et al., 1973; Gregersen and Ingerslev, 1979; Niwa et al., 1979). The origin of this adipic acid is thought to be hepatic ω-oxidation of fatty acids, which is usually minimal. Adipic acid excretion increases, however, during fasting, ketosis, and abnormalities of fatty acid metabolism (Gregersen and Ingerslev, 1979; Gregersen et al., 1976; Aleck et al., 1973; Griffiths et al., 1978).

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