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ACUTE TOXICITY OF MONOCHLOROPHENOLS, DICHLOROPHENOLS AND PENTACHLOROPHENOL IN THE MOUSE

(Chlorophenols; acute toxicity; mice)

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SUMMARY

Acute oral LD_{50} values were determined for 2-, 3-, and 4-chlorophenol, 2,3-, 2,4-, 2,5-, 2,6-, 3,4-, and 3,5 dichlorophenol and pentachlorophenol in male and female mice. LD_{50} values (mg/kg) ranged from 117 (females) and 177 (males) for pentachlorophenol to 2389 (females) and 2643 (males) for 3,5-dichlorophenol. It was found that 2-chlorophenol and 3-chlorophenol were considerably more toxic than the dichlorophenol series. Values for males and females were generally similar, the major differences being with pentachlorophenol and 2,5-dichlorophenol, where in both cases the female LD_{50} was lower.

INTRODUCTION

Chlorinated phenols have been found in drinking water as a result of the chlorination of water containing phenol or other phenolic compounds [1]. While some information on the acute oral toxicity of these substances is available, primarily in the rat, a systematic study of this series of compounds under similar experimental conditions is lacking. This investigation was designed to provide such comparative toxicity data and also to permit an analysis of the relationship between structure and degree of toxicity.

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MATERIALS AND METHODS

Six-week-old male and female CD-1 ICR mice (Charles River Labs, Wilmington, MA) were quarantined for 4 days, randomized and maintained in plastic cages in rooms at 21–24°C and relative humidity of 40–60% with a light–dark cycle of 12–12 h. Purina rodent chow and deionized water ware available ad lib.

TABLE I

ACUTE ORAL TOXICITY DATA OF CHLORINATED PHENOLS IN CD MICE AND IN RATS

Compound	M_r	Present mouse study				Previous rat studies	
		Purity	Vehicle/ solvent	Acute oral LD_{50}(mg/kg) Male	Acute oral LD_{50}(mg/kg) Female	Vehicle/ solvent	Acute oral LD_{50} (mg/kg)
2-Chlorophenol[b]	128.56	98+%	Deionized water	347 (239–393)[a]	345 (321–381)	Olive oil	670[3,4]
3-Chlorophenol	128.56	99%	Deionized water	521 (463–586)	530 (468–601)	Olive oil	570[3,4]
4-Chlorophenol	128.56	99+%	Corn oil	1373 (1191–1583)	1422 (1333–1518)	Olive oil	670[3,4]
2,3-Dichlorophenol	163.00	98%	Corn oil	2585 (2046–3266)	2376 (2186–2585)		
2,4-Dichlorophenol[c]	163.00	99%	Corn oil	1276 (982–1569)	1352 (1094–1670)	Fuel oil	580[3,4] 4000[5][c]
2,5-Dichlorophenol	163.00	98%	Corn oil	1600 (1233–2075)	946 (633–1438)		
2,6-Dichlorophenol	163.00	99%	Corn oil	2198 (1727–2797)	2120 (1799–2498)		
3,4-Dichlorophenol	163.00	99%	Corn oil	1685 (1504–1887)	2046 (1472–2846)		
3,5-Dichlorophenol	163.00	99%	Corn oil	2643 (2269–3078)	2389 (1829–3120)		
Pentachlorophenol	226.34	99%	10% Emulphor	177 (125–252)	117 (65–212)	Fuel oil Peanut oil ♂ : 146[6] Peanut oil ♀ : 175[6]	27[3,4]

[a]Confidence limits

[b]Bubnov, 1969; mouse LD_{50} 670 mg/kg

Chemicals were obtained from Aldrich Chemical Company, Milwaukee, WI. Identity and purity (98–99%) were confirmed. The compounds were administered in corn oil (Mazola Pure Corn Oil, Best Foods, Englewood Cliffs, NJ), deionized water or 10% emulphor (see Table I) by gavage at concentrations allowing all doses to be delivered in a volume of 10 ml/kg.

Five dose levels were employed with 10 mice of each sex per dosage group. The animals were fasted for 18 h prior to dosing; food was returned 1 h after dosing. The mice were continuously observed for 1 h after dosing, hourly for the next 4 h and then twice each day (9:00 a.m. and 4:00 p.m.) for the next 14 days. All mice that died during the observation period and those that survived were necropsied. The LD_{50} was computed by Log Probit Analysis as described by Finney [2].

RESULTS

The primary signs of toxicity were increased respiration, tremors, and slight convulsions followed by CNS depression for all compounds except pentachlorophenol, which elicited signs of CNS depression only. Mean times of death for most groups were less than 24 h.

The LD_{50} values are shown in Table I. The figures (mg/kg) ranged from 177–2643 for males and 117–2389 for females. In both sexes pentachlorophenol was the most toxic and 3,5-dichlorophenol the least toxic. There was generally very little difference in LD_{50} values between males and females. The major exceptions were 2,5-dichlorophenol and pentachlorophenol, both of which were more toxic to females.

In comparing the three classes of chlorophenols studied (monochloro-, dichloro-, and pentachloro-), the pentachloro-form was the most toxic and the dichloro-compounds the least toxic.

DISCUSSION

Other LD_{50} values reported [3–7] for these compounds in the mouse and rat appear in Table I. Deichmann [3, 4] studied the acute toxicity of chlorinated phenols in the rat and also found pentachlorophenol to be most toxic. In comparing toxicity in the 2 species (Table I), the LD_{50} values found in mice in this study are lower than those reported for the rat [3, 4] for 2- and 3-chlorophenol and higher for 4-chlorophenol and 2,4-dichlorophenol. The LD_{50} values found for 2,4-dichlorophenol in the mouse are considerably lower than the 4000 mg/kg reported for the rat by Kobayashi [5]. LD_{50} values reported by Gaines [6] for pentachlorophenol in the rat are 146 mg/kg for males and 175 mg/kg for females. The differences noted could be due to the solvent used. For example, the fuel oil vehicle used by Deichmann could be partly responsible for the lower figure. Gaines [6] used peanut oil and his data suggest that the sensitivity of the two species is comparable.

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