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Mutagenic Properties of Methyl- and Ethylbromophos in Mammals

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Although the mutagenic properties of some organophosphorus pesticides such as dichlorvos and trichlorfon have been extensively investigated (Moutschen et al., 1981), only a few data are available concerning some other substances of the same chemical group. This is the case for methylbromophos (dimethyl 4 bromo 2,5 dichlorophenyl phosphorothionate) and ethylbromophos (diethyl 4 bromo 2,5 dichlorophenyl phosphorothionate), two substances used for insect control on both animals and plants (Brofene, Bromophos, Nexion, Prosol, Nexagan).

The only published data does not reveal any mutagenic activity in Salmonella typhimurium (Lippens et al., 1983), Schizosaccharomyces pombe (Gilot-Delhalle et al., 1983) and Drosophila melanogaster (Benes and Sram, 1969).

The present research investigates the genetic (dominant lethal mutations) and cytogenetic (chromosome damage in bone marrow cells and spermatogonia) effects induced in male mice by an acute treatment with a very high dose (1000 mg/kg) of methylor ethylbromophos. The results are compared to those obtained with the well known mutagen mitomycin C selected as a positive control.

MATERIALS AND METHODS

Methylbromophos and ethylbromophos (Riedel-De Haen, Pestanal®, purity > 99%) being slightly soluble in water, the solutions were injected as suspensions in peanut oil.

Male mice (Q strain), 3–4 months old, received a single i.p. injection. The doses tested were 1 g/kg for the insecticides and 2 mg/kg for mitomycin C (Sigma Chemical).

Treated males were sacrificed from 12–36 h after the treatment for the analysis of chromosome damage in bone marrow cells and spermatogonia. Microscopic slides were prepared according to the air drying method (Evans et al., 1964).

Table 1: Cytogenetic effects induced in bone marrow cells by methylbromophos (1 g/kg), ethylbromophos (1 g/kg) and mitomycin C (2 mg/kg) (500 metaphases analyzed).

Treatment	Recovery period in h	Percentage of aberrations		
		Fragments	Exchanges	Gaps
Control	-	0.4	0.0	0.4
Mitomycin C	12	7.2	2.6	5.0
	24	45.2	8.2	8.6
	36	7.0	1.6	0.6
Methyl-	12	0.0	0.0	0.0
bromophos	24	0.4	0.0	0.0
	36	0.2	0.0	0.0
Ethyl-	12	0.2	0.0	0.2
bromophos	24	0.4	0.0	0.0
	36	0.6	0.0	0.0

Table 2: Cytogenetic effects induced in spermatogonia by methylbromophos (1 g/kg), ethylbromophos (1 g/kg) and mitomycin C (2 mg/kg).

Treatment	Recovery period in h	Number of metaphases analyzed	Percentage of aberrations		
			Fragments	Exchanges	Gaps
Control	-	386	0.26	0.00	0.26
Mitomycin C	12	132	15.91	9.09	6.82
	24	68	17.65	11.76	4.41
	36	33	27.27	6.06	3.03
Methyl-	12	143	1.40	0.00	0.70
bromophos	24	408	0.74	0.00	0.49
	36	336	0.30	0.00	0.00
Ethyl-	12	289	1.04	0.00	0.00
bromophos	24	366	0.54	0.00	0.27
	36	360	0.28	0.00	0.28

Table 3: Genetic effects induced by methylbromophos (1 g/kg), ethylbromophos (1 g/kg) and mitomycin C (2 mg/kg) in the dominant lethal mutation assay.

Treatment	Recovery period in days	Pregnant females	Corpora lutea per ♀	Implants per ♀	Preimplantation losses per ♀	Preimplantation losses % CL	Live embryos per ♀	Postimplantation losses per ♀	Postimplantation losses % IP	Total mortality per ♀	Total mortality %CL
Control	-	68	9.93	9.15	0.78	7.9	8.78	0.37	4.0	1.15	11.6
Mitomycin C	1- 7	11	9.73	9.64	0.09	0.9	8.91	0.73	7.5	0.82	8.4
	8-14	11	10.45	8.81	1.64	15.7	8.27	0.54	6.2	2.18	20.9
	15-21	14	8.78	6.57	2.21	25.2	5.57	1.00	15.2	3.21	36.6
	22-28	6	7.33	3.00	4.33	59.1	2.50	0.50	16.7	4.83	65.9
Methyl-	1- 7	12	8.58	7.17	1.41	16.5	7.00	0.17	2.3	1.58	18.4
bromophos	8-14	16	9.19	8.69	0.50	5.4	8.56	0.13	1.4	0.63	6.8
	15-21	12	8.92	8.42	0.50	5.6	7.92	0.50	5.9	1.00	11.2
	22-28	17	9.65	8.77	0.88	9.2	8.59	0.18	2.0	1.06	11.0
	29-35	12	9.58	9.25	0.33	3.5	9.08	0.17	1.8	0.50	5.2
	36-42	13	9.00	8.08	0.92	10.3	7.69	0.39	4.8	1.31	14.5
	43-49	14	8.71	7.71	1.00	11.5	7.57	0.14	1.9	1.14	13.1
Ethyl-	1- 7	17	9.65	8.65	1.00	10.4	8.35	0.30	3.4	1.30	13.4
bromophos	8-14	11	10.00	9.64	0.36	3.6	9.28	0.36	3.8	0.72	7.2
	15-21	16	10.00	9.38	0.62	6.2	9.25	0.13	1.3	0.75	7.5
	22-28	14	10.43	9.79	0.64	6.2	9.43	0.36	3.6	1.00	9.6
	29-35	15	10.47	9.53	0.94	8.9	9.33	0.20	2.1	1.14	10.8
	36-42	15	10.20	9.07	1.13	11.1	8.67	0.40	4.4	1.53	15.0
	43-49	18	9.83	8.72	1.11	11.3	8.61	0.11	1.3	1.22	12.4

Other males were mated with untreated virgin females according to the classical procedure for the dominant lethal mutation assay in mouse (Bateman, 1977).

Seven-day mating intervals were used for a total of seven weeks. Pregnant females were killed 14 days after verification of the vaginal plugs.

Statistical analysis was carried out by the Kastenbaum and Bowman tables and the χ^2 test.

RESULTS AND DISCUSSION

In bone marrow metaphases (table 1) the percentages of chromosome aberrations observed in animals treated with the insecticides were below the control level. Mitomycin C induced a great number of lesions, especially in the males killed 24 h after the treatment. In spermatogonia (table 2), both methyland ethylbromophos increased, though not significantly, the frequency of damaged cells. No chromosome exchange was observed. The total number of aberrations induced by mitomycin C exceeded 30%.

The number of live embryos per female was low, sometimes less than 8, in the females mated with males receiving methylbromophos (table 3). Nevertheless, the frequency of deciduomata and the total foetal mortality were not significantly higher than in the control group. The number of live embryos is likely to be correlated to the low number of corpora lutea per female.

The females mated with males injected with ethylbromophos did not show any increase in foetal lethality before and after implantation. On the other hand, mitomycin C induced both types of foetal mortality, increasing the recovery period.

Although conducted under drastic conditions at very high doses (1 g/kg), our experiments did not reveal cytogenetic effects in bone marrow cells and spermatogonia or genetic effects in the dominant lethal mutation assay. These results confirm the data concerning the mutagenic properties of methylbromophos in microorganisms and in Drosophila. This also parallels the lack of carcinogenic and teratogenic action of long term treatments in mammals (Vettorazzi, 1976).

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