

Preferential Effect of Dichlorvos (Vapona) on Bacteria Deficient in DNA Polymerase¹

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SUMMARY

Bacteria deficient in DNA polymerase are much more susceptible than are normal cells to the lethal action of dichlorvos [Vapona, *O,O*-dimethyl *O*-(2,2-dichlorovinyl) phosphate], a widely used insecticide. The results are taken to indicate that dichlorvos is capable of altering the cellular DNA.

The anticholinesterase compound DDVP³ is widely used as an insecticide in agriculture (9, 10), as an antimosquito agent for eradicating malaria (3, 4, 11, 17), as a disinfectant of commercial aircraft (16), and for the control of flea infections (10). Hence, human exposure to and inhalation of this pesticide occurs frequently. As normally used, this substance has not exhibited acute toxicity except for the occasional lowering of plasma cholinesterase levels (2-4, 6, 10, 12, 19, 21, 22). However, it was shown recently that DDVP and related phosphoric acid esters reacted with purified DNA and that this reaction was due to the methylation of guanine residues of DNA (8, 15). If the reaction were also to occur *in vivo*, then DDVP could present a real hazard to health in view of the established relationship between the ability of agents to alkylate DNA and their potential carcinogenicity and mutagenicity.

In this report it is shown (Tables 1 and 2) that bacteria (*Escherichia coli*) deficient in DNA polymerase are more sensitive to DDVP than are the parents from which they were derived. This is a property also exhibited by other DNA-alkylating agents (Table 2, Group 2) that are known to be carcinogens as well. On the other hand, substances that do not act on the cellular DNA did not inhibit the DNA polymerase-deficient strain preferentially (Table 2, Group 1).

DNA polymerase has been implicated in the DNA repair process (1, 7); bacterial strains lacking this enzyme are more sensitive than their parents to agents that react with the cellular DNA (1, 5, 18, 20), presumably, because they are unable to repair efficiently the damage to their DNA. The present data suggest that DDVP reacts with the DNA of living cells—a reaction which already has been demonstrated *in vitro*

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³ The abbreviation used is: DDVP, *O,O*-dimethyl-*O*-(2,2-dichlorovinyl)phosphate.

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Table 1

Effect of DDVP on the growth of bacteria deficient in DNA polymerase

Bacteria (*E. coli* W3110 *thy*⁻ (*pol A*⁺) and its DNA polymerase-deficient derivative *E. coli* p3478 (*pol A*₁⁻) (1) in Medium HA (13, 14) containing 5 μg of thymine per ml were brought to the early exponential growth phase, at which time portions of each culture received DDVP (6.4 × 10⁻³ M). At intervals, serial dilutions (0.1 ml) of cell cultures were plated on agar plates (Medium HA plus 5 μg thymine per ml) (13).

Time (hr)	Additions	No. of viable bacteria/ml with	
		<i>Pol A</i> ⁺	<i>Pol A</i> ₁ ⁻
0	None	1.1 × 10 ⁸	1.4 × 10 ⁸
0.5	None	1.8 × 10 ⁸	2.3 × 10 ⁸
1	None	4.3 × 10 ⁸	4.5 × 10 ⁸
2	None	9.3 × 10 ⁸	8.7 × 10 ⁸
0	DDVP	1.1 × 10 ⁸	1.4 × 10 ⁸
0.5	DDVP	7.1 × 10 ⁷	2.6 × 10 ⁷
1	DDVP	4.3 × 10 ⁷	5.0 × 10 ⁶
2	DDVP	1.0 × 10 ⁷	1.5 × 10 ⁵

(8, 15). A reexamination of the potential hazard (carcinogenicity and mutagenicity) to human health of this widely used substance seems, therefore, imperative.

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Table 2

Effects of agents on the growth of a DNA polymerase-deficient strain of E. coli

The procedure used has been described (18). Bacteria [*E. coli* W3110 *thy*⁻ (*pol A*⁺), the parent strain, and *E. coli* p3478 (*pol A*⁻), the DNA polymerase-deficient strain (1)]. were spread onto the surface of agar plates [Medium HA plus 5 µg thymine per ml (13, 14)]. When the plates had dried, discs impregnated with the substances to be tested were deposited on the surface of the agar; after incubation at 37° for 16 hr, the diameters of the zones of inhibition were measured.

Group	Agent	Amount	Diameter of zone of inhibition (mm)	
			<i>pol A</i> ⁺	<i>pol A</i> ⁻
1	Chloramphenicol	30 µg	24	24
	Streptomycin	10 µg	17	17
	Kanamycin	30 µg	19	19
	Erythromycin	15 µg	9	9
2	Methylmethanesulfonate	0.13 µmole	42	59
	Ethylmethanesulfonate	0.11 µmole	4	30
	<i>N</i> -Methyl- <i>N</i> -nitrosourea	0.05 µmole	0	16
	<i>N</i> -Methyl- <i>N</i> -nitrosourethan	0.02 µmole	0	22
	<i>N</i> -Ethyl- <i>N</i> -nitrosourethan	1 µmole	2	33
3	DDVP	0.06 µmole	21	26

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