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INFORMATION PROFILES ON POTENTIAL OCCUPATIONAL HAZARDS

VOLUME I. SINGLE CHEMICALS

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16. Abstract (Limit: 200 words) <p>ABSTRACT: This information profile on*N,N-dimethyl acetamide (127195) is part of a group of 46 such profiles that provide information about chemicals or industrial processes considered to be potential occupational hazards. Each profile contains summary data on known and suspected health effects, the extent of worker exposure and the industrial importance of either a single chemical, class of chemicals, or a particular industrial process. The report was developed for use by occupational safety and health professionals in industry, and labor and other areas, to provide them with a synopsis of information in their workplaces.</p>				
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INTRODUCTION

An information profile is a working paper used by the National Institute for Occupational Safety and Health (NIOSH) to assist in establishing Institute priorities. It is an initial step in determining the need to develop comprehensive documents or to initiate research. Each profile summarizes data on known and suspected health effects, the extent of worker exposure, physical and chemical properties, and the industrial importance of individual chemicals and classes of chemicals. The profile may also be used by industry, labor, and the occupational health community as a synopsis of information on each subject and to identify possible health hazards associated with their workplaces.

Although detailed literature searches are conducted using computerized and manual searching techniques to identify pertinent and recent information, not all the literature obtained is incorporated in the report due to the summary nature of the profiles. Further, literature published after 1978 may not be included in these profiles because it was generally unavailable at the time the search was completed.

N,N-DIMETHYL ACETAMIDE

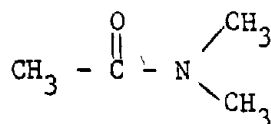
SUMMARY

Approximately 65 million pounds of dimethylacetamide (DMA) and dimethylformamide were produced in 1977; production figures were not available on the individual chemicals. Approximately 8,476 workers are exposed to DMA annually. The major use of DMA is as a solvent for synthetic and natural resins.

Animal and human data indicate that dimethylacetamide is readily absorbed into the blood stream via dermal contact or inhalation. Skin and lung irritation may also occur. Dermal exposure to liquid DMA at any concentration is considered significant. The prime target organ of DMA exposure is the liver, where cord-cell degeneration occurs. Degeneration of the heart, kidney, and brain may also occur.

Rodent tests indicated no mutagenic or carcinogenic effects; however, DMA was embryotoxic to rats, and had teratogenic effects on rabbits.

1. Synonyms: Acetamide, N,N-dimethyl
Acetdimethylamide
Acetic acid, dimethyl amide
Dimethylacetone amide
Dimethylamide acetate
DMA
DMAC
2. Chemical Abstracts Service Number: 127-19-5
3. Registry of Toxic Effects of Chemical Substances Number: AB77000
4. Molecular Formula: C_4H_9NO
5. Chemical Structure:



6. Physical and Chemical Properties:

Molecular Weight	87.12
Physical State	Liquid
Boiling Point	165°C at 758 mm
Melting Point	-20°C
Vapor Pressure	1.3 mm at 25°C
Evaporation Rate	
Solubility	Infinite (H_2O)
Specific Gravity	0.9366 (25°C)
Stability	

7. Producer and User Data

Production and Trends

The combined production of dimethylacetamide and dimethylformamide in 1977 was roughly 65 million pounds. This figure is derived from the fact that both chemicals are produced from dimethylamine; 71.8 million lbs of dimethylamine were manufactured in 1977 (USITC, 1977), and 50% of dimethylamine production is used to make dimethylacetamide and dimethylformamide (Chem. Prof., 1976). A break-down of individual production figures for each chemical is not available.

Based upon growth projections for dimethylamine (Chem. Prof., 1976), growth for dimethylacetamide and dimethylformamide should average 7% per year through 1980.

Uses

Dimethylacetamide is used primarily as a solvent for synthetic and natural resins, especially acrylic fibers and spandex (Siegle, 1978; Lawler, 1977). About 15% of dimethylacetamide production is used to make alkyl (C₁₂-C₁₄) dimethylamine oxide (a surfactant) and rubber chemicals (Blackford, 1974). Dimethylacetamide is also used as an extraction solvent for butadiene manufacture (Lawler, 1977).

Producers and Distributors

Dimethylacetamide is produced by DuPont in Belle, W.V. (SRI, 1978).

Distributors include the following (OPD, 1978; Chem. Week, 1978):

BASF Wyandotte
Eastern Chem.
Pioneer Salt & Chem.
Wall Chem.
Ashland Chem.

Manufacturing Process

Dimethylacetamide can be produced by the reaction of acetic acid and dimethylamine as shown below (Siegle, 1978):



The product of the reaction can be removed as an azeotrope (84.1% amide, 15.9% acetic acid). The acid present in the azeotrope can be removed by the addition of solid caustic soda followed by distillation (Siegle, 1978).

8. Biological Effects of Exposure

a) Acute Effects

Laboratory studies with experimental animals are summarized in Table 1. These data show that single exposures to DMA are only slightly toxic.

Female rats and mice exhibited a greater sensitivity to intraperitoneal and oral administration of DMA than did males (Bartsch et al., 1976). In rabbits, only minor skin irritation resulted 24 hrs after 0.01 ml DMA was applied to the stomach area. Slight to moderate corneal injury was observed when DMA was applied directly to the eye in liquid form (Smyth et al., 1962).

Barnes and Ranta (1972) analyzed the urine of 20 young adult rats 72 hours after the rats had been given two subcutaneous injections of 300 mg DMA on two consecutive days. N-methylacetamide and acetamide were identified in the urine, indicating that the metabolism transformation proceeds via a selective demethylation.

Table 1. Acute Toxicity

Species	Route	Dose	Result	Reference
mouse	i.v.	3.2 ml/kg	LD ₅₀	Bartsch <u>et al.</u> , 1976
	i.p.	3.4 ml/kg	LD ₅₀	Bartsch <u>et al.</u> , 1976
	p.o.	4.9 ml/kg	LD ₅₀	Bartsch <u>et al.</u> , 1976
rat	i.v.	2.8 ml/kg	LD ₅₀	Bartsch <u>et al.</u> , 1976
	i.p.	3.0 ml/kg	LD ₅₀	Bartsch <u>et al.</u> , 1976
	p.o.	5.4 ml/kg	LD ₅₀	Bartsch <u>et al.</u> , 1976
	p.o.	5.63 ml/kg	LD ₅₀	Smyth <u>et al.</u> , 1962
rabbit	dermal	2.24 ml/kg		Smyth <u>et al.</u> , 1962
rabbit	i.v.	8340 mg/kg	LD _{Lo}	NIOSH, 1977
chicken	i.v.	14 g/kg	LD _{Lo}	NIOSH, 1977

b) Subchronic Effects

Horn (1961) applied DMA to the clipped trunks of dogs for 5 hr/day, 5 days/wk, for 6 weeks. The concentrations used were 0.10, 0.32, 1.0, and 4.0 ml/kg/day. Dogs showed progressive impairment of health after 15 days of exposure; one of the two dogs receiving the highest dose level died. Dogs at the two highest dose rates showed weight loss, mild to moderate skin irritation, anorexia, depression, weakness, ataxia, and abdominal tenderness. No noticeable changes occurred below the 1.0 ml/kg/day dosage.

When 0.10 and 0.32 ml/kg/day were applied dermally for 6 months, toxic symptoms did not develop as rapidly and were not as severe as those observed at the two higher dosage levels (Horn, 1961).

Chronic inhalation studies on rats and dogs were conducted at 40, 64, 103, and 195 ppm DMA for 6 months on a 6 hr/day, 5 day/wk basis. No signs of toxicity appeared for either species except for rats exposed to 195 ppm. These rats had an unkempt appearance, red-tinged discharge around the eyes, and loss of weight. The blood and urine of the dogs were analyzed and no abnormalities were detected. Microscopic examination of the tissues of dogs exposed to 103 and 115 ppm DMA showed degeneration of the liver cord cells which was apparently periportal fatty metamorphosis. No toxic histological effects were observed below 103 ppm.

In rats, mild to significant liver cell degeneration occurred in the groups administered 103 and 195 ppm DMA. No degeneration was observed below 103 ppm. Microscopic examination showed varying degrees of cytoplasmic disturbance, cholangitis, periangitis, and small discrete areas of focal necrosis of the parenchymal cells.

c) Chronic Effects

i. Carcinogenicity

No data were encountered.

ii. Mutagenicity

No data were encountered.

iii. Teratogenicity

DMA was applied at full strength to the skin of pregnant rats and rabbits during the period of fetal organogenesis (Stula and Krauss, 1977). A marked incidence of embryo mortality resulted at doses that did not affect the maternal body weight during the time of application (Table 2). No other clinical signs of toxicity occurred. Application of DMA on gestation days 12 and 13 produced a lesser incidence of embryo lethality than that produced by application on days 10 and 11. Teratogenic effects (3 of 34 fetuses with encephalocele; 1 of 8 with diffuse subcutaneous edema) were found only when DMA was applied on gestation days 10 and 11 at a total dose of 2400 mg/kg. No embryotoxic effects were found in rabbits.

Table 2. Embryotoxic Effects of N,N-Dimethylacetamide Applied to Skin of Pregnant Rats and Rabbits (Stula and Krauss, 1977)

Number of pregnant animals in group	Daily dose [mg/kg] (fraction of ALD)	Gestation days applied	48-hr Mother body weight change (%)	Embryomortality (%)	Average fetal weight (g)	Fetal abnormalities ^a
Rats						
8	600 H ₂ O Control	10 + 11	+6	6	2.7	—
7	600 (1/12)	9	— ^b	15	2.5	—
7	600 (1/12)	10 + 11	+4	12	2.2	—
8	600 (1/12)	11 + 12	+4	16	2.1	—
8	600 (1/12)	12 + 13	+2	4	2.1	—
7	1200 (1/6)	9	— ^b	10	2.4	—
5	1200 (1/6)	10 + 11	-1	45	2.2	3 of 34: encephalocele; all from one mother
8	1200 (1/6)	11 + 12	+1	19	2.2	—
Rats						
7	600 H ₂ O Control	10 + 11	+4	3	2.3	—
8	600 (1/12)	10 + 11	+4	14	2.3	—
8	1200 (1/6)	10 + 11	+1	89	1.9	1 of 8: diffuse subcutaneous edema
6	2400 (1/3)	10 + 11	-1	100	—	—
Rabbits						
4	200 H ₂ O Control	8-16	— ^b	3	28.4	—
5	200 (1/25)	8-16	— ^b	0	32.6	—

^a No entry under "Fetal abnormalities" indicates "none."

^b Not weighed.

iv. Other Effects

No data were encountered.

d) Human Effects

Dermal absorption from cutaneously applied DMA resulted in injury at levels above 0.1 ml/kg/day (ACGIH, 1974). The dermal factor is considered to be so significant that no air concentration, however low, will provide protection if skin contact to DMA (liquid) is permitted. Neat DMA applied dermally did not affect epidermal mitosis in humans (Fisher and Maibach, 1975).

Jaundice has been noted in workers chronically exposed to 20 to 25 ppm DMA; in addition to exposure through inhalation, skin absorption may have occurred (ACGIH, 1974). Liver injury consists of cord cell degeneration, but recovery is usually rapid. Symptoms from large oral doses of DMA given as an anticancer drug include depression, lethargy, and visual and auditory hallucinations (Occupational Diseases, 1977).

9. Threshold Limit Values, OSHA Standards, NIOSH Recommended Standards

	<u>Dimethyl acetamide</u>		<u>Reference</u>
Threshold Limit Value	10 ppm	35 mg/cu m (skin)	ACGIH, 1977
OSHA Standard	10 ppm	35 mg/cu m (skin)	OSHA, 1976
NIOSH Recommended Std.	None		

The Threshold Limit Value is considered low enough to prevent liver injury as long as skin contact is prevented (ACGIH, 1974).

10. Other Standards

The following table lists national standards (other than U.S.) for concentrations of DMA allowable in the occupational environment (Wills, 1979):

<u>Standard</u>	<u>Country</u>
20 mg/cu m	Romania (average)
30 mg/cu m	Romania (ceiling)
35 mg/cu m	Australia, Belgium, Finland, BRD, the Netherlands, Switzerland, Yugoslavia

11. Occupational Exposures

According to the National Occupational Hazard Survey, 8,476 workers are exposed to N,N-dimethylacetamide yearly (oral communication from Vera Hudson, Division of Criteria Documentation and Standards Development, NIOSH, 1978).

References

- ACGIH (1977), American Conference of Governmental Industrial Hygienists, Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment, Cincinnati, Ohio.
- ACGIH (1974), American Conference of Governmental Industrial Hygienists, Documentation of the Threshold Limit Values, Cincinnati, Ohio.
- Barnes, J.R. and K.E. Ranta (1972), The Metabolism of Dimethylformamide and Dimethylacetamide, Toxicol. Appl. Pharmac., 23:271-276.
- Bartsch, W., G. Sponer, K. Dietman, and G. Fuchs (1976), Acute Toxicity of Various Solvents in the Mouse and Rat, Arzneim.-Forsch., 26(8):1581-1583.
- Blackford, J.L. (1974), Methanol (Methyl Alcohol), Chemical Economics Handbook, Stanford Research Institute, Menlo Park, Calif.
- Chemical Prof. (1976), Methylamines, Chem. Mktg. Reporter, Jan. 19.
- Chemical Week (1978), 1979 Buyers Guide Issue, Chemical Week, Part 2, October 25, 1978.
- Fisher, L.B. and H.I. Maibach (1975), Effect of Some Irritants on Human Epidermal Mitosis, Contact Dermatitis, 1:273-276.
- Horn, H.J. (1961), Toxicology of Dimethylacetamide, Toxicol. Appl. Pharmac., 3:12-24.
- Lawler, G.M. (Ed.) (1977), Chemical Origins and Markets, Chemical Information Services, Stanford Research Institute, Menlo Park, Calif.
- NIOSH (1977), Registry of Toxic Effects of Chemical Substances, National Institute for Occupational Safety and Health, Rockville, Maryland.
- Occupational Diseases (1977), Occupational Diseases - A Guide to Their Recognition, USDHEW Public Health Service, Publication No. 77-181, U.S. Gov't Printing Office.
- OPD (1978), 1978-79 OPD Chemical Buyers Directory, 66th annual edition, Schnell Publ. Co., New York.
- OSHA (1976), OSHA Safety and Health Standards (29CFR1910), U.S. Dept. Labor, Revised Jan. 1976.

Siegle, J.C. (1978), Acetic Acid Derivatives (DMAC), Kirk-Othmer Encycl. Chem. Technol., 3rd Ed., 1:167-171.

Smyth, H.F., C.P. Carpenter, C.S. Weil, U.C. Pozzani, and J.A. Striegel (1962), Range-Finding Toxicity Data: List VI, Amer. Ind. Hyg. Assoc. J., 28:95-107.

SRI (1978), Directory of Chemical Producers: United States, Stanford Research Institute, Menlo Park, Calif.

Stula, E.F. and W.C. Krauss (1977), Embryotoxicity in Rats and Rabbits from Cutaneous Application of Amide-Type Solvents and Substituted Ureas, Toxicol. Appl. Pharmacol., 41:35-55.

USITC (Annual), Synthetic Organic Chemicals U.S. Production and Sales, U.S. International Trade Commission, Washington, D.C.

Wills, J.H., Senior Reviewer, DCDS (1979), Memorandum to Donald A. Hensel, Acting Director, DCDS, NIOSH, March 26, 1979.