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VINYLIDENE CHLORIDE

I. An Overview

II. A Literature Collection 1947 to 1977

H. S. Warren and B. E. Ricci

APRIL 1978

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Toxicology Information Response Center
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APRIL 1978

OAK RIDGE NATIONAL LABORATORY
Oak Ridge, Tennessee 37830
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DEPARTMENT OF ENERGY

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VINYLIDENE CHLORIDE

I. An Overview

INTRODUCTION

Vinylidene chloride (VDC), a clear, pleasantly sweet-smelling liquid, is related to vinyl chloride in structure, use, and reactivity and the two compounds often coexist as contaminants in workroom air. VDC was first reported by V. Regnault in 1838, but not until almost 100 years later (1930–1940) were commercial uses developed. The monomer copolymerizes readily with other vinyl monomers into latex, fiber, film, and resin forms, with outstanding resistance to chemicals and abrasion. Marketed by Dow Chemical Company under the name "Saran," these copolymers have found wide and increasing use (Dow Bulletin, 7).

The monomer is characterized as follows:

Chemical formula: $H_2C{=}CCl_2$

Synonyms: 1,1-dichloroethylene; 1,1-dichloroethene; DCE; VDC

Chemical Abstracts Service (CAS) Registry Number: 75-35-4

Physical state: clear, colorless liquid

Molecular weight: 96.95

Freezing point: -122.5°C

Boiling point: 31.5°C

Specific gravity: 1.3

Vapor density: 3.34 (air = 1)

Explosive limits in air (28°): 7.3 - 16.0%

Solubility: insoluble in water; soluble in organic solvents

VDC monomer is stored and shipped either with an inhibitor, or refrigerated under an inert gas with light and air excluded, to prevent polymerization and/or development of peroxides.

TOXICITY

Animal Toxicity

Experimental animal studies indicate that VDC is slightly more toxic than ethylene dichloride and slightly less toxic than carbon tetrachloride. Either a single prolonged inhalation exposure or repeated short-term exposures of concentrations too low to cause anesthesia may produce organic injury to liver and kidneys (Dow Bulletin, 7). Continuous 90-day exposures and repeated daily exposures of 8 hr/day, five days per week for six weeks to VDC (and other halogenated hydrocarbons) were studied in rats, guinea pigs, dogs, rabbits, and monkeys. Growth depression and significant mortality were noted in continuous exposures to VDC at 61, 101, and 189 mg/m^3. Significant increases in the activities of serum glutamic-pyruvic transaminase and liver alkaline phosphatase were found in rats and guinea pigs exposed continually to the 189 mg/m^3 level; also, histopathologic study revealed liver damage. Similar liver damage was also

found in those animals with repeated exposures to 395 and 515 mg/m^3 (Prendergast et al., *41*). Minimal but significant injury to liver and kidney at concentrations as low as 25 ppm has been shown after several months exposure (Irish, *24*).

Nasal irritation, retarded weight gain, and liver cell degeneration were noted in rats exposed 20 times to 500 ppm for 6 hr at each exposure, but only a slight nasal irritation was noted for the same exposures to 200 ppm (Gage, *20*). Siegel et al. (*48*) arrived at an LC_{50} of 6350 ppm for VDC in rats in a comparative toxicity test of a series of halogenated hydrocarbons. Carpenter, Smyth, and Pozzani (*16*) reported that four of six rats died within 14 days after a single 4-hr inhalation exposure to 32,000 ppm VDC.

Rylova (*45*) found the lethal vapor concentration to be 15 mg/liter for white mice and also reported hyperemia of laryngeal and pulmonary mucosa in guinea pigs.

A concentration of 8 mg/liter caused irritation of respiratory mucosa in white mice with death occurring within 24 hr. In rabbits, 0.2-2 mg/liter slowed reflexes within 40 min. Postmortem examination after chronic exposure to similar concentrations for 3 hr/day over a four-month period showed bronchitis, liver changes, swelling of renal tubules, and an increase in spleen follicles (Roubal, *44*).

Aqueous and oil extracts of VDC-based polymer administered in food and/or drinking water to mice and rats failed to produce any visible effects on viability, body weight, or organ size (Sporn et al., *50*).

The effects of adrenalectomy on the hepatotoxicity of VDC to rats were tested in an effort to determine mechanisms of toxicity, since it is known that CCl_4 hepatotoxicity is affected by adrenalectomy (Jenkins, Trabulus, and Murphy, *33*). Removal of the adrenals 10 to 14 days prior to oral administration of VDC drastically reduced the 24-hr LD_{50}. A single oral dose of 400 mg/kg resulted in decreased hepatic injury as measured by serum alanine-α-ketoglutarate transaminase (AKT).

The toxicity of VDC to rats was also markedly affected by the nutritional state. Prolonged fasting (45 hr) potentiated hepatic injury as measured by the 4-hr elevation of serum AKT (Jaeger, Trabulus, and Murphy, *32*). Inhalation LC_{50} in fed rats was between 10,000 and 15,000 ppm, while in fasted rats it ranged between 500 and 2500 ppm.

The effects of adrenalectomy and fasting are outlined below:

Oral LD_{50}:	Rats, adrenalectomized - 84 mg/kg/24 hr
	Rats, normal - 1550 mg/kg/24 hr
Inhalation LC_{50}:	Rats, fed - 10,000 to 15,000 ppm/4 hr
	Rats, fasted - 500 to 2500 ppm/4 hr

Human Toxicity

Very little information is available on the toxicology of VDC in humans. Because of its high volatility and lack of adequate warning properties such as odor or color, VDC presents a definite inhalation hazard. A single exposure for a few minutes to 4000 ppm may cause "drunkenness," progressing to unconsciousness if the exposure becomes prolonged. Industrial experience indicates a prompt and complete recovery from the anesthetic effects of short exposures to VDC if the patient is moved immediately to fresh air (Dow Bulletin, *7*).

Skin irritation, due at least partly to the polymerization inhibitor (phenol or monomethyl ether of hydroquinone), may occur on contact with inhibited VDC. The inhibited monomer is also irritating to the eyes, but permanent damage is not likely (Dow Bulletin, *7*). Rylova (*45*) reported irritation of corneal mucosa and respiratory passages in humans at 0.1 mg/liter.

Neurological symptoms of two patients who had manually cleaned a tank used in transport of an aqueous dispersion of VDC resembled the "polyneuritis cranialis" caused by trichloroethylene. Irreversible lesions of the trigeminal area of face, mouth, and tongue developed, spreading later to the second and third cervical segments. Electromyographic evaluation of the trigemino-facial reflexes indicated a functional disorder of the interneuronal system. The toxic chemical appeared to be either VDC or mono- and/or dichloroacetylene (Broser, Henschler, and Hopf, *13*; Henschler, Broser, and Hopf, *22*).

A long-term mortality study (Ott, Langner, and Holder, *39*) of 594 employees exposed to vinyl chloride (VC) together with small amounts of VDC and other contaminants revealed no deaths due to liver malignancy, and fewer than expected deaths at all levels of exposure with the exception of the high level (over 200 ppm VC). The concomitant exposure to VDC, now a suspected toxicant, was acknowledged as a factor in the study.

A threshold limit value of 10 ppm set in 1974 is believed to be low enough to avoid liver and kidney injury (American Conference of Governmental Industrial Hygienists, *3*). Prior to that time it was generally understood by industry that the vapor concentration should be maintained below 25 ppm for repeated exposures 8 hr/day, five days per week.

BIOCHEMISTRY AND METABOLISM

Oral Administration

Jenkins, Trabulus, and Murphy (*33, 34*) undertook the task of clarifying the biochemical response of rats to VDC and of comparing the influence of factors that might alter that response. Oral administration of VDC in 100, 300, and 500 mg/kg doses in corn oil resulted in decreased liver alkaline phosphatase, tyrosine transaminase, plasma alkaline phosphatase, and alanine transaminase. A definite dose-response relationship was shown. Female rats were more susceptible than males as shown by the decreased liver glucose-6-phosphatase and increased alkaline phosphatase activity. Phenobarbital pretreatment caused a reduction in response of liver

glucose-6-phosphatase, alkaline phosphatase, tyrosine transaminase, and plasma alanine transaminase. Adrenalectomized animals were more susceptible to acute lethal action indicating that the adrenals may be involved in resistance to the monomer's toxicity. These observations suggested that metabolism of VDC results in products which are less hepatotoxic than VDC itself.

Studies by Jaeger, Trabulus, and Murphy (*31*) on dose-response and time course of hepatic injury by VDC confirmed the results reported by Jenkins. The time sequence of enzyme changes and measurements designed to detect lipid peroxidation indicated that VDC was dissimilar to CCl_4 in its mechanism of action.

An oral dose of 400 mg/kg was shown to prolong pentobarbital sleeping time in rats (a measure of hepatic mixed function oxidase activity) probably because of altered absorption or distribution of the pentobarbital (Jaeger and Murphy, *30*).

Inhalation Studies

In inhalation studies with rats, control animals tolerated exposures of 32,500 ppm VDC for 1 hr. Lethality was increased by pretreatment with either phenobarbital or 3-methylcholanthrene, and most pretreated animals died either during the exposure period or shortly thereafter. No increase was observed in hepatotoxicity as measured in terms of serum glutamic-pyruvic and glutamic-oxalacetic transaminases or liver glucose-6-phosphatase. Changes were not evident in wet or dry lung weight nor in the gross appearance of the lungs (Carlson and Fuller, *15*).

Since lethality in phenobarbital-treated rats was increased without apparent enhancement of hepatotoxicity or lung damage, cardiotoxic effects were suspected (Siletchnik and Carlson, *49*). A dose of 4 μg/kg of epinephrine failed to produce arrhythmia in air-exposed rats, but a 0.5 μg/kg dose produced continuous ventricular contractions in rats exposed to VDC. Cardiac sensitization by VDC was further enhanced when rats were pretreated with phenobarbital. Metabolism of VDC by hepatic microsomal enzymes may have been induced by the phenobarbital, thereby hastening the amount of cardiotoxic metabolite formed (Siletchnik and Carlson, *49*).

Jaeger (*25*) conducted research toward understanding the mechanisms by which inhalation toxicity of compounds in the rat is altered. Overnight (18 hr) fasting of rats lowered the 24-hr LC_{50} from 15,000 ppm for rats fed ad libitum to 600 ppm in the fasted rats. Elevation of serum AKT was found at 150 ppm in fasted rats but only at 2000 ppm and higher in the fed rats. Increased hepatic injury appeared to be related to decreased hepatic glutathione concentration associated with fasting (Jaeger, Conolly, and Murphy, *27*). Diurnal variations in liver glutathione concentration were shown in both fed and fasted rats with increased sensitivity to lethal and hepatotoxic effects of foreign compounds occurring when the glutathione concentration was at the lower levels (Jaeger, Conolly, and Murphy, *26*). The fasted rats which had received VDC, either by inhalation or orally, were hypoglycemic at death, while fed rats were hyperglycemic. Both groups had bloody ascites. Blood volumes were reduced and death appeared to be due to vascular collapse and shock (Jaeger, Trabulus, and Murphy, *32*).

When VC was administered simultaneously with VDC in a molar ratio of 5:1, fasted rats appeared to be completely protected from VDC damage as judged by serum AKT activity. Only when concentrations were approximately equimolar did serum AKT activity appear and injury occur, with some degree of protection still apparent (Jaeger et al., *29*). Prior administration of VC resulted in diminished glutathione and an enhanced degree of liver injury.

Morphologic studies showed massive mid-zonal hepatic necrosis with hepatic thrombosis and chromatolysis within 2 hr after a 4-hr exposure of fasted rats to 200 ppm VDC (Jaeger, *25*). Following formation of this mid-zonal lesion, the central portion of the lobule collapsed, accompanied by congestion, bloody ascites, and increased hematocrit. Serum transaminase and sorbital dehydrogenase were elevated after 6 hr.

MUTAGENICITY

A linear dose-dependent mutagenic response to 0.2-2% vol VDC in air was seen in *Salmonella typhimurium* TA1530 and TA100. Mutagenicity was higher in the assays mediated with mouse liver, kidney, and lung fractions than with rat fractions and was dependent on mixed function oxidase cofactors. Pretreatment of mice and rats with phenobarbitone increased the mutagenic response. The addition of sulfur-containing compounds (e.g., *N*-acetyl-cysteine or *N*-acetyl-methionine) caused reduced mutagenic response indicating that the mutagenic VDC metabolite may be trapped by nucleophilic sulfur groups thus competing for binding sites in bacterial DNA (Bartsch et al., *12*).

LITERATURE COLLECTION

A review of the literature by Haley (*21*) stresses the necessity for further study of VDC in general.

References in this collection span the time period 1947 to 1977 and were drawn from:

Biological Abstracts, Vols. 21:1947-64:1977
Chemical Abstracts, Vols. 41:1947-87:1977
Excerpta Medica
  Cancer, Vols. 25:1974-36:1977
  Pharmacology and Toxicology, Vols. 18:1965-41:1977
Current Contents, 1975-1977
Current Journals, 1974-1977
MEDLINE Data System
TOXLINE Data System
ORNL Data Systems

Search terms used for retrieval of references were vinylidene chloride; 1,1-dichloroethylene; 1,1-dichloroethene; DCE; and VDC.

VINYLIDENE CHLORIDE

II. A Literature Collection

1947 to 1977

ABBREVIATIONS

CA.....Chemical Abstracts

BA.....Biological Abstracts

LITERATURE COLLECTION

<1>
Agranovskii, Z.N.; Shiba, V.V.; Dotsenko, V.A. Sanitary inspection of new packaging materials for food products. Vopr. Pitan. 3: 55-59 (1974). (BA 59(10):58113).

Analysis of packaging materials made of vinylidene chloride (VDC) and vinyl chloride (VC) polymers established the presence of free volatile monomers. Absorption of the monomers by food packaged in similar material was examined in wheat flour, soup concentrates, cookies, tea, and bay leaves. Negative results were obtained, except in cookies with a 3-month shelf life. These results stress the importance of extending the experiments beyond the recommended shelf life of food products.

Russ; Eng. Transl.

PACKAGING; FOOD; ABSORPTION; ANALYSIS

<2>
Allen, T.H. Spacecraft atmospheres. Part II. Contaminants. Environmental Biology. Altman, P.L.; Dittmer, D.S. (Eds.) Federation of American Societies for Experimental Biology. MD; USA 326 (1966).

Forty-seven compounds were identified as contaminants of Mercury spacecraft atmospheres after a space flight. Of these, twenty-four compounds were quantitatively determined. Vinylidene chloride was detected in the concentration 0-2 ppm range.

CONTAMINANT; SPACECRAFT

<3>
American Conference of Governmental Industrial Hygienists Vinylidene chloride Documentation of the Threshold Limit Values for Substances in Workroom Air. Supplement for Those Substances Added or Changed since 1971. p. 351-2 (1971).

Continued exposure to vinylidene chloride (VDC) appears to cause less injury in laboratory animals than continued exposure to carbon tetrachloride (CCl4), although mortality due to VDC may be greater than in those similarly exposed to CCl4. Time-weighted average exposure for workers should not exceed 25 ppm. VDC threshold limit value in workroom air of 10 ppm (approx. 40 mg/m3) is believed low enough to prevent liver and kidney injury.

ANIMAL; TOXICITY; THRESHOLD LIMIT

<4>
Anderson, W.L.; Saunders, R.A. Evolution of materials in the closed system. A Symposium on Toxicity in the Closed Ecological System. Homma, M.; Crosby, H.J. (Eds.), Lockheed Missiles and Space Co., Research Lab., Palo Alto, CA 9-18 (1963).

Data were collected and compiled during actual manned operation in confined atmospheres (submarine and spacecraft). Table 4 lists all contaminants identified in the atmospheres of Mercury Spacecraft. Vinylidene chloride was found in a concentration of 0-2 ppm.

SPACECRAFT; SUBMARINES; CONTAMINANT

<5>
Anonymous Vinylidene chloride. Chem. Sources-U.S.A., Directories Publishing Co., Inc., Flemington, NJ 573, 711 (1974).

Producers (manufacturers) are listed for vinylidene chloride and polyvinylidene chloride. Producers of vinylidene chloride monomer are Dow Chemical Co. and PPG Industries, Inc. Chemical Division.

MANUFACTURE

<6>
Anonymous Vinylidene chloride Fire Protection Guide on Hazardous Materials, National Fire Protection Association, Boston, MA 5th ed. 279-280 (1972).

Different hazards linked with the handling of vinylidene chloride, as well as the measures to be taken in case of fire, are described. Special care should be taken with the electrical equipment for use in atmospheres containing vinylidene chloride vapors.

FIRE; EQUIPMENT

<7>
Anonymous Vinylidene chloride monomer Bulletin, Plastics Department, The Dow Chemical Company, Midland, Michigan, (1966).

This bulletin makes pertinent data on the safe handling of vinylidene chloride monomers (VDC) available to customers. Dow Chemical Company started research and development of VDC in the early 1930's. "Saran" copolymers were first marketed in the early 1940's. These copolymers are noted for their resistance to chemicals and solvents, low water absorption and water vapor transmission, and excellent stability. They are odorless, tasteless, tough, and virtually non-toxic. Commercial VDC consists of 1,2-dichloroethylene (900 ppm), vinyl chloride (850 ppm), vinylidene chloride (99.8 ppm) and an inhibitor, monoethyl ether of hydroquinone, or MEHQ (200 ppm). It also contains phenol (0.6 to 0.8 ppm) and a small amount of impurities (chlorinated hydrocarbons). Inhibitors are added to VDC during manufacturing to prevent polymerization of the product. "Physical properties and constants", "Hazards and their control," and "Storage" are sections of the Bulletin which give information on safe handling and use of the monomer.

PLASTIC; PROPERTIES; INDUSTRIAL HYGIENE

<8>
Anonymous MCA undertakes monomer study. Chemecology (Feb. 1975).

The Manufacturing Chemists Association has announced plans to administer research on the occupational health aspects of vinylidene chloride monomer (VDC) and styrene monomer. Twelve firms will sponsor the research on

<8> CONT.
styrene, and thirteen will fund the work on VDC. Projects include animal tests on ingestion, inhalation, fetal development, toxicity, and metabolism.

MANUFACTURE; INGESTION; TOXICITY; METABOLISM; TERATOGENICITY; ANIMAL; STYRENE

<9>
Anonymous; Societe pour la Protection des Cultures Melanges producteurs d'aerosols et leurs applications. (Mixed aerosol products and their applications.) Brevet d'Invention (French Patent) 942,680 (Feb. 15, 1949).

The patented mixture consists of dichloroethylene (CCl2:CH2) (I) or dimethylsilane (MeSiH2Me) (II) mixed with active ingredients and kept under pressure in an aerosol can: an insecticidal mixture contains 1% crystalline rotenone and 0.5% citral; a disinfectant mixture, 4.5% pine oil and 0.5% citral; a therapeutic compound, 3% pine oil and 0.5% thymol, and an anticryptogamic compound 5% hexachlorobenzene. I and II act in two ways: as dispersive agents for the mixture and as activators of the effect of the insecticide agents.

Fr.

AEROSOL; PATENT; INSECTICIDE

<10>
Bando, B.M.; Rosenbaum, M.J. Toxicity in HeLa cells mediated by plastic wraps. Lab. Pract. 22(1): 26, 31 (1973).

Cytotoxicity in tubed HeLa cell cultures was observed from using a particular brand of plastic film in the "sandwich" sealing technique for tissue culture tubes. Cell cultures covered with Vitafilm plastic wrap (Goodyear, Ohio, U.S.A.) developed 75% cytotoxicity within 4 hrs and were destroyed in 72 hrs. "Saran Wrap", "Handi-Wrap" (Dow Chemical, Michigan, U.S.A.) and "Glad Wrap" (Union Carbide Co. New York, U.S.A.) produced no cytotoxicity in testing experiments. 1,1-Dichloroethylene is used as a monomer in the manufacture of Saran Wraps. "Vitafilm", according to the manufacturer does not contain 1,1-dichloroethylene. Apparently the toxic substance in "Vitafilm" was transferred to the cell culture and might be volatile.

PLASTIC; CELL CULTURE; TOXICITY

<11>
Barr, R.F.; Watts, H. Diffusion of some organic and inorganic compounds in air. J. Chem. Eng. Data 17(1): 45-46 (1972).

Diffusion coefficients in air at 298.2 degrees K and 1 atm. have been determined for carbon dioxide, nitrous oxide, propane, isobutane, n-pentane, dichlorodifluoromethane, vinyl chloride, and vinylidene chloride. The infrared frequency for vinylidene chloride at cm-1 was in the range of 940 and 1024. The experimental value at cm2, sec-1 was 0.1144 plus or minus 0.0087. This precision of the vinylidene chloride value is low probably because it reacts with oxygen to form peroxides in the diffusion cell.

DIFFUSION COEFFICIENT; SPECTROPHOTOMETRY; PROPERTIES

<12>
Bartsch, H.; Malaveille, C.; Montesano, R.; Tomatis, L. Tissue-mediated mutagenicity of vinylidene chloride and 2-chlorobutadiene in Salmonella typhimurium. Nature (London) 255(5510): 641-643 (1975).

The mutagenicity of vinylidene chloride, VDC, (I) and 2-chlorobutadiene (II) to Salmonella typhimurium TA1530 and TA100 strains was examined by mouse and rat tissue-mediated assay systems. A dose-dependent mutagenic response to I (0.2 to 2% vol. in air) and II (0.5 to 8% vol. vapour in air) was observed. Pretreating mice with phenobarbitone (0.1% in drinking water for 7 days) increased the response to I and II in the presence of 9,000 g liver supernatant fractions. The mutagenic response increased in both strains after exposure to up to 2% VDC in air. Exposure to 2 or 20% VDC in air for 4 hr was used to assay rat and mouse liver, kidney, and lung fractions for their ability to produce mutagenic metabolites of I. Mutagenic activity of I was highest with mouse microsomal fractions and minimal with the lung fractions. Pretreatment of rats and mice with pregnenolone-16a-carbonitrile (50 mg/kg) or aminoacetonitrile (500 mg/kg) was followed by addition of N-acetylcysteine and N-acetyl methionine (12 u mole of each per ml) to assays containing mouse liver fractions. An 80% reduction in the mutagenic response to I was observed, suggesting that mutagenic metabolites of I are trapped by nucleophilic S groups. I and II are mutagenic and exposure of workers to them must be controlled.

MUTAGENICITY; INTERACTION; SALMONELLA; ENZYME

<13>
Broser, F.; Henschler, D.; Hopf, H.C. Chlorierte Acetylene als Ursache einer irreparablen Trigeminusstoerung bei zwei Patienten. (Irreversible lesions of the trigeminal nerve caused by chlorinated acetylenes in two patients). Dent. Z. Nervenheilk. 197: 163-170 (1970).

Two workers exhibited symptoms of poisoning especially in the trigeminal area within 9 to 30 hr after exposure to vinylidene chloride (I). Symptoms were similar to "polyneuritis cranialis" associated with trichloroethylene poisoning; both patients developed sensory disturbances in face, mouth, and tongue. An electromyographic analysis showed the disorder to be of interneuronal origin. I is suggested as the toxic agent.

Ger.; Eng. Summ.

OCCUPATIONAL EXPOSURE; NEUROTOXICITY; CASE REPORT

<14>
C&EN Health hazards of monomers probed. Chem. Eng. News 53(3): 8 (Jan. 20, 1975).

P.L. Viola (Regina Elena Institute of Cancer Research, Rome) found liver tumors in animals exposed to high inhalation concentrations of vinylidene chloride (VDC). Dow Chemical is five months along on inhalation and feeding studies.

<14> CONT.
The Manufacturing Chemists Association has contracted to study the occupational health aspects of VDC and styrene. Effects on fetal development and metabolism will be investigated. Estimated total costs for both projects approximate $500,000 to $600,000.

RESEARCH; TUMOR; ANIMAL; MANUFACTURE; INGESTION; METABOLISM

<15>
Carlson, G.P.; Fuller, G.C. Interaction of modifiers of hepatic microsomal drug metabolism and the inhalation toxicity of 1, 1-dichloroethylene. Res. Commun. Chem. Pathol. Pharmacol. 4(3): 553-560(1972).

The inhalation lethality of 1, 1-dichloroethylene (1,1-DCE) was increased by administration of the hepatic microsomal enzyme inducing agents phenobarbital (PB) and 3-methylcholanthrene (3MC); no increase in hepatotoxicity and no lung damage were found. Other inhibitors, SKF 525A and Lilly 18947, also increased 1, 1-DCE lethality, with shortened survival time during inhalation.

TOXICITY; ENZYME; RAT; INHALATON

<16>
Carpenter, C.P.; Smyth, H.F. Jr.; Pozzani, U.C. The assay of acute vapor toxicity, and the grading and interpretation of results on ninety-six chemical compounds. J. Ind. Hyg. Toxicol. 31(6): 343-346 (1949).

The response of rats to a 4 hr vapor exposure in a 14 day observation period is used as a basis for grading the single exposure toxicity of a chemical. A list of 96 compounds is tabulated according to toxicity data on ingestion, skin penetration, vapor inhalation, skin irritation, and eye injury. At exposures of 32,000 ppm of 1, 1-dichloroethylene, 2/6, 3/6 and 4/6 rats tested were killed.

RAT; TOXICITY

<17>
Chivers, C.P. Two cases of occupational leucoderma following contact with hydroquinone monomethyl ether. Brit. J. Ind. Med. 29: 105-107(1972).

Two out of eight process workers handling hydroquinone monomethyl ether in a vinylidene chloride plant developed depigmentation (occupational leucoderma) of the skin of the forearms. One of thes experienced depigmentation of the skin of the forehead. The process operation and case reports are described. Of the eight operators, two worked the process for more than three years, three for between two and three years, and three for less than one year. Those affected had the longest service: one (aged 53 years) worked for 22 years and another (aged 38 years) worked for 14 years. Both experienced depigmentation of the skin. Repigmentation was hoped to be completed.

LEUCODERMA; OCCUPATIONAL EXPOSURE; CASE REPORT

<18>
Christensen, H.E.; Luginbyhl, T.T. (Eds.) Ethylene, 1, 1-dichloro. The Toxic Substances List (1974 edition) U.S. Dep. of Health, Education and Welfare 352, 824, 826, (1974).

Data on vinylidene chloride toxicity (lowest published lethal concentration) to rats, dogs, and rabbits are: oral toxic dose for rats 400 mg/kg.; inhalation toxic dose for rats : 500 ppm in 4 hr.; intravenous toxic dose for dogs: 225 mg/kg; subcutaneous toxic dose for rabbits: 3700 mg/kg.

TOXICITY; ANIMAL

<19>
Fed. Register; Kirk, J.K. Food additives. Packaging materials for use during the irradiation of prepackaged foods. Fed. Register 33(54): 4659 (1968).

Several food packaging materials that may be subjected to irradiation have been added to the list of food additives. Among them is vinylidene chloride copolymer containing a minimum of 85% vinylidene chloride with one or more of the following elastomers: acrylic acid, acrylonitrile, itaconic acid, methyl acrylate and methyl methacrylate.

FOOD ADDITIVE; COATINGS; CONTAINERS; FOOD

<20>
Gage, J.C. The subacute inhalation toxicity of 109 industrial chemicals. Brit. J. Ind. Med. 27(1): 1-18 (1970).

Rats were exposed to known concentrations of 109 chemicals in air for periods of about three weeks. The toxic properties of the substances are reviewed in relation to the effects of similar compounds on animals and on man. Five hundred ppm of 1, 1-dichloroethylene 6 hr/day for 20 days, was found to be of moderate toxicity, producing nose irritation and liver cell degeneration effects. Two hundred ppm for the same time of exposure also produced slight nose irritation but organs were normal on autopsy.

RAT; TOXICITY; INHALATION

<21>
Haley, T.J. Vinylidene chloride. A review of the literature. Clin. Toxicol. 8(6): 633-643 (1975).

This review is taken from 38 references on vinylidene chloride (VDC). Following a brief introduction, the chemistry section is divided into synthesis, analysis, biochemistry, and metabolism. A paragraph on industrial hygiene precedes the toxicity section.

TOXICITY; RESEARCH; INDUSTRIAL HYGIENE; REVIEW; HUMAN; ANIMAL

<22>
Henschler, D.; Broser, F.; Hopf, H.C. (Polyneuritis cranialis following poisoning with chlorinated acetylenes while handling vinylidene copolymers). Arch. Toxikol. (Translation 101-4521-1, Ralph McElroy Co., Austin, Tex.) 26: 62-75 (1970).

Two workers developed cranial nerve disorders after an attempt to clean out tank cars containing residues of an aqueous dispersion of vinylidene chloride copolymers. Primarily involved was the trigeminal nerve. The occipital, auricular, and cervical nerves as well as mastication, eye, and hypoglossus muscles were affected. The poisoning agent(s) was identified as monochloroacetylene and/or dichloroacetylene, present as highly toxic contaminants in vinylidene chloride (I) or developing from other contaminants (such as tetrachloroethane and trichloroethylene) during production and storage of (I). Strict caution is absolute for handling preparations of polyvinyl chloride as well as the above monomers.

Ger.; Eng. Summ.

OCCUPATIONAL EXPOSURE; HANDLING; NEUROTOXICITY; CASE REPORT

<23>
Huebner, V.R.; Eaton, H.G.; Chaudet, J.H. Gas chromatograph for the Apollo spacecraft. Preliminary report. J. Gas Chromatog. 4(4): 121-125 (1966).

A 3-column gas chromatograph was designed to analyze toxic contaminants which may appear in the atmosphere of Apollo spacecraft during flight. Separation of a large number of compounds, including 1,1-dichloroethylene, was achieved in laboratory tests. Less than 10 ppm concentrations of practically all compounds were easily detectable.

GAS CHROMATOGRAPHY; CONTAMINANT; SPACECRAFT

<24>
Irish, D.D. Vinylidene chloride. Industrial Hygiene and Toxicology. Patty, F.A., (Ed.), Interscience Publishers, N.Y. 2nd. ed., 2: 1305-1307 (1963).

Physical and chemical properties of vinylidene chloride (I) are given. An extensive review of the physiological response to I includes acute and chronic vapor exposures, eye and skin contact, and absorption by breathing. Hygienic standards, flammability, and odor and warning properties are also included.

PHYSIOLOGY; TOXICITY; PROPERTIES

<25>
Jaeger, R.J. Vinyl chloride monomer: comments on its hepatotoxicity and interaction with 1, 1-dichloroethylene. Ann. N.Y. Acad. Sci. 246: 150-1 (1975).

Vinyl chloride monomer (VCM) and 1, 1-dichloroethylene (1, 1-DCE) are used together in the manufacture of polyvinyl polymers. 1,1-DCE is more reactive and more hepatotoxic than VCM. The mechanism of inhalation toxicity and of interaction between the two chemicals were studied. In previous experiments it was demonstrated that fasted rats were more sensitive to 1,1-DCE induced injury than fed rats. When fasted rats were exposed to 0.02% (v/v), 1, 1-DCE in air, serum alanine-alpha-ketoglutarate-transaminase (AKT) activity was elevated about 50-fold 2 hr after a 4-hr inhalation exposure. Exposure of fasted rats to 0.1% VCM (v/v) had no effect on serum AKT. When 0.02% 1, 1-DCE and 0.1% VCM were administered simultaneously to fasted rats for 4 hr, no injury was found in the animals killed and assayed 2 hr later. It was concluded that 0.1% VCM prevented 1, 1-DCE injury. These data may prove useful for research on mechanisms of hepatotoxicity.

HEPATOTOXICITY; INTERACTION; RAT; VINYL CHLORIDE MONOMER

<26>
Jaeger, R.J.; Conolly, R.B.; Murphy, S.D. Diurnal variation of hepatic glutathione concentration and its correlation with 1, 1-dichloroethylene inhalation toxicity in rats. Res. Commun. Chem. Pathol. Pharmacol. 6(2): 465-471 (1973).

Lethal effects and hepatotoxicity were increased in 18-hr fasted rats after inhalation exposure to 1, 1-dichloroethylene (1, 1-DCE). Hepatic glutathione (GSH) concentrations decreased in fasted animals. Day-night variation in hepatic GSH concentration was studied in both fed and fasted rats. The minimum GSH concentration in fed rats occurred between 7 pm and 1 am. The maximum hepatic GSH concentration occurred between 7 am and 1 pm. Fasted rats had less diurnal variation. In 2 groups of fed rats exposed to a concentration of 2,000 ppm of 1, 1-DCE, the animals with an exposure time period between 10 pm and 2 am (low hepatic GSH concentration) were more susceptible to 1, 1-DCE induced liver injury and lethality.

RAT; LIVER; TOXICITY; FASTING; INHALATION

<27>
Jaeger, R.J.; Conolly, R.B.; Murphy, S.D. Effect of 18 hr fast and glutathione depletion on 1, 1-dichloroethylene-induced hepatotoxicity and lethality in rats. Exp. Mol. Pathol. 20: 187-198 (1974).

Four-hour inhalation exposure to 1, 1-dichloroethylene (1, 1-vinylidene chloride) was more injurious to 18-hr fasted rats than to fed rats. The estimated 24 hr LC50 for fed rats was 15, 000 ppm while the same value for fasted rats was 600 ppm. The minimum lethal concentration was 200 ppm for fasted rats and 10, 000 ppm for fed rats. Elevated serum alanine-alpha-keto-glutarate transaminase (AKT) was seen at 150 ppm in fasted rats but only at 2, 000 ppm in fed rats, and preceded hepatic necrosis and death. Hepatic injury was proportional to hepatic glutathione (GHS) depletion caused by fasting. If applied to humans, these findings would suggest that GHS depletion in night-shift workers exposed to 1, 1-dichloroethylene could result in an enhanced work-related injury.

TOXICITY; RAT; LIVER; FASTING

<28>
Jaeger, R.J.; Conolly, R.B.; Murphy, S.D. Short-term inhalation toxicity of halogenated hydrocarbons. Effects on fasting rats. Arch. Environ. Health 30; 26-31 (1975).

Vinyl chloride monomer (VC) and 1, 1-dichloroethylene (DCE) were administered (short-term inhalation) simultaneously to fed and fasted rats, and serum alanine-alpha-ketoglutarate-transaminase (AKT) activity determined. VC was not toxic at 1,122 ppm in fasted rats; DCE produced injury at 205 ppm. The combined exposure of 1,056 ppm VC with 195 ppm DCE in a molar ratio of 5 to 1, protected fasted rats from DCE injury. Simultaneous exposure of fasted rats to 12,093 ppm VC and 1,971 ppm DCE did not increase either serum AKT or sorbitol dehydrogenase (SDH). Vinyl chloride was therefore antagonistic to the hepatotoxic effect of DCE, probably by a competitive interaction.

RAT; HEPATOTOXICITY; FASTING; ANTAGONISM

<29>
Jaeger, R.J.; Conolly, R.B.; Reynolds, E.S.; Murphy, S.D. Biochemical toxicology of unsaturated halogenated monomers. Environ. Health Perspect. 11: 121-128 (1975).

Effects of inhalation exposure to vinyl chloride monomer (VC); 1,1-dichloroethylene (1,1-DCE); or 2-chloro-1,3-butadiene (2-CBD) were studied in fed and fasted rats. Within 2 hr after a 4 hr inhalation exposure to 200 ppm 1,1-DCE, fasted rats developed distinctive morphological changes in liver cells. In fed rats the hepatotoxicity was greater during the night, time of glutathione (GHS) depletion. Fasted rats were more sensitive to 1,1-DCE and 2-CBD. Diethyl maleate (DEM), which depletes GHS in fed rats, potentiated the hepatotoxicity of 1,1-DCE and 2-CBD. Acetone exposure (10,000 ppm) enhanced the hepatotoxic response, while cysteine (500 mg/kg) protected the animals against lethality and serum AKT elevation. Both the time course and dose response data suggested that 2-CBD was a less potent and less rapid hepatotoxin than 1,1-DCE. No fed-fasting difference and no hepatotoxicity were found with VC. Protection against 1,1-DCE was found in rats exposed to VC, which suggests a competitive interaction. The results of this research encourage future investigation in exposure of night shift workers to hepatotoxic chemicals like 1,1-DCE or 2-CBD. Food intake patterns and conditions such as alcoholism and diabetes are some factors worth further study.

RAT; INHALATION; LIVER; TOXICITY; FASTING

<30>
Jaeger, R.J.; Murphy, S.D. Alterations of barbiturate action following 1, 1-dichloroethylene, corticosterone, or acrolein. Arch. Int. Pharmacodyn. 205: 281-292 (1973).

1, 1-Dichloroethylene (1, 1-DCE) prolonged pentobarbital sleeping time in rats between 2 and 4 hr after oral administration with no liver injury but did not affect hexobarbital sleeping time. Corticosterone prolonged pentobarbital sleeping time only. Acrolein prolonged both pento- and hexobarbital sleeping time. The mechanism of these effects differed. 1,1-Dichloroethylene altered the absorption or distribution of pentobarbital. The action of pentobarbital was more easily altered by changes in absorption, distribution, or increased CNS sensitivity than was the action of hexobarbital.

RAT; BARBITURATES; METABOLISM

<31>
Jaeger, R.J.; Trabulus, M.J.; Murphy, S.D. Biochemical effects of 1, 1-dichloroethylene in rats: Dissociation of its hepatotoxicity from a lipoperoxidative mechanism. Toxicol. Appl. Pharmacol. 24(3): 457-467 (1973).

A comparison was made of the ability of 1,1-dichloroethylene (1, 1-DCE) and carbon tetrachloride (CCl4) to stimulate lipoperoxidation both in vivo and in vitro. The results, following oral administration of 100-800 mg 1, 1-DCE/ kg to rats, indicate that 1,1-DCE causes hepatic glucose-6-phosphatase (G-6-Pase) depression, serum alanine-alpha-ketoglutarate transaminase (SAKT) elevation, hepatic triglyceride (HTG) elevation and pentobarbital sleeping time (PST) prolongation. 1,1-DCE was dissimilar to CCl4 in terms of a proposed lipoperoxidative mechanism.

LIVER; RAT; ENZYME; LIPOPEROXIDATION

<32>
Jaeger, R.J.; Trabulus, M.J.; Murphy, S.D. The interaction of adrenalectomy, partial adrenal replacement therapy, and starvation with hepatotoxicity and lethality after 1, 1-dichloroethylene intoxication. Toxicol. Appl. Pharmacol. 25: 491, Abs. 133 (1973).

Several stress-related factors were studied in the modifications of acute lethality and hepatotoxicity in rats after 1, 1-dichloroethylene intoxication. Following a single oral dose (400 mg/kg) of 1, 1-DCE, both adrenalectomized (ADX) and sham rats had similar 24-hr mortalities, but ADX resulted in an apparent decrease of liver injury. Corticosterone (CS) treatment resulted in a slight decrease of lethal effects of 1, 1-DCE in both ADX and sham rats. Prolonged (45 hr) fasting also potentiated hepatic injury. The estimated 4-hr inhalation LC50 of 1, 1-DCE in fed rats was between 10,000 and 15,000 ppm, whereas the LC50 in fasted rats was between 500 and 2500 ppm.

LIVER; RAT; ADRENAL; FASTING

<33>
Jenkins, L.J., Jr.; Trabulus, J.; Murphy, S.D. Effect of adrenalectomy and phenobarbital pretreatment on the toxicity and biochemical effects of 1,1-dichloroethylene. Toxicol. Appl. Pharmacol. 19: 391 abs. 76 (1971).

1, 1-Dichloroethylene (vinylidene chloride) used in industry in the manufacture of thermoplastic polymers, has been identified as a contaminant of closed atmospheres such as nuclear submarines and spacecraft. Vinylidene chloride is both a CNS depressant and hepatotoxic. To clarify these biochemical effects, 500 mg/kg of 1,1-dichloroethylene were administered orally to male rats. Liver alkaline phosphatase (AP) activity and liver tyrosine transaminase (TT) activity were increased. Plasma alanine transaminase (AT) and plasma AP activities were also increased. A depression of liver glucose -6- phosphatase activity was noted.

<33> CONT.
Adrenalectomy 10-14 days prior to the experiment and phenobarbital pretreatment for 5 days reduced the toxicity of 1, 1-dichloroethylene.

RAT; TOXICITY; ENZYME; METABOLISM

<34>
Jenkins, L.J., Jr.; Trabulus, M.J.; Murphy, S.D. Biochemical effects of 1,1-dichloroethylene in rats: Comparison with carbon tetrachloride and 1,2-dichloroethylene. Toxicol. Appl. Pharmacol. 23(3): 501-510 (1972).

The biochemical effects of oral administration of 1,1-dichloroethylene (1,1-DCE) in rats were compared with the effects of carbon tetrachloride (CCl4) and 1,2-dichloroethylene (1,2-DCE). Following administration of 1,1-DCE a depression of liver glucose-6-phosphatase (G-6-Pase) activity, and increased activities of liver alkaline phosphatase (AP), tyrosine transaminase (TT), and of plasma AP and alanine transaminase (AT) were observed. The effects caused by 1,1-DCE were similar but more pronounced than effects caused by CCl4, with female rats more susceptible to 1,1-DCE than males. Altered effects from phenobarbital pretreatment and adrenalectomy were also studied.

RAT; ENZYME; SOLVENT; METABOLISM

<35>
Kovalev, O.A.; Blinova, T.S.; Severovostokova, V.I.; Broitman, A.Ya. (Hygienic assessment of some coatings for concrete vats for sauerkraut). Gig. Sanit. (Hyg. Sanit.) 35 (182-184) (1970).

Tests performed with aqueous extracts of KhS-76 varnish (a copolymer of vinyl and vinylidene chlorides, dissolved in a mixture of acetone, butyl acetate, and toluene) showed a slow increase of weight for female mice and rats after 10 months, delayed excretion of sodium benzoate, and pronounced dystrophic lesions of the internal organs, especially that of the liver. The copolymer had been used as a coating in concrete vats for the storage of sauerkraut.

Russ.; Eng. Transl.

RAT; MICE; VARNISH; COPOLYMER; LIVER; TOXICITY

<36>
Lehman, A.J. Chemicals in foods: A report to the Association of Food and Drug Officials on current developments. Assoc. Food Drug Officials U.S. Quart Bull. 15: 82-89 (1951)

New pharmacology data (unreported) are used to classify a number of food additives as suitable or unsuitable. Included in the food packaging materials, and considered suitable, is vinylidene chloride. Suitability is based on the low solubility of the resin components of the plastic film so as to be considered toxicologically insignificant as a food contaminant. An "unsuitable" list of chemicals in food is also given.

FOOD ADDITIVE; CLASSIFICATION

<37>
McBirney, R.S. Trichloroethylene and dichloroethylene poisoning. Arch. Ind. Hyg. Occup. Med. 10(2): 130-133 (1954).

Dichloroethylene (DCE) was used to extract oil from fish livers in vessels which contained each 25 gal. of DCE. The vessels, 24 in. in diameter, were not provided with exhaust air ventilation or a cover, which resulted in a great amount of evaporation of the solvent into the workroom air. A 35 year old male worker, supervising the operation 8 hr a day and in constant exposure to the vessels, complained of nausea, vomited several times and appeared intoxicated within a few days after being hired. He was taken to the hospital where he died of congestion of brain, heart, kidneys and spleen, lung emphysema and bronchopneumonia, and liver degeneration.

TOXICITY; SOLVENT; LUNGS; LIVER; OCCUPATIONAL EXPOSURE; CASE REPORT

<38>
Newman, D.R., Ed. Another potential vinyl chloride-like scare... Toxic Material News 1(15): 113 (1974).

Attention is directed to the potential hazards of vinylidene chloride, which is used in the production of Saran and other clear plastic wrappings.

PLASTIC; INDUSTRIAL HYGIENE

<39>
Ott, M.G.; Langner, R.R.; Holder, B.B. Vinyl chloride exposure in a controlled industrial environment. A long-term mortality experience in 594 employees. Arch. Environ. Health 30(7): 333-339 (1975).

In a long-term study, Dow Chemical Company (Medical Dept.) examined the mortality rate of workers exposed to vinyl chloride (I) and lesser amounts of vinylidene chloride (II). The analytical strategy was to examine the relationship between tumor incidence and the highest levels of exposure to I and II experienced by the employers. Data were initiated in 1950 and surveys of the work environment were continuously updated and recorded through 1974. Job classifications were categorized as low (< than 25 ppm), intermediate (25 to 200 ppm), or high (> 200 ppm) exposure levels, based on estimated time-weighted average concentrations for an eight-hour day. In the analysis, duration of exposure was separated into two categories: <1 year exposure and 1 plus year exposure. Observed deaths among V.C. workers were 91% of the expected deaths. Total malignant neoplasms were 13 versus 16.0. Of the 13 malignancies, 9 were observed in the higher exposure group. The distribution of the malignant neoplasms with respect to exposure category suggests a possible dose-response relationship.

MORTALITY; OCCUPATIONAL EXPOSURE; CASE REPORT; CANCER

<40>
Piatt, V.R. Chemical constituents of nuclear

<40> CONT.
submarine atmospheres. Part 1. Quantitatively identified. Environmental Biology. Altman, P.L.; Dittmer, D.S. (Eds.) Federation of American Societies for Experimental Biology. MD; (USA) 327-328 (1966).

Thirty-two compounds were quantitatively identified as chemical constituents of nuclear submarine atmospheres. The highest concentration of vinylidene chloride normally found was 2 ppm.

CONTAMINANT; SUBMARINES

<41>
Prendergast, J.A.; Jones, R.A.; Jenkins, L.J., Jr.; Siegel, J. Effects on experimental animals of long-term inhalation of trichloroethylene, carbon tetrachloride, 1, 1, 1-trichloroethane, dichlorodifluoromethane, and 1, 1-dichloroethylene. Toxicol. Appl. Pharmacol. 10(2): 270-289 (1967).

Rats, guinea pigs, dogs, rabbits, and monkeys were exposed to the title compounds. Inhalation exposures were either continuous (90 days), to simulate submarine conditions, or repeated for 8 hrs/day, 5 days/week for 6 weeks to mimic industrial exposures. Parameters included mortality, toxicity, and biological changes. As a result of 1, 1-dichloroethylene repeated exposure (395 mg/m3) no animals died and no visible signs of toxicity were observed; guinea pig serum urea nitrogen concentration was normal. Liver damage was also noticed at this concentration. Significant mortality was found in continuous exposures to 1,1-dichloroethylene at 189, 101, and 61 mg/m3. Growth depression in varying degrees was found in all continuous exposures. Serum urea nitrogen levels were in their control limits. Significant elevations of serum glutamic-pyruvic transaminase and liver alkaline phosphatase activities and liver damage was found in rats and guinea pigs with continuous exposure to 189 mg/m3 of 1,1-dichloroethylene.

ANIMAL; INHALATION; TOXICITY; MORTALITY

<42>
Reinhardt, R.C. Handling vinylidene chloride. Chem. Eng. News 25(30): 2136 (1974).

When vinylidene chloride (I) is stored at temperatures between minus 40 degrees and plus 25 degrees C in the presence of air, a peroxide compound which is violently explosive is formed and may act as a polymerization catalyst. Any polymer containing more than 15% of the peroxide will, if dry, detonate from a slight mechanical shock or from heat. Phenol-type polymerization inhibitors are recommended for storage of I. Residues of I in industrial equipment should be destroyed by washing in hot water. Vapor exposures to I and or repeated contact with the skin should be avoided because of its toxicity.

STORAGE; EXPLOSIVE; HANDLING; TOXICITY; SAFETY

<43>
Reynolds, E.S.; Moslen, M.T.; Szabo, S.; Jaeger, R.J.; Murphy, S.D. Hepatotoxicity of vinyl chloride and 1,1-dichloroethylene. Role of mixed function oxidase system. Amer. J. Pathol. 81(1): 219-231 (1975).

A single 5-hr exposure to 5% vinyl chloride monomer (VC) produces acute liver injury in phenobarbital-pretreated rats. Phenobarbital induces the cytochrome P-450-centered multienzyme system located in the endoplasmic reticulum of the liver parenchymal cells, thus potentiating the hepatotoxicity of VC. 1,1-Dichloroethylene (1,1-DCE), and trichloroethylene (TCE) also cause hepatic injury, but different from that caused by VC. Various xenobiotics (enzyme inducers) including phenobarbital and Aroclor, were given to rats (400 u moles/kg). After 8 days rats were exposed to 200 ppm (0.02%) 1,1-DCE for 4 hr or 50,000 ppm (5%) VC% for 6 hr. Hepatic injury and necrosis were higher in the phenobarbital-pretreated animals exposed to VC. Exposure of pretreated animals to 1,1-DCE produced injury to the hepatic plasma membranes, mitochondria, and nuclear chromatin but spared endoplasmic reticulum. Thus, induction of cytochrome P-450 appears to protect the liver against 1,1-DCE but not against VC.

ENZYME; LIVER; TOXICITY; RAT; INTERACTION

<44>
Roubal, J. Vinylidene chloride. Encyclopaedia of Occupational Health and Safety, International Labour Office, Geneva 2: 1468 (1972).

Chemical and physical properties, toxicity of vapor inhalation, and skin irritation of vinylidene chloride are given. Pure vinylidene chloride between -40 degrees C and +25 degrees C in the presence of air or oxygen will form an explosive peroxide. Vapors of vinylidene chloride are irritating to the eyes and contact of the liquid with skin should be avoided. Treatment entails removal from the inhalation source or washing of contaminated skin.

PROPERTIES; TOXICITY; EXPLOSIVE

<45>
Rylova, M.L. (Toxicity of 1,1-ethene dichloride). Farmakol. Toksikol. (Pharmacol. and Toxicol.) USSR 16(1): 42-44 (1953). (CA 47, 11559i)

At concentrations ranging from 0.5 to 45 mg/l, 1,1-ethene dichloride is mildly narcotic to mice, cats, rabbits, and guinea pigs. Vinylidene chloride is highly volatile, with a lethal vapor concentration of 15 mg/l (mice). Human corneal mucosa and respiratory passages are affected at 0.1 mg/l. In vapor form, it causes hyperemia of laryngeal and pulmonary mucosa, and dermal erythema in 5 minutes.

Russ.; Eng. Transl.

VAPOR; TOXICITY

<46>
Sax, N.I. Vinylidene chloride. Dangerous Properties of Industrial Materials, Van Nostrand Reinhold Co., NY 3rd ed., p. 1229 (1969).

Vinylidene chloride is dangerous when exposed to heat or flame. The disaster hazard is rated as highly dangerous because it reacts vigorously with oxidizing materials. A list of countermeasures (ventilation control, storage and

<46> CONT.
handling, and shipping regulations) is included.

STORAGE; HANDLING

<47>
Severn, L.W.; Skory, L.K. Monitoring personnel exposure to vinyl chloride, vinylidene chloride and methyl chloride in an industrial work environment. Amer. Ind. Hyg. Assoc. J. 36(9): 669-676 (1975).

The 1974 OSHA exposure standard stated that the permissible eight hour average exposure to vinyl chloride (VC) is not over 1 ppm, with a ceiling of 5 ppm per sampling period. A study was undertaken to develop a reliable method for long and short term personnel sampling and analysis of vinyl chloride (I), vinylidene chloride (II), and methyl chloride (III). Of the various commercially available carbons, Pittsburg PCB 12 X 30 Activated Carbon, a cocoanut carbon, was found the most suitable for the personnel sampling technique. One gram in a steel tube can be used to collect (I), (II), and (III). The carbon is further desorbed with CS, at dry ice temperature, or by thermal desorption.

ANALYSIS; OCCUPATIONAL EXPOSURE; MONITORING

<48>
Siegel, J.; Jones, R.A.; Coon, R.A.; Lyon, J.P. Effects on experimental animals of acute, repeated and continuous inhalation exposures to dichloroacetylene mixtures. Toxicol. Appl. Pharmacol. 18: 168-174 (1971).

The 4-hr LC50 of a dichloroacetylene-trichloroethylene mixture (DCA-TCE) in rats was compared with the LC50 of trichloroethylene, carbon tetrachloride, methyl chloroform, and vinylidene chloride. LC50 of vinylidene chloride was determined to be 6,350 ppm for rats, with a mortality ratio of 1/16 at 4,900 ppm, and 7/16 at 6,150 ppm.

RAT; CHLORINATED HYDROCARBONS; MIXTURES; TOXICITY

<49>
Siletchnik, L.M.; Carlson, G.P. Cardiac sensitizing effects of 1, 1-dichloroethylene: Enhancement by phenobarbital pretreatment. Arch. Int. Pharmacodyn. 210: 359-364 (1974).

Rats were injected with epinephrine at a dose of 4 ug/kg and then exposed to DCE (26,000 ppm plus or minus 700 ppm) for 10 min. or more. Another group was exposed to DCE alone and did not receive epinephrine. In phenobarbital (PB) pretreatment studies, one animal in a pair of the same weight was pretreated with PB (50 mg/kg ip for 4 days) and the control rat received saline. Although the dose of 4 ug/kg failed to induce cardiac arrythmias in air-exposed animals, 0.5 ug/kg did so in rats exposed to DCE. This cardiotoxicity was further enhanced in rats pretreated with PB, with a lower epinephrine dose required for severe arrythmias than in controls. Since PB induces the enzymatic metabolism of foreign substances, some metabolite of DCE may be responsible for the increased cardiotoxicity.

CARDIOTOXICITY; ARRYTHMIA; PHENOBARBITAL; EPINEPHRINE; RAT

<50>
Sporn, A.; Cirstea, A.; Dinu, I.; Ghizelea, L.G.; Stoenescu, L. (Contributions to investigations on the toxicity of vinylidene chloride polymer extracts). Igiena 19(10): 587-594 (1970).

Aqueous and oil extracts of vinylidene chloride copolymer were tested in mice and rats. Administration of the aqueous extract in 50% drinking water for 60 days produced a decrease of 13-17% in aldolase, glutamic oxalacetic transaminase, succinoxidase, and acid and alkaline phosphatase activity, without affecting blood picture, succindehydrogenase activity, and the adrenal ascorbic acid content. The oil extract (8% in the food) did not have any effect on the animals. The alterations produced by the aqueous extract are attributed to the presence of chlorhydrin in the plastic mass.

Rom.; Eng. Summ.

COPOLYMER; TOXICITY; RAT; MICE; EXTRACT

<51>
Stecher, P.G., (Ed.) Vinylidene chloride. The Merck Index. Merck and Co., Inc. Rahway, NJ 8th ed., 1109 (1968).

Chemical and physical properties of vinylidene chloride are given. An intermediate in the production of vinylidene polymer plastics such as Saran and Velon, its toxicity is reported as irritant to the mucous membranes, narcotic in high concentrations, and the toxic agent of kidney and liver injuries in humans and experimental animals. Vinylidene chloride polymerizes to a plastic: uncontrolled polymerization may lead to explosion. Preservation of the monomer requires inhibitors.

TOXICITY; HUMAN; ANIMAL

<52>
Stewart, R.D.; Dodd, H.C.; Duncan, S.E.; Holder, E.E. Diagnosis of solvent poisoning. JAMA 193(13); 1097-2000 (1965).

Solvent poisoning or exposure can be rapidly diagnosed by breath analysis. For identification of unknown solvents, the breath is collected in a 10-liter plastic bag and analyzed by infrared spectrometry. Once the identity of the solvent is known, breath collection and analysis techniques are simplified. Small breath samples are collected in 10 to 50 ml glass pipettes and analyzed in small aliquots by vapor phase chromatography. A table of data obtained by infrared analysis lists the solvents most commonly present in the expired breath of exposed workers (Dow Chemical Co.) up to several weeks after exposure, and the minimum amount which must be present in the breath for identification. Vinylidene chloride can be identified as a concentration of 0.1 ppm (vapor phase chromatographic sensitivity) and 5 ppm (infrared sensitivity) with an infrared analytical wavelength of 12.60 ug. The rate of excretion or "decay" of a solvent in the breath is dependent upon the rate at which the compound is metabolized; each solvent possesses a characteristic excretion or "decay" curve in breath. Serial breath analyses following solvent exposure produce an excretion curve, which may be

<52> CONT.
compared to excretion curves of known quantities in order to determine if a potentially toxic amount of solvent has been absorbed.

SOLVENT; BREATH; ANALYSIS

<53>
von Oettingen, W.F. 1,1-dichloroethylene The Halogenated Aliphatic, Olefinic, Cyclic, Aromatic, And Aliphatic-Aromatic Hydrocarbons Including The Halogenated Insecticides, Their Toxicity And Potential Dangers. U.S. Department of Health, Education and Welfare Publication No. 414 198-200 (1955).

Vinylidene chloride polymerizes rapidly and is therefore the basic monomer used in the manufacture of plastic polymers. If kept at temperatures between -40 degree C and +25 degree C in the presence of air or oxygen it forms a potentially explosive peroxide compound that requires careful handling. Vinylidene chloride therefore should not be handled or stored in the presence of air.

PEROXIDE; HANDLING; EXPLOSIVE

<54>
Wessling, R.; Edwards, F.G. Vinylidene chloride. Kirk-Othmer Encyclopedia of Chemical Technology, Standen, A.(Ed.), Interscience Publishers, N.Y. 2nd ed., 21: 275-303 (1970).

The physical properties, manufacture, analysis, and safety of vinylidene chloride are given. For repeated exposures (8hr/day, 5 days a week) the vapor concentration of vinylidene chloride should be below 25 ppm. Single exposure of 1000 ppm for up to one hr or 200 ppm for up to 8 hr will probably be safe. Single exposure to a high concentration (4,000 ppm) even for a few minutes can be dangerous and produce liver and kidney injury. Skin and eye contact with vinylidene chloride should be avoided. Vinylidene chloride reacts with air or oxygen to form a peroxide compound which is violently explosive. Residues of vinylidene chloride should be handled with care and peroxides destroyed by washing with water at room temperature.

PROPERTIES; MANUFACTURE; ANALYSIS; TOXICITY

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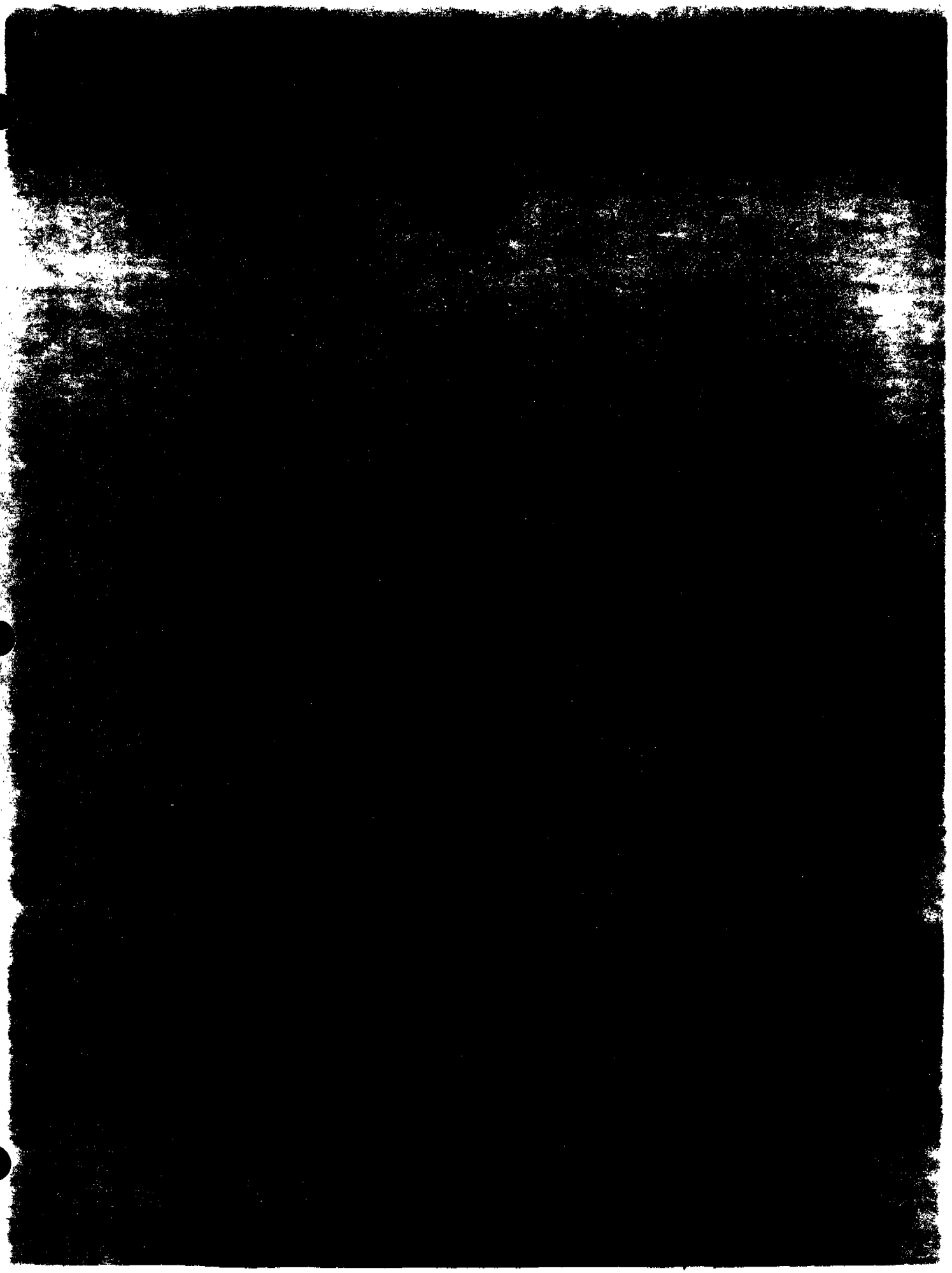

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