fetal in order to prevent secondary disease.

Over the long period, the 92 percent survival of radiation chimeras inoculated with allogeneic fetal liver and thymus cells is presumptive evidence that these mice have an adequate immune system. In addition, GVH disease was at the minimum in view of the relative absence of secondary disease and the healthy and vigorous appearance of the mice. Our results suggest that a state of immunological tolerance exists in these allogeneic radiation chimeras, despite the histocompatibility differences between the strains of mice tested. We believe that the postulated inverse relation between immune inadequacy and GVH disease has been abrogated by the use of fetal liver cells and fetal thymus cells in combination.

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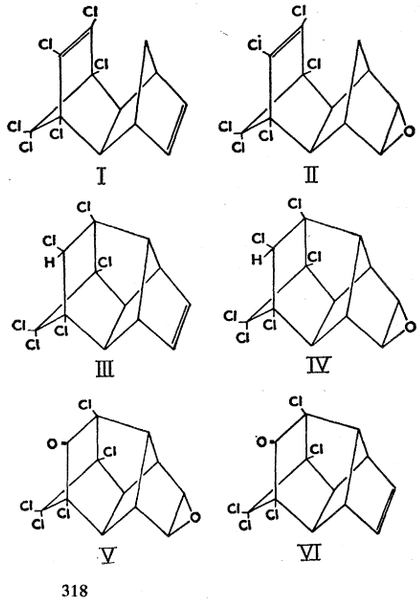
Insect Metabolism of Photoaldrin and Photodieldrin

Abstract. *Photoaldrin and photodieldrin, sunlight products of aldrin and dieldrin, are rapidly metabolized to a more toxic material by flies and mosquito larvae. It is suggested that this conversion is the cause for the enhanced toxicities of the photoproducts.*

Solar irradiation of the cyclodiene insecticides aldrin (I) and dieldrin (II), either as dry films (*1*, *2*) or in aqueous solution (*3*), yields the photoisomers photoaldrin (III) and photodieldrin (IV). The latter is two to ten times more toxic than dieldrin is to several vertebrates (*2*, *4*), while both photoisomers are more toxic to insects (*1*, *2*). Photoaldrin is as much as 11 times more toxic to mosquito larvae than aldrin (*5*). In order to determine the possible reason for their increased toxicity, we have investigated the metabolism of compounds III and IV in insects.



Each compound (0.285 mg/ml) was applied topically in acetone (1 μl) to 50 female multiresistant *Musca domestica* L. (4 days old) (*6*). After 2 hours, the flies were immobilized with carbon dioxide and rinsed with acetone. The flies were then homogenized in 10 ml of water and the homogenate was extracted with 50 ml of a mixture of hexane and isopropanol (3:2); it was then extracted with 30 ml of hexane. The extract was dried over anhydrous sodium sulfate and analyzed on a gas chromatograph (MicroTek MT-220), equipped with a Ni^{63} electron-capture detector and a glass column (122 by 0.159 cm) containing 0.15 percent DC-710 on Corning-0201 glass beads DMCS, 60 to 80 mesh. The chromatograph was operated at column, detector, and injection port temperatures of 135°, 230°, and 215°C, respectively, and at a flow rate of 60 ml/min. A peak with a retention time equal to that of Klein's metabolite (V) [a metabolite of dieldrin in male mice (*7*)] was obtained from flies treated with photoaldrin or photodieldrin. In addition to compound V, flies treated with photoaldrin also contained photodieldrin. Tissue extracts of flies to which aldrin or dieldrin had been applied did not contain compound V. Identical retention times for our metabolic material and compound V were also observed on the very same instrument and column (DC-200) reported on recently (*7*). Although this is the only evidence available at present for the formation of compound V in insects, the finding is logical on the basis of the structures of the applied starting materials, compounds I and II.

The metabolite, after topical application to susceptible flies, caused 52 percent mortality within 4 hours, compared to 28 percent for equimolar amounts of photoaldrin and no mortality for dieldrin. The increased and more rapid toxicity of compound V has been observed earlier (*7*).

In another experiment, 500 mosquito larvae [*Aedes aegypti* (L.)] were placed in 500 ml of water containing 0.014 part per million of photoaldrin or photodieldrin for periods of 1, 2, and 4 hours; the mortality was then determined, and the larvae were prepared for chromatographic analysis. The results (Table 1) indicate that compound V is formed very rapidly. After photoaldrin treatment, only compound V was found in the larval tissue after 4 hours. At this time 90 percent of the larvae were dead. Treatment with photodieldrin resulted in 78 percent mortality after 4 hours, by which time 90 percent of the absorbed photodieldrin had been converted to

Table 1. Concentration (ng/larva) of materials and percent mortality (M) after varying periods of exposure to 0.014 part per million of photoaldrin (III) and photodieldrin (IV).

Exposure time (hr)	Compound (ng)		M (%)	Compound (ng)		M (%)
	III	V		IV	V	
1	1.6	0.2	5	0.99	0	0
2	1.5	2.6	22	1.2	2.3	10
4	0	4.5	90	0.5	4	78

compound V. The results strongly suggest that the photoisomers are more toxic than their parent compounds because of rapid metabolism to compound V, itself a more toxic material than the photoisomers. Aldrin and dieldrin are not metabolized to compound V in insects, although this transformation has been observed in male mice (*7*).

No photodieldrin was detected in mosquito larvae (in contrast to flies) which were treated with photoaldrin. This suggests that photodieldrin is either metabolized to compound V much more rapidly in this species than in flies, or that, in mosquitoes, conversion to the ketone VI (not found) precedes epoxidation. Possibly ketone formation and epoxidation occur at the same enzymatic site.

Only negligible amounts of photodieldrin have been recovered in certain foods, and it has been concluded that photolysis of cyclodienes does not represent an increase in the toxicological significance of cyclodiene residues (*4*). However, the rapid biological activation of the photoisomers to the more toxic compound V in insects and possibly similar metabolism in other organisms suggests that residues of compound V might be important.

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Multiplicity Reactivation as a Test for Recombination Function

Abstract. *Multiplicity reactivation of bacteriophage inactivated by ultraviolet light is dependent on the recombination function of either the host bacterial cell or the infecting bacteriophage. Absence of both recombination systems leads to a loss of multiplicity reactivation.*

The inactivation of bacteriophage by ultraviolet light is essentially a first-order reaction (*1*) and can be expressed as:

$$P/P_0 = e^{-kT} \quad (1)$$

where P_0 is the initial bacteriophage titer, P is the bacteriophage titer after the ultraviolet dose T (measured in seconds), and k is a constant dependent on the sensitivity of the bacteriophage and the ability of the host bacterium to repair ultraviolet damage. If bacteria are infected with irradiated bacteriophage at a multiplicity greater than one, the survival of infective centers as a function of dose is expected to be (*2*)

$$Y/Y_0 = 1 - (1 - e^{-kT})^m \quad (2)$$

where Y_0 is the initial infective center titer, Y is the infective center titer after ultraviolet dose T, and m is the multiplicity of infection. As the dose increases, Eq. 2 reduces to

$$Y/Y_0 = me^{-kT} \quad (3)$$

Thus the ratio of survivors of multiple infection to those of single infection at any dose T will be the multiplicity of infection, m.

This is not the case for a number of bacteriophages. The ratio of survivors of multiple infection to those of single infection increases with dose to values much greater than the multiplicity used (*3*). This phenomenon is termed muliplicity reactivation, and its explanation is based on the observation that ultraviolet irradiation stimulates recombination in bacteriophage; and recombination acts between two damaged genomes may lead to an undamaged genome and, eventually, to an infective center (*4*). With the isolation of both bacterial and bacteriophage mutants deficient in recombination, it is possible to test the recombination theory for multiple reactivation.

Bacteriophage lambda undergoes multiplicity reactivation (*5*) especially in strains of *Escherichia coli* which do not efficiently repair radiation damage (*uvr*−) (*6*). These bacterial strains are more sensitive to killing by ultraviolet light because of the low efficiency for repair of radiation damage. Similarly, bacteriophage lambda is more sensitive to radiation killing on *uvr*− bacteria than on *uvr*+. Moreover, the fact that the recombination system of the host cell is not required for reactivation is in agreement with the observation that lambda contains information for its own recombination system (*7*). Bacteri-

Table 1. Effect of recombination (*rec*) functions on multiplicity reactivation of bacteriophages irradiated with ultraviolet. Bacteriophage lambda, *rec*+, and φtde120R, *rec*−, were irradiated with ultraviolet by a germicidal lamp (General Electric). Samples removed at stated times were adsorbed to either *Escherichia coli* AB1886 *rec*+ or AB2480 *rec*− at a multiplicity much less than one (monocomplexes) or greater than one (multicomplexes). The infected bacteria were assayed for infective centers on AB2480. The multiplicity of infection (MOI) for multicomplexes was calculated from a microscopic count of bacterial cells and the initial titer of bacteriophage. The entire experiment was conducted under yellow light to avoid photoreactivation.

Dose (sec)	P/P_0		B/A	MOI
	A monocomplex	B multicomplex		
	Phage, rec+; *host*, rec+			
15	1.8×10^{-1}	1.7×10^{-1}	0.9	3
30	1.4×10^{-2}	1.0×10^{-1}	7.1	
45	6.3×10^{-4}	6.6×10^{-2}	100	
60	5.5×10^{-5}	3.8×10^{-2}	690	
90	2.2×10^{-5}	1.7×10^{-2}	770	
120	1.1×10^{-5}	5.9×10^{-3}	540	
	Phage, rec+; *host*, rec−			
15	4.8×10^{-2}	3.5×10^{-1}	7.3	5
30	9.3×10^{-4}	1.0×10^{-1}	110	
45	3.1×10^{-5}	1.7×10^{-2}	550	
	Phage, rec+; *host*, rec−			
15	4.8×10^{-2}	1.8×10^{-1}	3.8	2.5
30	9.3×10^{-4}	3.7×10^{-2}	40	
45	3.1×10^{-5}	3.5×10^{-3}	110	
60	3.9×10^{-6}	5.9×10^{-4}	150	
	Phage, rec−; *host*, rec+			
15	2.3×10^{-1}	2.7×10^{-1}	1.2	3
30	3.4×10^{-2}	1.8×10^{-1}	5.3	
45	4.9×10^{-3}	1.3×10^{-1}	27	
60	5.1×10^{-4}	1.0×10^{-1}	200	
90	1.0×10^{-4}	3.8×10^{-2}	380	
120	5.5×10^{-5}	1.5×10^{-2}	270	
	Phage, rec−; *host*, rec−			
15	3.8×10^{-2}	1.7×10^{-1}	4.5	4
30	8.4×10^{-4}	3.2×10^{-3}	3.8	
45	2.2×10^{-5}	1.2×10^{-4}	5.5	
60	2.0×10^{-6}	7.0×10^{-6}	3.5	
90	1.5×10^{-7}	5.6×10^{-7}	3.7	
	Phage, rec−; *host*, rec−			
15	3.8×10^{-2}	1.1×10^{-1}	2.9	2
30	8.4×10^{-4}	2.1×10^{-3}	2.5	
45	2.0×10^{-5}	7.6×10^{-5}	3.5	
60	2.0×10^{-6}	5.2×10^{-6}	3.1	