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Acute Toxicity and Skin Corrosion Data for Some Organic and Inorganic Compounds and Aqueous Solutions

E. H. VERNOT, J. D. MACEWEN, C. C. HAUN, AND E. R. KINKEAD

University of California, Irvine, Toxic Hazards Research Unit, Overlook Branch, Dayton, Ohio 45431

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Acute Toxicity and Skin Corrosion Data for Some Organic and Inorganic Compounds and Aqueous Solutions. VERNOT, E. H., MACEWEN, J. D., HAUN, C. C., AND KINKEAD, E. R. (1977). *Toxicol. Appl. Pharmacol.* **42**, 417–423. A table of acute toxicity and skin corrosion data is presented for about 110 organic and inorganic compounds and aqueous solutions. Although the chemicals tested are not new, either as commercial materials or as potential hazards to humans, basic toxicological data was lacking in many areas. The present report is an attempt to provide such fundamental acute toxicity data for these compounds.

The utility of acute toxicity data in identification of materials as manifestly hazardous under certain conditions has been recognized for many years. Since 1944, the group at the Carnegie–Mellon Institute of Research, previously the Mellon Institute of Industrial Research, has published a series of articles presenting range-finding toxicity data: Smyth and Carpenter (1944, 1948); Smyth *et al.* (1949, 1951, 1954, 1962, 1969); and Carpenter *et al.* (1974).

These reports have outlined the ways in which data can be applied and the precautions which must be taken against identifying chemicals as safe on the basis of acute toxicity tests. They have noted that these tests yield information which can be applied to single or infrequent contact with a chemical and that the information is most useful when compared with similar data obtained from long-used chemicals. They can be performed as the first in a series of studies giving information on concentrations to be used in more extensive tests but are not sufficient to classify a material as safe for repeated daily use or contact.

Most of the compounds listed in the present report are not newly introduced to manufacture and marketing. Testing of these materials was not undertaken until examination of the literature revealed that adequate data were not available. The criterion applied to the judgement of adequacy was open literature publication with references to or precise accounts of the methods used.

METHODS

Single oral dose toxicity was usually determined by the method of Smyth *et al.* (1962) in which the LD50 and its 95% confidence limits are estimated by the moving average technique (Thompson, 1947; Weil, 1952). When fractional mortality was not noted, the LD50 value was listed without a confidence interval. Occasionally enough data were obtained to use the probit method (Finney, 1971) for calculation.

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TABLE 1

ACUTE TOXICITY DATA ON ORGANIC AND INORGANIC COMPOUNDS

Material studied	Single oral LD50 (mg/kg)		Single skin penetration LD50	Inhalation, 1-hr LC50 (ppm)		Skin corrosion
	Male rats	Other	Rabbits (mg/kg)	Male rats	Other	
Aromatic compounds						
Aniline hydrochloride	1,070 (730–1,590)	840 (470–1,490)[a]				
Benzenesulfonic chloride				32 0/5[b,c]	32 0/5[a,b,c]	
Benzonitrile				900 0/6[b,c,d]		
Benzyl chloride	1,230 (1,150–1,660)	1,620 (1,150–2,185)[e]				
Benzylidene chloride	3,250 (2,360–4,470)	2,460 (1,790–3,390)[e]				
1-Chloronaphthalene	1,540 (1,310–1,720)	1,090 (960–1,180)[e]				
2-Chloronaphthalene	2,080 (1,610–2,670)	890 (735–1,070)[e]				
1-Chloro-2-nitrobenzene	270 (1,80–400)	140 (110–200)[e]				
1-Chloro-4-nitrobenzene	810 (590–1,120)	1,410 (1,070–2,040)[e]				
Cresol, technical			2,000 (700–5,900)			+
o-Cresol			890 (460–1,690)			+ +
m-Cresol			2,830			+ +
p-Cresol			300 (130–910)			+
2,4-Dichlorophenol	2,830 (2,050–3,890)	1,630 (1,010–2,620)[e]				
2,3-Dinitrotoluene	1,120 (500–2,520)	1,070 (730–1,590)[e]				
2,4-Dinitrotoluene	270 (180–400)	1,630 (1,180–2,240)[e]				
2,5-Dinitrotoluene	710 (510–970)	1,230 (730–2,080)[e]				
2,6-Dinitrotoluene	180 (130–240)	1,000 (590–1,700)[e]				
3,4-Dinitrotoluene	1,070 (730–1,590)	1,410 (460–4,380)[e]				
4,4′-Dioctyl-diphenylamine	8,000 0/5[c]					
2,2′-Dithiobis (benzothiazole)	12,000 0/5[c]	12,000 0/5[c,e]				
2-Methyl-4,6-dinitrophenol	33 (22–49)	21 (12–37)[e]				
o-Nitroaniline	3,560 (2,590–4,910)	1,290 (1,130–1,470)[e]	20,000 0/3[c]			
m-Nitroaniline	540 (360–790)	310 (230–420)[e]				
p-Nitroaniline	3,250 (1,980–5,700)	810 (590–1,120)[e]				
o-Nitrophenol	2,830 (2,050–3,890)	1,300 (890–1,700)[e]				
m-Nitrophenol	930 (640–1,350)	1,410 (No CL)[e]				
p-Nitrophenol	620 (450–850)	470 (320–690)[e]				

o-Nitrotoluene	*890 (500–1,580)*	*2,460 (1,790–3,390)[e]*			
m-Nitrotoluene	*1,070 (730–1,580)*	*1,230 (890–1,700)[e]*			
p-Nitrotoluene	*2,140 (1,450–3,170)*	*1,230 (890–1,700)[e]*			
N-Octylphenyl-1-naphthylamine	8,000 0/5[c]				
Phenol			1,400 (740–2,670)		
N-Phenyl-1-naphthylamine	1,630 (1,200–2,200)				
Pyridine				9,010 (8,220–9,880)	9,020 (8,160–9,970)[a]
2,3-Xylidine	930 (630–1,380)	1,070 (730–1,590)[e]			
2,4-Xylidine	470 (320–690)	250 (150–420)[e]			
2,5-Xylidine	1,300 (940–2,140)	840 (470–1,490)[e]			
2,6-Xylidine	1,230 (890–1,700)	710 (520–960)[e]			
3,4-Xylidine	810 (590–1,120)	710 (520–960)[e]			
3,5-Xylidine	710 (470–1,070)	420 (280–640)[e]			
Organic acids					
Acetic acid, glacial					
Fumaric acid	10,700 (7,200–15,800)	9,300 (6,300–13,800)[a]	20,000 0/3[c]		
3-Methylbutyric acid			3,560 (1,880–6,770)		
Oxalic acid, 5%[f]	9.5 (5.4–12.3) [ml/kg]	7.5 (5.0–11.0) [ml/kg][a]	20,000 0/3[c]		
Propionic acid, 15%[f]					
Esters					
Acrylic acid, *n*-butyl ester	6,170 (4,570–8,330)	4,920 (4,320–5,600)[a]	5,660 (1,450–22,100)	6,360[b] 2/5[c]	5,100 4/5[a,c]
Acrylic acid, methyl ester				33,000[b] 1/5[c]	34,000[b] 3/5[a,c]
Chloroacetic acid, ethyl ester			230 (120–430)		
Chloroformic acid, ethyl ester	470 (320–690)	270 (180–400)[a]	7,120	145 (140–150)	170 (150–180)[a]
Chloroformic acid, methyl ester	190 (130–280)	110 (70–160)[a]	7,120	88 (64–123)	103 (90–118)[a]
Diethyl sulfate	1,410 (1,100–1,550)	650 (510–830)[e]			
Isocyanic acid, methyl ester	140 (55–340)	120 (78–200)[e]	1,800 (950–3,410)		
Isocyanic acid, phenyl ester			7,130 (3,740–13,540)		
Isocyanic acid, tris-2-hydroxyethyl ester	20,000 0/5[c]	10,000 0/5[c] 20,000 3/5[a,c]			

TABLE 1—*Continued*

Material studied	Single oral LD50 (mg/kg)		Single skin penetration LD50	Inhalation, 1-hr LC50 (ppm)		Skin corrosion
	Male rats	Other	Rabbits (mg/kg)	Male rats	Other	
Isothiocyanic acid, allyl ester	490 (240–1,010)	310 (190–690)[e]	88			
Isothiocyanic acid, methyl ester	220 (110–440)	110 (40–300)[e]	33 (18–64)			
Methyl nitrate	340 (310–380)[g]	1,820 (1,740–1,910)[c, g]		1,280 (1,200–1,360)[d, g]	5,940 (5,830–6,510)[d, c, g]	
Miscellaneous organic compounds						
2-Amino ethanol	1,970 (1,430–2,710)	1,720 (1,160–2,540)[a]				
Ethanethiol				28,400 0/5[c, h]	15,000[a] 0/5[c] 27,000[a] 3/5[c, h]	
Ethyl bromide				27,000 (25,400–28,700)	16,200 (15,400–18,600)[c]	
Bis(3-fluoro salicyl-aldehyde)ethylenedi-amine cobalt (II)	190 (130–270)	120 (93–170)[e]		710 (640–790) [mg/m³]	890 (mg/m³)[c] 0/10[c]	
1,6-Hexanediamine	800 (470–1,360)	750 (510–1,100)[a]	1,110 (600–2,120)			
Maleic anhydride			2,620 (1,930–3,550)			
Nicotine sulfate)	75 (44–127)	16 (12–21)[e]				
2-Propyne-1-ol	93 (58–150)[g]	54 (37–78)[a, g]	88	1,200 (1,180–1,220)[g]	1,040 (970–1,120)[a, g]	
Tetranitromethane	130 (83–210)	380 (260–510)[c]		18 (16–19)[d, g]	54 (48–62)[d, c, g]	
Trichloroethylene				26,300 (23,700–29,200)	25,700 (22,300–29,500)[a]	
Trichloromethane-sulfenyl chloride			1,410 (360–5,510)	11 (10–13)[g]	16 (13–22)[a, g]	
Trichloro-*s*-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione	406 (295–559)	466 (315–690)[a]	20,000 0/3[c]			
Triphenyl stibine	187 (129–270)	650 (472–895)[e]				
Inorganic compounds						
Ammonia, gas				7,338 (6,822–7,893)	4,837 (4,409–5,305)[c]	
Ammonia, 10%[f]						–
Ammonia, 12%[f]						+
Boron trichloride				**2,541 (2,243–2,878)[g]**	**4,418 (3,940–4,953)[a, g]**	
Boron trifluoride				**387 (320–467)[g]**	**371 (293–469)[a, g]**	

Calcium arsenate	***812 (712–924)***				
Calcium chromate	***746 (627–887)***	***327 (260–410)[a]***			
Carbon monoxide			14,200 (13,400–15,100)[g,i]		
Chlorine			293 (260–327)	137 (119–159)[c]	
Chlorine trifluoride			299 (260–344)[g]	178 (169–187)[c,g]	
Chromic nitrate, nonahydrate	1,540 (1,270–3,010)	1,410 (900–2,170)[a]			
Deuterium fluoride, gas			1,100 (1,010–1,190)[g]	324 (301–349)[c,g]	
Hydrochloric acid, 15%[f]					–
Hydrochloric acid, 17%[f]					+
Hydrogen bromide, gas			2,860 (2,580–3,160)[g]	814 (701–947)[c,g]	
Hydrogen chloride, gas			3,120 (2,830–3,450)[g]	1,110 (874–1,400)[c,g]	
Hydrogen cyanide, gas			484 (442–535)[g,i]	323 (276–377)[c,g,i]	
Hydrogen fluoride, gas			966 (785–1,190)[g]	456 (426–489)[c,g]	
Hydrogen sulfide			712 (662–765)	634 (576–688)[c]	
Nitric acid, 6%[f]					–
Nitric acid, 8%[f]					+
Mercuric acetate	76 (55–105)	62 (41–92)[c]			
Mercuric cyanide	26 (15–46)	33 (22–49)[c]			
Mercuric oxide	18 (7–44)	22 (10–48)[c]			
Mercuric sulfate	57 (27–120)	40 (30–50)[c]			
Mercurous nitrate	297 (248–362)	388 (290–530)[c]			
Oxygen difluoride			2.6 (2.5–2.7)[g]	1.5 (1.2–2.0)[c,g]	
Phosphotungstic acid	3,300 (2,560–4,250)	4,930 (3,580–6,780)[a]			
Potassium hydroxide, 1%[f]					–
Potassium hydroxide, 2%[f]					+
Silane			9,600 0/5[c,d,j]		
Sodium hydrosulfide, 45%[f]					+
Sodium hydroxide, 1%[f]					–
Sodium hydroxide, 2%[f]					+
Sodium sulfide, 25–27%[f]					+
Sulfuric acid, 4%[f]					–
Sulfuric acid, fuming			420 (397–444)	347 (260–464)[a]	
Sulfuryl fluoride			3,730 (3,090–4,510)	3,020 (2,830–3,220)[a]	

[a] Female rats.
[b] Saturated vapor.
[c] Single exposure mortality.
[d] 4-Hr LC50 value.
[e] Mice.
[f] Percentage by weight in aqueous solution.
[g] Calculated using probit technique (Finney, 1971).
[h] Lower explosive limit.
[i] 5-Min LC50.
[j] Auto ignition concentration.

The method used for skin absorption toxicity was essentially that of Smyth *et al.* (1962), except that three female albino New Zealand rabbits were used per dose and the doses were kept in place by 8-ply gauze patches under a latex rubber film.

Skin corrosion was tested using rabbits that had been clipped of all possible hair on backs and flanks 24 hr prior to exposure to allow for recovery of the skin from any irritation resulting from clipping. Six areas on the back, three on each side, were designated as patch areas to allow for the simultaneous testing of six materials per rabbit with six rabbits used for replicate testing of each series.

The test material was applied in the amount of 0.5 g for solids and 0.5 ml for liquids or aqueous solutions. Aqueous solutions were made up by diluting pure materials or concentrated solutions to give percentages by weight. Solid materials were applied as powders. The material was applied to the designated patch areas and covered by a 1-in. square of surgical gauze two single layers thick. The gauze patches were held in place with strips of Elastoplast tape. The entire area was covered with a latex rubber film and secured with more Elastoplast tape. The patches remained in place for 4 hr. During that time, the rabbits were fitted with leather restraining collars to prevent disturbance of the patch area, while allowing the rabbits freedom of movement and access to food and water.

After 4 hr, the wrap and patches were carefully removed, and the test areas were evaluated for visible tissue destruction. When such severe skin damage occurred in at least two of six rabbits, the materials were classified as corrosive. This method was obtained through private communication with the Carnegie–Mellon Institute of Research where it was developed.

Inhalation experiments were usually performed in bell jars or large desiccators using five rats per exposure level with 1-hr LC50 values determined for males and females by the method of Thompson (1947) and Weil (1952), or, where enough information was available, by the probit method. Some of the inhalation data reported here were obtained in male mice and some for times other than 1 hr. All such instances are noted in Table 1. In all cases, the chamber contaminant concentrations were measured by standard techniques or by methods developed in this laboratory and checked to give relative SD of 5% or less.

The animals used in this study were Sprague–Dawley rats, 200–300 g; male CF-1 mice, 22–28 g; and female New Zealand albino rabbits, 3–4 kg. The rodents were maintained on Purina Formulab Chow 5008 and the rabbits on Purina Rabbit Chow.

RESULTS

The data obtained are summarized in Table 1.

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REFERENCES

CARPENTER, C. P., WEIL, C. S., AND SMYTH, H. F., JR. (1974). Range-finding toxicity data: List VIII. *Toxicol. Appl. Pharmacol.* **28**, 313–319.

FINNEY, D. J. (1971). *Probit Analysis.* Cambridge University Press, London.

SMYTH, H. F., JR., AND CARPENTER, C. P. (1944). The place of the range-finding test in the industrial toxicology laboratory. *J. Ind. Hyg. Toxicol.* **26**, 269–273.

SMYTH, H. F., JR., AND CARPENTER, C. P. (1948). Further experience with the range-finding test in the industrial toxicology laboratory. *J. Ind. Hyg. Toxicol.* **30**, 63–68.

SMYTH, H. F., JR., CARPENTER, C. P., AND WEIL, C. S. (1949). Rangefinding toxicity data: List III. *J. Ind. Hyg. Toxicol.* **31**, 60–62.

SMYTH, H. F., JR., CARPENTER, C. P., AND WEIL, C. S. (1951). Range-finding toxicity data: List IV. *Arch. Ind. Hyg. Occup. Med.* **4**, 119–122.

SMYTH, H. F., JR., CARPENTER, C. P., WEIL, C. S., AND POZZANI, U. C. (1954). Range-finding toxicity data: List V. *Arch. Ind. Hyg. Occup. Med.* **10**, 61–68.

SMYTH, H. F., JR., CARPENTER, C. P., WEIL, C. S., POZZANI, U. C., AND STRIEGEL, J. A. (1962). Range-finding toxicity data: List VI. *Amer. Ind. Hyg. Ass. J.* **23**, 95–107.

SMYTH, H. F., JR., CARPENTER, C. P., WEIL, C. S., POZZANI, U. C., STRIEGEL, J. A., AND NYCUM, J. S. (1969). Range-finding toxicity data: List VII. *Amer. Ind. Hyg. Ass. J.* **30**, 470–476.

THOMPSON, W. R. (1947). Use of moving averages and interpolation to estimate median-effective dose. I. Fundamental formulae, estimation and error, and relation to other methods: *Bact. Rev.* **11**, 115–145.

WEIL, C. S. (1952). Tables for convenient calculations of median-effective dose and instructions in their use. *Biometrics* **8**, 249–263.