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ACUTE, ORAL TOXICITY TO LABORATORY ANIMALS OF FENTHION (O-O-DIMETHYL-O-(3-METHYL-4-METHYL-MERCAPTO-PHENYL)-THIOPHOSPHATE) IN DIFFERENT FORMULATIONS

By

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Fenthion is an organophosphorus compound (see Fig. 1) marketed under various trade names as a broad-spectrum insecticide. Specifications given by the manufacturers indicate that it is relatively resistant to light and alkalies, with a low vapour pressure at ordinary room temperatures. Furthermore, the available data suggest a moderate toxicity to mammals. The compound is accordingly advertised as being well suited for use as a residual wall deposit against insects in barns and stables. Some experimental results concerning the acute toxicity of fenthion are listed in Table 1. The work of *DuBois & Kinoshita* (1964) cited was published after the present investigations were finished.

The oral toxicity of a given compound will vary as it is applied with different vehicles. In the experiments referred to in Table 1, fenthion was administered in solution with alcohols or oils. The compound is commercially marketed as emulsions and wettable powders to be diluted with water before use. It therefore appeared

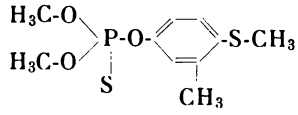

Fig. 1. O,O-dimethyl-O-(3-methyl-4-methylmercapto-phenyl) thiophosphate, O,O-dimethyl O-(4-methylthio-m-tolyl) phosphorothioate.
Common names: fenthion, mercaptophos.
Other designations: S 1752, Bayer 29493, DMTP.
Trade names: Baytex, Lebaycid.

Table 1. Some experimental results concerning the acute, oral toxicity of fenthion to laboratory animals.

Species	Sex	LD50 mg/kg	Reference
Rat	Females	310	*DuBois & Kinoshita* (1964)
Rat	Males	190	
Guinea pig	Males	260	
Rat	Females	245	*Gaines* (1960)
Rat	Males	215	
Rat	Males and females	325	*Brady et al.* (1960)

of interest to study the toxicity of fenthion in formulations corresponding to those used under practical conditions. Simultaneously the relative toxicities of fenthion preparations varying in purity could be investigated.

MATERIAL AND METHODS

The experiments with *rats* were performed using the following formulations:

Test 1: Chemically pure fenthion: S 1752, chemisch rein.*)

Test 2: Technical fenthion: S 1752, technisch Reinheitsgrad 95 %.*)

Test 3: Baytex: wettable powder declared to contain 40 % fenthion, 60 % spreading and sticking agents.

Test 4: Lebaycid: emulsion declared to contain 50 % fenthion, 50 % spreading agents and emulgator. Samples analysed after a procedure described by the manufacturers contained 51, 49 and 53 %.

In *Test 5 Lebaycid* was given to *mice.*

The test formulations were emulgated in water by vigorous mechanical shaking for 2 hours. It became necessary to stabilize the emulsions in Tests 1 and 2 by adding 5 % (w/v) Arabic Gum. To obtain uniform experimental conditions this was also done in Tests 3 and 4.

*) Supplied by Farbenfabriken Bayer AG, Leverkusen.

The concentrations of the test compounds were adjusted to keep the ratio of dose volume to weight of animal constant. The doses were administered to unanaesthetized animals through a glass stomach tube mounted on an injection syringe.

The investigations were performed with adult, male white rats (weight 190—260 g) and adult, male, white mice (weight 25—30 g) of the department's own breed. The rats were fed a pelleted standard feed (*Tollersrud & Slagsvold* 1962). The mice were fed a granulated chicken feed. All animals were fasted 20—24 hours before administration. They stayed in their usual quarters and at a temperature of 20—24°C during the complete experiments, with free access to feed and water during the observation periods which lasted for 72 to 96 hours after administration.

RESULTS

In rats the symptoms of poisoning would appear 30—60 minutes after administration. They rapidly increased in severity, reached a maximum after 6—10 hours and then decreased. They consisted of copious lachrymation and salivation, incontinence of urine, diarrhoea, laborious breathing and muscle fasciculations. After a few hours most animals were lying prostrate, and they stayed in this position until death or recovery supervened. The first deaths might occur 8 to 12 hours after administration, but as a rule there were only a few deaths for the first 24 hours. Most deaths occurred between 24 to 36 hours after administration, very few animals would die after this period. At 48 hours after administration the survivors often had started to recover, even if the symptoms persisted much longer. In a few groups there could still be seen single animals who were severely affected, these would always die in a couple of hours.

Table 2. Regression coefficients (b) with standard errors (s_b) for the probit regression lines fitted to the dose/response data of fenthion toxicity tests.

Test	b	s_b
1	10.78	± 1.62
2	6.05	± 1.40
3	9.96	± 1.76
4	7.80	± 1.78
5	7.34	± 1.95

In mice the poisoning ran a similar course but far more rapidly. All deaths occurred within 24 hours after administration.

Maximum likelihood estimates of probit regression lines (*Finney* 1952) were fitted to the number of dead and moribund animals in each group at 48 hours after administration. The regression coefficients are listed in Table 2, and the lines with

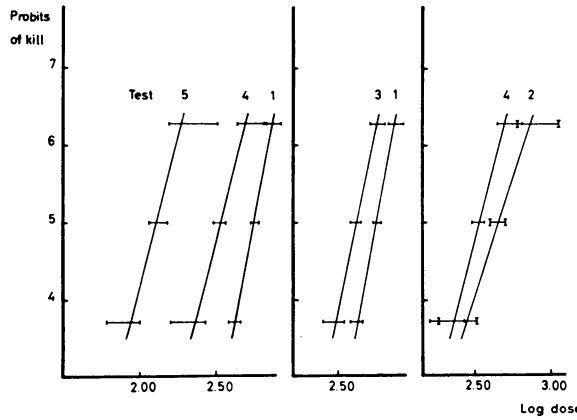

Fig. 2. Relationship between dosage of fenthion and kill, showing probit regression lines with 95 % fiducial limits indicated at three levels of effect.

Test 1: Chemically pure fenthion to rats.
Test 2: Technical fenthion to rats.
Test 3: Baytex to rats.
Test 4: Lebaycid to rats.
Test 5: Lebaycid to mice.

Table 3. Approximate LD-values for rat and mouse of fenthion in different formulations.

Test	Species	Sex	Formulation	LD in mg fenthion per kg with 95 % fiducial limits LD10	LD50	LD90	No. of animals
1			Chemically pure	425 (380—460)	560 (530—600)	740 (675—855)	120
2	Rat	Males	Technical	275 (180—325)	445 (400—495)	725 (610—1120)	120
3			Baytex	310 (255—345)	415 (385—445)	560 (510—650)	120
4			Lebaycid	230 (160—270)	340 (305—365)	490 (435—650)	100
5	Mouse	Males	Lebaycid	85 (60—100)	125 (115—150)	185 (155—325)	61

indications of 95 % fiducial limits at three levels of effect are compared in Fig. 2. The corresponding approximate values for LD10, LD50 and LD90 with 95 % fiducial limits are given in Table 3.

DISCUSSION

The results of these experiments indicate that fenthion emulgated in water has a moderate to low acute, oral toxicity to male, white rats. It is somewhat more toxic to male, white mice.

From Table 2 it may be seen that the regression lines are not parallel. Accordingly the results will not serve as a basis for direct statistical evaluation of the relative toxic potencies of the different formulations. But as no systemic heterogenicity was found in the results of any experiment, it has been assumed justified to compare the toxicity to rats at three levels of effect.

The value for LD50 found in Test 1 is significantly higher than in the three other tests. Furthermore is the LD50 in Test 4 significantly lower than in Tests 2 and 3. At doses giving very high and very low effect levels (90 % and 10 % kill) the difference in toxicity is only significant between Test 1 on one side and Tests 3 and 4 on the other.

The results suggest that technical fenthion in the commercial formulations Baytex and Lebaycid under the conditions of these experiments has a higher acute, oral toxicity than the chemically pure compound to male, white rats. The difference is small but significant within 95 % fiducial limits. It may be due to contaminating agents in the technical compound. There is however no satisfactory evidence to prove that technical fenthion as such is more toxic than the chemically pure product. It should accordingly be justified to presume that the toxicity of fenthion is also affected by the additives found in commercial formulations (spreading and sticking agents or emulgators). These additives may themselves be toxic, or they may enhance the specific toxicity of fenthion simply by increasing the rate of absorption from the intestine.

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SUMMARY

The acute, oral toxicity of fenthion (O,O-dimethyl-O-(3-methyl-4-methylmercapto-phenyl)thiophosphate) in different formulations emulgated in water was studied. For male, white rats the approximate values for LD50 found varied from 340 to 560 mg per kg, technical fenthion in commercial products being more toxic than the chemically pure compound. Fenthion in the commercial preparation Lebaycid was more toxic for male, white mice (LD50 approx. 125 mg per kg) than for rats.

ZUSAMMENFASSUNG

Die akute, orale Toxizität verschiedener Emulsionen des Stoffes Fenthion (O-O-Dimethyl-O-(3-Methyl-4-Methylmercapto-Phenyl)-Thiophosphat) gegenüber Ratten und Mäusen.

Die akute, orale Toxizität von Fenthion (O,O-Dimethyl-O-(3-Methyl-4-Methylmercapto-Phenyl)Thiophosphat) in verschiedenen in Wasser emulgierten Formen ist untersucht worden. Die annähernden Werte für LD50 variierten in Versuchen mit weissen Ratten (♂) von 340 bis 560 mg pro kg. Technisches Fenthion in commerziellen Produkten erwies sich giftiger als der chemisch reine Stoff. Fenthion in dem commerziellen Präparat Lebaycid zeigte grössere toxische Wirkung gegenüber weissen Mäusen (♂) (LD50 annähernd 125 mg pro kg) als bei Ratten.

SAMMENDRAG

Den akutte, orale toksisitet for rotte og mus av fenthion (O,O-dimethyl-O-(3-methyl-4-methylmercapto-fenyl)-thiofosfat) i forskjellige formuleringer.

Undersøkelsene er utført med fire forskjellige fenthionformuleringer emulgert i vann. De tilnærmede LD50-verdier for voksne, hvite hanrotter varierte mellom 340—560 mg/kg, idet teknisk fenthion i handelspreparater var noe mer giftig enn det kjemisk rene stoff. Fenthion i form av handelspreparatet Lebaycid var mer giftig for hvite hanmus (LD50 ca. 125 mg/kg) enn for rotter.

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