chemicals against the house fly seem to be independent. Judging from percernt mortality, sesoxane or p. butoxide with pyrethrins indicated highest effect and MGK-264 and synepirin 500 were lowest, while the moralities of S-421, sesoxane or safroxane mixed with allethrin solution were most excellent.

5. The knockdown effect of isobornyl thiocyanoacetate was remarkably increased by mixing with pyrethrins and allethrin, especially with the latter. By 20 times of mixing ratio of isobornyl thiocyanoacetate for pyrethrins or allethrin, the highest effect was obtained. But, lethal effect was comparatively low.

Metabolic Fate of Parathion and Paraoxon in Parathion Susceptible and Resistant Larvae of the Rice Stem Borer, *Chilo suppressalis*.* By Ken'ichi KOJIMA, Tadayoshi ISHIIZUKA and Setuo KITAKATA (Institute of Agricultural Chemicals, Toa Noyaku Co., Ltd., Odawara, Kanagawa)
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9. Parathion 感受性および抵抗性ニカメイガ幼虫における parathion と paraoxon の代謝

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1960年夏，香川県の一部で，parathion がニカメイガ幼虫の防除に役立たなかつたという事例にそう遇したので，香川県において parathion の防除効果に疑念のあつた地帯の幼虫と，その効果に問題のなかつた静岡県の幼虫をもちいて parathion に対する感受性を滴下施用法によつて検定し，両者の間には明らかに感受性に相違のあることを知つた．さらに parathion に対して感受性の低い香川産幼虫は paraoxon に対しても抵抗性のあることを見出した．そこで同年秋，parathion に対して感受性の異なる香川産と静岡産幼虫について，parathion と paraoxon の代謝を，ヒト血漿による抗コリンエステラーゼ法によつて定量的に比較検討した．その結果，幼虫体内への parathion や paraoxon の表皮透過性には両者間に差があるとはおもわれなかつた．また体内での parathion の paraoxon への酸化活性化にも両者間に差異は認められなかつた．そして両産幼虫とも parathion および paraoxon を分解解毒するが，その解毒力は静岡産幼虫より香川産のそれの方が強く，paraoxon は parathion より速かに分解解毒された．これらの実験結果から，香川産幼虫の parathion および paraoxon に対する抵抗性は体内における毒物の速かな解毒が一要因であると推察した．また両産幼虫における parathion の代謝の様相を代謝平衡指数 (Metabolic balance index, MBI)，すなわち体内での酸化活性化と分解解毒の代謝のつりあいを示すひとつの指数で表わしてみた．

The metabolic fates of parathion and paraoxon in parathion susceptible and resistant larvae of the rice stem borer were studied. The cuticle penetration of parathion and paraoxon, or activation of parathion to paraoxon in the bodies of larvae, did not differ between susceptible and resistant larvae. Although both parathion and paraoxon were detoxified by the larvae, resistant larvae detoxified them more rapidly than susceptible larvae. Paraoxon was detoxified much more rapidly than parathion in resistant larvae. It is considered that the more active detoxication of paraoxon as well as parathion was one of the major mechanisms of parathion resistance in the rice stem borer larvae. Metabolic balance index (MBI) presented the aspect of parathion metabolism in both susceptible and resistant larvae.

In order to solve the problem of insect resistance to insecticide, it is certainly important to clarify the metabolic fate of the insecticide in insects. Working with normal and parathion resistant house fly, *Musca domestica*, Oppenoorth[9] demonstrated that susceptibility of flies to parathion was inversely related to the ability by which flies detoxified the insecticide or its activated derivative, paraoxon. March[8] reported the similar finding, that a malathion resistant strain of flies metabolized malaoxon as twice as fast in a susceptible strain. According to their opinions, the resistance of the house fly to organophosphorus insecticides does not relate primarily to changing the systems concerning

* Studies on detoxication of insecticides, Part X.

the toxic action mechanism of organophosphorus insecticides such as activity and inhibitor-sensitivity of cholinesterase and the efficiency of toxifying systems, but is owing to detoxication mechanisms and rate of destruction of the active compound in relation to its rate of accumulation at the action site. Lord and Solly[7], however, could not find out an apparent difference in the rate of detoxication of paraoxon between a normal and a tolerant strains of house flies.

In 1960, it was found that an organophosphorus insecticide, parathion, applied to paddy fields was less effective against larvae of the rice stem borer, *Chilo suppressalis*, in some districts of Kagawa and Ehime Prefectures. This suggested the development of parathion resistance in the larvae[2,10]. Previously, Kojima *et al.*[4] reported the detoxication mechanism of parathion in parathion susceptible and resistant larvae of the insect. The present paper gives a further information on the metabolism of parathion and paraoxon in both strains of the rice stem borer larvae.

Materials and Methods

Insecticides. Chromatographically pure parathion and paraoxon were used for the present experiments. Acetone was used as solvent.

Test insects. Parathion resistant larvae of the second generation were collected in Sakaide City, Kagawa Prefecture in September, 1960. They were reared on rice plants at temperature of 25°C. Parathion susceptible larvae were collected in Shizuoka City, Shizuoka Prefecture in September, 1960, and kept under the similar condition.

Bioassay. Larvae were treated with parathion in 1.0μl of acetone by applying topically to the dorsal surface using an 'Agla' micrometer syringe attached to capillary tube. Then they were kept at temperature of 25°C. Mortality was recorded at 72 hours after the treatment.

Insecticide metabolism. Larvae of 60 to 80mg body weight were used throughout the present experiments. The metabolic fates of both insecticides in susceptible and resistant larvae were examined at the levels of parathion 0.05, 0.10, 0.25 and 0.50μg, and paraoxon 0.50μg per larva. Five larvae were used for each treatment. Just before the treatment, larvae were anaesthetized with carbon dioxide. After treatment they were placed in a petri dish, 9cm in diameter and 2cm high, and kept at 25°C without food. Both sexes of larvae were used without discrimination in the experiments.

The rates of cuticle penetration in larvae were determined as follows: At various intervals after treatment, treated larvae were placed on a piece of filter paper, Toyo-roshi No. 7, in a funnel, and washed three times with small quantity of chloroform to remove off unabsorbed insecticide on the surface of larval body. Insecticide content of the combined chloroform washes was determined and reported as the insecticide remaining externally.

Detoxication studies were performed on the same larvae used in the penetration studies. Larvae washed with chloroform were frozen at the fixed intervals, and then homogenized in a mortar with small amounts of anhydrous sodium sulfate. To the homogenate a small quantity of chloroform was added for extracting the insecticide present in the larval bodies. Chloroform extraction was repeated three times. Insecticide content of the combined chloroform extracts was determined and reported as insecticide present in the larval bodies.

The amounts of parathion and paraoxon were separately determined by means of the anticholinesterase method using human plasma cholinesterase as described by Kojima and Ishizuka[3]. The possible conversion of parathion to paraoxon was measured by this technique.

Results and Discussion

Susceptibility of larvae to parathion and paraoxon. The data on susceptibility of susceptible and resistant larvae to parathion and paraoxon are given in Tables 1 and 2. These indicate that the parathion resistant larvae are highly tolerable to paraoxon as well as to parathion.

Parathion metabolism. Right after the treatment, total recovery of insecticides from the larvae was observed 53 to 62 per cent in parathion, and 89 to 90 per cent in paraoxon, by the analytical method adopted here. Total recovery of parathion

Table 1. Susceptibility to parathion applied topically on susceptible and resistant larvae of the rice stem borer, second generation, 1960.

Larvae	Average body weight (mg)	Regression equation	Lethal dose (μg/g)	
			LD_{50}	LD_{95}
Sus.	53.3	$Y=4.9900+2.531(X-0.8434)$	1.32	5.90
Res.	58.2	$Y=4.9720+3.767(X-1.8741)$	13.08	35.74

Table 2. Percentage of intoxifying and death in susceptible and resistant larvae of the rice stem borer applied parathion and paraoxon topically.

Insecticide	Applied dosage (μg/larva)	Time after treatment (hr.)	Sus.		Res.	
			Paralysis (%)	Death (%)	Paralysis (%)	Death (%)
Parathion	0.05	1	0	0	0	0
		2	0	0	0	0
		4	0	0	0	0
		6	0	0	0	0
		24	0	40	0	0
		48	0	20	0	0
	0.10	1	0	0	0	0
		2	0	0	0	0
		4	0	0	0	0
		6	0	0	0	0
		24	40	0	0	0
		48	0	40	0	0
	0.25	1	0	0	0	0
		2	0	0	0	0
		4	20	0	40	0
		6	60	0	40	0
		24	0	100	60	20
		48	0	80	40	20
	0.50	1	0	0	0	0
		2	0	0	0	0
		4	80	0	60	0
		6	60	0	40	0
		24	20	80	40	60
		48	0	100	0	40
Paraoxon	0.50	1	20	0	0	0
		2	80	0	40	0
		4	100	0	60	0
		6	40	60	20	0
		8	60	40	40	0
		12	40	60	100	0
		24	0	100	40	20
		48	40	60	40	0

from a glass plate, on the other hand, was observed 70 per cent on an average, when 0.1μg of parathion in acetone was applied topically onto the plate and extracted with chloroform by the same procedure. It is likely that parathion and paraoxon could not be extracted completely with chloroform from larval tissue homogenates, unless the homogenate was treated with trichloroacetic acid. It is convenient that doses of parathion recovered from treated larvae at given hours after treatment were given as percentages to total dose recovered from larvae right after the treatment, and also, outwardly penetrated dose was determined on the basis of initial external dose.

Table 3 shows the quick disappearance of parathion from the body surface of larvae, but

Table 3. Penetration, activation and detoxication of parathion in susceptible (S) and resistant (R) larvae of the rice stem borers applied parathion topically.

Applied dosage (μg/larva)	Time after treatment (hr.)	Outwardly penetrated dose (%)		Total recovery (%)		Found dose (μg/larva)								Activation rate		Detoxication rate		Metabolic balance index	
						External		Internal											
						Parathion		Parathion		Paraoxon		Total							
		S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R
0.05	0	0	0	100	100	0.0260	0.0276	0.0010	0.0010	0	0	0.0010	0.0010	0	0	0	0	0	0
	2	87	86	17	18	0.0035	0.0038	0.0004	0.0009	0.0007	0.0005	0.0011	0.0014	64	36	0	0	64	36
	4	94	90	9	10	0.0015	0.0028	0	0	0.0008	0	0.0008	0	100	100	38	57	62	43
	6	97	98	7	5	0.0008	0.0007	0.0003	0	0.0008	0.0007	0.0011	0.0007	73	100	61	71	12	29
	24	89	90	13	12	0.0028	0.0028	0	0.0002	0.0006	0.0004	0.0006	0.0006	100	67	28	33	72	34
	48	98	96	4	6	0.0006	0.0010	0	0.0006	0.0004	0	0.0004	0.0006	100	100	74	72	26	28
0.10	0	0	0	100	100	0.0552	0.0520	0.0007	0.0007	0	0	0.0007	0.0007	0	0	0	0	0	0
	1	75	69	27	36	0.0138	0.0159	0.0015	0.0022	0	0.0006	0.0015	0.0028	0	21	0	0	0	21
	2	85	95	17	8	0.0081	0.0028	0.0007	0.0006	0.0006	0.0006	0.0013	0.0012	46	50	0	0	46	50
	4	98	98	8	3	0.0014	0.0011	0.0011	0	0.0021	0.0007	0.0032	0.0007	66	100	30	68	36	32
	6	99	97	4	5	0.0006	0.0014	0.0002	0.0008	0.0012	0	0.0014	0.0008	86	100	62	70	24	30
	24	100	99	3	4	0	0.0008	0	0	0.0018	0.0011	0.0018	0.0011	100	100	65	75	35	25
	48	99	98	5	4	0.0007	0.0011	0.0007	0	0.0012	0.0007	0.0018	0.0007	67	100	58	74	9	26
0.25	0	0	0	100	100	0.1410	0.1450	0.0015	0.0017	0	0	0.0015	0.0017	0	0	0	0	0	0
	1	72	58	33	46	0.0390	0.0604	0.0074	0.0061	0.0005	0.0013	0.0079	0.0074	6	18	0	0	6	18
	2	85	97	24	16	0.0210	0.0039	0.0103	0.0138	0.0032	0.0053	0.0135	0.0191	24	28	0	0	24	28
	4	99	98	15	7	0.0014	0.0028	0.0150	0.0044	0.0054	0.0032	0.0204	0.0076	27	42	13	69	14	-27
	6	98	98	9	6	0.0028	0.0030	0.0061	0.0040	0.0042	0.0013	0.0103	0.0053	41	25	49	74	-8	-49
	24	99	100	8	3	0.0011	0.0007	0.0065	0.0009	0.0038	0.0021	0.0103	0.0030	37	70	55	86	-18	-16
	48	99	99	3	1	0.0013	0.0014	0.0023	0	0.0013	0	0.0036	0	36	100	81	96	-45	4
0.50	0	0	0	100	100	0.3040	0.2760	0.0059	0.0059	0	0	0.0059	0.0059	0	0	0	0	0	0
	2	92	81	16	27	0.0252	0.0528	0.0203	0.0185	0.0032	0.0035	0.0235	0.0220	14	16	0	0	14	16
	4	98	95	12	13	0.0053	0.0145	0.0205	0.0115	0.0159	0.0115	0.0364	0.0230	44	50	26	46	18	4
	6	99	97	10	7	0.0023	0.0087	0.0215	0.0094	0.0076	0.0026	0.0291	0.0120	26	22	45	71	-19	-49
	24	99	100	13	2	0.0019	0	0.0265	0.0051	0.0118	0.0014	0.0382	0.0065	31	22	37	88	-6	-66
	48	99	100	7	1	0.0023	0.0010	0.0149	0.0010	0.0029	0.0004	0.0178	0.0014	16	29	69	95	-53	-66

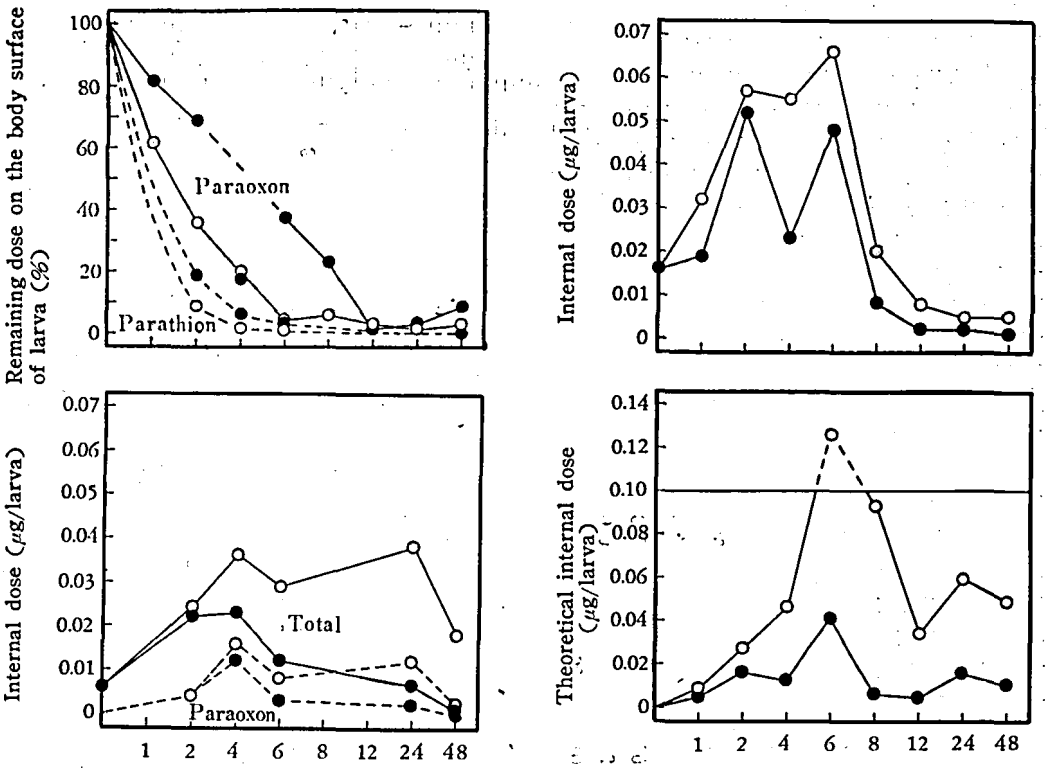

Fig. 1. Disappearence rate of the body surface and penetration rate into the bodies of susceptible and resistant larvae of the rice stem borer applied 0.50μg of parathion or paraoxon per larva topically.
○ Susceptible ● Resistant

this disapearance rate does not mean the true penetration rate of parathion into the larval bodies. The remaining dose of parathion on the body surface was much more in resistant larvae than in susceptible larvae during first 6 hours after treatment with 0.5μg parathion, as shown in Fig. 1. Total recovery rate was very low in susceptible and resistant larvae during 1 to 48 hours after treatment on each applied dose. With treatment of paraoxon at doses of 0.1 and 0.25μg, total recovery rate at one hour after treatment, was 27 to 30 per cent of initial dose in susceptible larvae and 36 to 46 per cent in resistant larvae. These figures correspond with the total recovery right after treatment, 44 to 62 per cent in susceptible larvae and 58 to 87 per cent in resistant larvae. It seemed that a portion of the topically applied parathion was rubbed off rapidly from larvae.

Generally the more dose remained on the body surface of resistant larvae than susceptible larvae, since susceptible larvae were immobilized rapidly by the insecticide application, as compared with resistant larvae. This phenomenon was contrary to the case of o-p insecticide resistant house fly, as observed by Krueger, O'Brien and Dauterman[6].

Total initial doses of parathion and paraoxon do not differ between susceptible and resistant larvae during first 2 hours after treatment. Therefore, it can be said that the cuticle penetration of parathion is not the cause of the resistance of larvae of the rice stem borer to parathion.

Total dose in the body of larva gradually increased with the advancement of time after the application of parathion in both susceptible and resistant larvae. The maximum amount in susceptible larvae was detected 4 hours later from the treatment in all the doses applied, but in the resistant larvae it was found 1 hour later from the treatment with 0.1μg, 2 hours with 0.05 and

0.25μg, and 4 hours with 0.5μg, respectively, indicating the high ability of metabolic detoxication.

The ability of oxidative activation of parathion to paraoxon in the bodies of larvae did not differ between susceptible and resistant larvae at the doses tested, but the activation rate of both susceptible and resistant larvae was lower when they were applied with larger doses, 0.25 or 0.5μg per larva, than with smaller doses, 0.05 and 0.1μg. It might be said that the oxidizing system saturated with relatively low doses, as pointed out previously by Krueger and O'Brien[6]. Though the activation rate was relatively higher in resistant larvae than in susceptible larvae, this difference might be due to the higher ability for detoxifying insecticides in the resistant larvae.

In the doses applied, the resistant larvae metabolized parathion and paraoxon more rapidly than the susceptible larvae. The detoxifying systems of the both larvae, however, did not saturate even in the highest dose. The detoxication rate was calculated by the following equation:

$$\text{Detoxication rate} = 100 - \frac{\text{Average external dose at the fixed intervals} + \text{Internal dose at the fixed intervals}}{\text{Average external dose at 2 hours later} + \text{Internal dose at 2 hours later}} \times 100$$

Average external dose is obtained by dividing by two the sum of external dose in the susceptible and the resistant larvae at each time of examination. The results show that there are systems capable of activating and detoxifying parathion in susceptible and resistant larvae, and that the selective toxicity of parathion against susceptible and resistant larvae might be due to different relative rates of the two processes.

The metabolic balance index (hereafter abbreviated MBI) represents the balance of the two opposing processes of activation and detoxication of parathion. Negative numbers of MBI, marked (−), indicate that detoxication rate is higher than activation rate, and positive numbers, without (−) marks, indicate the reverse relation between activation and detoxication rates, as stated above.

Table 4. Metabolic balance index indicating parathion metabolism in susceptible (S) and resistant (R) larvae of the rice stem borers applied parathion topically.

Internal toxicant	Applied dosage (μg/larva)	Internal dose (μg/larva)					
		S			R		
		0–4**	4–48	0–48	0–4	4–48	0–48
Parathion	0.05	0.0004	0.0003	0.0007	0.0009	0.0008	0.0017
	0.10	0.0033	0.0009	0.0042	0.0028	0.0008	0.0036
	0.25	0.0327	0.0149	0.0476	0.0243	0.0049	0.0292
	0.50	0.0408	0.0629	0.1037	0.0300	0.0155	0.0455
Paraoxon	0.05	0.0015	0.0018	0.0033	0.0005	0.0011	0.0016
	0.10	0.0027	0.0042	0.0069	0.0019	0.0018	0.0037
	0.25	0.0091	0.0093	0.0184	0.0098	0.0034	0.0132
	0.50	0.0191	0.0123	0.0314	0.0150	0.0044	0.0194
Total	0.05	0.0019	0.0021	0.0040	0.0014	0.0019	0.0033
	0.10	0.0060	0.0050	0.0110	0.0048	0.0026	0.0074
	0.25	0.0418	0.0242	0.0660	0.0341	0.0083	0.0424
	0.50	0.0599	0.0851	0.1450	0.0450	0.0199	0.0649
MBI*	0.05	128	110	238	79	91	170
	0.10	82	68	150	103	81	184
	0.25	44	−71	−27	19	−61	−42
	0.50	32	−78	−42	20	−181	−161

* Metabolic balance index.
** Time intervals (hours).

Relations on internal doses of parathion and paraoxon, and MBI are summarized in Table 4. With regard to susceptible and resistant larvae, MBI indicates positive numbers at the lower doses of 0.05 and 0.1μg per larva, where internal doses of parathion and paraoxon and total internal insecticides were less than 0.011 per cent, respectively. On the other hand, at the higher applied doses of 0.25 and 0.5μg, MBI indicates negative numbers in both resistant and susceptible larvae.

Internal dose of parathion was lower during 4 to 48 hours after treatment than during first 4 hours, especially less in resistant larvae than in susceptible larvae at the higher levels of application doses. Also internal paraoxon was lower during 4 to 48 hours than during first 4 hours in resistant larvae, but in susceptible larvae there was little difference between during first 4 hours and thereafter.

The results suggested that the relatively less toxicity of parathion against resistant larvae was due to the vigorous hydrolytic detoxication of parathion and paraoxon in the larvae. This detoxication process outstriped the paraoxon accumulation caused by oxidation of parathion. In the susceptible larvae, on the other hand, oxidation of parathion was much more rapid than the hydrolytic detoxication, and then paraoxon was accumulated gradually to a lethal level. Therefore, it is certainly that more rapid detoxication of parathion as well as the toxic oxygen analog, paraoxon, was one of the important factors responsible for the parathion resistance of the rice stem borer.

Paraoxon metabolism. The percentages of intoxication and death of both susceptible and resistant larvae which were applied with paraoxon topically, are given in Table 2. Also the data on paraoxon metabolism are given in Table 5 and Fig. 1. Parathion resistant larvae had also lower susceptibility to paraoxon than susceptible larvae.

In Table 5, the total recovery and outward penetrated dose of paraoxon are calculated similarly in the case of parathion experiment. There are considerable differences in external dose of paraoxon between the susceptible and the resistant larvae; this suggests that the rate of rubbing doses from the body surface differs between both

Table 5. Penetration and detoxication of paraoxon in susceptible (S) and resistant (R) larvae of the rice stem borers applied paraoxon topically.

Applied dosage (μg/larva)	Time after treatment (hr.)	Outwardly penetrated dose (%)		Total recovery (%)		Found paraoxon (μg/larva)				Theoretical internal dose applied topically 0.10 μg/larva (μg/larva)		Ratio of detoxication (S/R)
						External		Internal				
		S	R	S	R	S	R	S	R	S	R	
0.05	0	0	0	100	100	0.4300	0.4360	0.0155	0.0155	0	0	0
	1	39	18	67	83	0.2640	0.3560	0.0324	0.0187	0.0093	0.0047	2.0
	2	65	31	47	78	0.1510	0.3020	0.0566	0.0516	0.0273	0.0157	1.7
	4	80	83	32	22	0.0871	0.0760	0.0550	0.0230	0.0462	0.0122	3.8
	6	96	67	19	46	0.0179	0.1592	0.0662	0.0480	0.1256	0.0409	3.1
	8	94	77	10	24	0.0258	0.1000	0.0204	0.0080	0.0932	0.0062	15.0
	12	97	98	4	3	0.0110	0.0098	0.0080	0.0020	0.0340	0.0036	9.4
	24	99	97	2	4	0.0054	0.0148	0.0048	0.0018	0.0585	0.0146	4.0
	48	97	99	4	1	0.0145	0.0035	0.0049	0.0009	0.0490	0.0098	5.0

larvae. As shown in Fig. 1, however, it is interesting that the paraoxon dose remaining body surface of susceptible and resistant larvae differs from that of parathion. This might be due to the difference of affinities of both materials to the cuticles of these larvae. Working on distribution of some insecticides, Yamamoto[11] and Kobayashi and Yamamoto[1] pointed out that insecticides which have higher distribution, were adherent very well onto insects. Paraoxon has larger partition coefficient than parathion.

Though the external dose of paraoxon was much more in resistant larvae than in susceptible larvae, the internal dose of paraoxon was less in resistant larvae. Paraoxon penetrated more rapidly than parathion, as shown in Fig. 1. The internal dose of paraoxon increased gradually in susceptible and resistant larvae, and became a maximum at 6 hours after treatment, then decreased rapidly.

In the present experiment, the vicissitudes of internal dose at each time of examination are considered to be influenced by the degradation of paraoxon in the body or decrease of external dose, and average external dose is calculated by dividing the total external dose at examination time by two. For example, average external dose of susceptible larvae during first 1 hour after treatment is

$$\frac{0.4300\mu g+0.2640\mu g}{2}=0.3470\mu g$$

Basing on this average external dose, the quantity of paraoxon in the body was calculated theoretically. The results are given in Table 5 and Fig. 1.

If the detoxifying activity is negligible, theoretical quantity of paraoxon present in bodies of both susceptible and resistant larvae, is $0.10\mu g$ in maximum, and is always expected to show the fixed figures. The calculated quantity of paraoxon in the body, with some experimental errors, was observed as $0.1256\mu g$ in susceptible larvae at 6 hours after treatment. These values decrease thereafter, and it is considered to show the extinction caused by detoxication. The theoretical quantity of paraoxon in the body of resistant larvae was remarkably small as compared with susceptible larvae and showed as $0.0409\mu g$ in maximum at 6 hours after treatment.

Comparing the detoxifying abilities of both susceptible and resistant larvae at each time of examination, the ability of resistant larvae is stronger about two times than that of susceptible larvae. Although this ratio is recognized to increase up until 8 hours after treatment, it is considered that the physiological function, especially the detoxifying ability, is decreased remarkably by the strong toxic effects of paraoxon. During the above metabolism tests with parathion and paraoxon, the excrement of larvae was very small. Furthermore, the activities of cholinesterase, A-esterase (aromatic, aryl-esterase) and B-esterase (aliphatic, ali-esterase), or the sensitivity of these enzymes to paraoxon, did not differ between susceptible and resistant larvae. Also, it could not be found any close relation between A-esterase activity and hydrolysis of parathion and paraoxon. Therefore it might be said that paraoxon and parathion were detoxified by the other enzymes than A-esterases[2].

Summary

1) Parathion resistant larvae of the rice stem borer had lower susceptibility to paraoxon than susceptible larvae in the topical application test.

2) Parathion and paraoxon readily penetrated through the cuticles of both susceptible and resistant larvae when they were applied topically. Paraoxon penetrated more rapidly than parathion. The cuticle penetration of insecticides had no correlation with resistance.

3) The activation of parathion to paraoxon in the body did not differ between susceptible and resistant larvae.

4) Both parathion and paraoxon were readily detoxified by resistant larvae as well as susceptible larvae, especially paraoxon detoxified more rapidly than parathion. The results agreed with many reports on the more rapid detoxication of paraoxon by parathion resistant house flies.

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Studies on the Selective Toxicities of Organic Phosphorous Insecticides. (I). Activation of ethyl parathion in mammal and insect (Part 1). Jun-ichi Fukami* and Takashi Shishido (The 1st Laboratory of Pesticides, The Institute of Physical and Chemical Research, Komagome, Tokyo and Division of Agricultural Chemicals, National Institute of Agricultural Sciences, Nishigahara, Tokyo). Received July 26, 1963. *Botyu-Kagaku*, **28**, 63, 1963.

10. 有機リン殺虫剤の選択的殺虫作用 第1報. 高等動物およびこん虫におけるエチルパラチオンの活性化について (その 1). 深見順一 (理化学研究所農薬第一研究室)・宍戸孝 (農林省農業技術研究所農薬科) 38. 7. 26. 受理

生体内でパラチオンを活性化せしめる実験については数多くの報告がなされている. この論文においては, これらの実験の追試を, ラッテおよびニカメイチュウを材料としておこない, 新しい知見を得たので報告する. ラッテの臓器の切片による活性化は肝および腎臓において認められたが, 脳および後脚の筋肉では認められなかつた. つぎに肝臓の細胞分画における活性化の実験では, マイクロゾームにおいて最も強く, 上清がこれにつぎ, ミトコンドリアの画分では認められなかつた. またニカメイチュウについては, 直接細胞分画における活性化の実験をおこない, ラッテと同じくマイクロゾームにおいて認められたが, ミトコンドリアでは認められなかつた. しかしこの際ラッテの場合と相違して活性化の条件における助酵素としてニコチンアマイドアデニンディヌクレオタイドリン酸 (NADP ; 助酵素 II) を必要とした. またこれら活性化物はパラオクソンであることをクロマトグラフィーにより同定することができた.

Ethyl parathion (*O, O*-diethyl *O*-*p*-nitrophenyl thiophosphate), when administered to animals, causes a decrease in the cholinesterase levels of blood and tissues which is accompanied by typical signes of acetylcholine poisoning despite its weak potency to inhibit cholinesterase (ChE) *in vitro*.[1,3]

It has been shown that, in the presence of oxygen, ethyl parathion was oxidized by mammalian liver slices to ethyl paraoxon (*O, O*-diethyl *O*-*p*-nitrophenyl phosphate), a highly active inhibitor of ChE.[5,8] The capacity of the liver preparation to activate parathion was completely lost by homogenization. Davison[2] found that activating capacity of ethyl parathion in rat liver

* This is an account of investigations performed during his stay at the Division of Entomology, National Institute of Agricultural Sciences.