

lower concentrations of catecholamines though still significantly higher concentrations of tryptophan and tyrosine than the heterozygotes. The concentration of serotonin did not differ between the groups.

The wet weights of the brains from the homozygous DI rats were less than those of the heterozygous group (mean weight: 1.44 and 1.54 g, respectively).

Table II. Content of biogenic amines, their precursors and  $\gamma$ -aminobutyric acid in the brains of rats homozygous and heterozygous for hereditary hypothalamic diabetes insipidus

Amine/amino acid	Heterozygous		Homozygous	
	Total	Concentration ( $\mu\text{g/g}$ )	Total	Concentration ( $\mu\text{g/g}$ )
Noradrenaline	1.03	0.66	1.04 (-7, +9)	0.73 <sup>a</sup> (+1, +16)
Dopamine	1.85	1.20	1.82 (-10, +5)	1.24 (-8, +16)
Serotonin	0.90	0.58	1.03 <sup>a</sup> (+4, +26)	0.72 <sup>a</sup> (+11, +37)
Tyrosine	14.88	9.64	15.56 (-6, +16)	10.84 <sup>a</sup> (0, +26)
Tryptophan	3.60	2.34	3.34 (-18, +4)	2.32 (-11, +12)
GABA	702	453	723 (-1, +7)	504 <sup>a</sup> (+7, +15)

Values are the mean of 19 determinations. Concentrations are given as  $\mu\text{g/g}$  wet weight of whole brain. See further legend to Table I.

The brain levels of monoamines, their precursor amino acids and GABA are given in Table II. Homozygous DI rats had a significantly higher whole brain content of serotonin but did not differ with respect to whole brain content of noradrenaline, dopamine, tyrosine, tryptophan and GABA. However, in terms of the concentration of amine or amino acid per g wet weight of the brain, homozygous DI rats appeared to have higher brain concentrations of noradrenaline, serotonin, tyrosine and GABA than their heterozygous littermates.

In conclusion, the present results indicate that there are marked differences between homozygous DI and heterozygous Brattleboro rats with respect to brain and urine levels of monoamines and their precursor amino acids. There is no clear interpretation of these neurochemical differences as seen in relation to the vasopressin deficiency of homozygous DI rats. The sustained levels of activity in homozygous DI rats due to the frequent bouts of drinking may produce changes in amine turnover rates. Furthermore, the high urine content of monoamines and their precursor amino acids in homozygous DI rats may either be due to an increased filtration or excretion or a reduced resorption in the kidney. In addition, the vasopressin deficiency is not the only endocrine anomaly in these rats: the oxytocin content of pituitaries of homozygous DI rats, but not heterozygous rats is greatly reduced, although synthesis of oxytocin is unimpaired<sup>15</sup>. It is not known whether this phenomenon bears any relevance to the findings of the present experiment.

<sup>15</sup> H. VALTIN, W. H. SAWYER and H. A. SOKOL, *Endocrinology* 77, 701 (1965).

## A Paradoxical Concentration Effect in the Toxicity of Fentin Acetate for Insects

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**Summary.** Triphenyltin (fentin) acetate residues on glass resulting from the evaporation of acetic solutions, turned out to be less toxic on contact and finally non-toxic to houseflies and *Spodoptera littoralis* larvae with rising concentration. This paradoxical concentration effect may be due to polymerization of the compound in concentrated solutions.

Under specific conditions, certain compounds may be biologically more active, e.g. more toxic, at lower than at higher concentrations. Such so-called 'paradoxical concentration effects', which seem to be wide-spread in various biological systems, have been reviewed repeatedly by SCHATZ et al.<sup>2</sup>. We wish to report on an easily-reproducible paradoxical toxic effect of fentin (triphenyltin) acetate (henceforth abbreviated to FA) in insects. FA is an agricultural fungicide<sup>3</sup> possessing insect antifeedant<sup>4</sup> properties, but it is only weakly insecticidal in the conventional sense<sup>5</sup>.

The toxicity of FA residues for the housefly was assayed by a short-term tarsal contact method<sup>6</sup>: 1.37 ml acetic solutions of FA<sup>7</sup> of various concentrations (w/v) were introduced into 150 ml round glass jars (inner wall surface area, 137 cm<sup>2</sup>), which were then rolled so that a uniform layer formed on their inner surface after the evaporation of the solvent. By this procedure the value of the percentage concentration of the applied solution is the same number as g/m<sup>2</sup> of substance ultimately deposited. 24 h

later, 2–3-day-old housefly (*Musca domestica vicina* Macq.) females, immobilized with cold anaesthesia, were introduced into the jars, 10 per jar; there were 4 replications per concentration in an experiment, and each experiment was repeated 4–8 times. The flies were allowed

<sup>1</sup> Contribution from the ARO, The Volcani Center, 1976 Series, No. 106-E.

<sup>2</sup> A. SCHATZ, E. B. SCHALSCHA and V. SCHATZ, *Compost Sci.* 5, 26 (1964). – A. SCHATZ and J. J. MARTIN, *Pakist. dent. Rev.* 14, 113 (1964). – V. SCHATZ and A. SCHATZ, *Can. J. Microbiol.* 11, 1029 (1965).

<sup>3</sup> K. HÄRTEL, *Agric. vet. Chem.* 3, (1) 19 (1962).

<sup>4</sup> K. R. S. ASCHER and GERTA RONES, *Int. Pest Control* 6, (3) 6 (1964). – K. R. S. ASCHER and J. MEISNER, *Z. PflKrankh. PflSchutz* 76, 564 (1969).

<sup>5</sup> K. R. S. ASCHER, unpublished data.

<sup>6</sup> C. KOCHER, W. ROTH and J. TREBOUX, *Anz. Schädlingssk.* 26, 65 (1953). – K. R. S. ASCHER, *Riv. Parassit.* 18, 113 (1957).

<sup>7</sup> If a slight opalescence appeared in any solution, the latter was filtered before use.

The toxicity against housefly females of 24-h-old FA residues obtained on glass by evaporation of 1–4% FA solutions in various solvents

Solvents			FA Residues				
Name	Dielectric constant	Solubility of FA in the solvent (g/l)	FA concentration in solution				Visual aspect of residue
			1%	2%	3%	4%	
			Percentage of housefly mortality observed 24 h after a 45-min tarsal contact with FA residues				
Diethyl ether	4.33	37	98.7	100	100		Heavy white, somewhat transparent
Ethanol	24.3		8.4	23.1	48.5	100	White, crystalline
Methanol	32.6	70	56.8	57.3	42.5	66.6	White, crystalline
Benzene	2.28	50	9.1	33.2	17.0	17.1	Some white crystals dispersed over a colourless, transparent layer
Carbon tetrachloride	2.24	72	0	0	0	0	Colourless, transparent
Chloroform	4.8		0	0	0	0	Colourless, transparent
2-Butanone	18.5		0	0	0	0	Colourless, transparent
Acetone	20.7	40	88.7	49.7	2.8		Heavy white, somewhat transparent

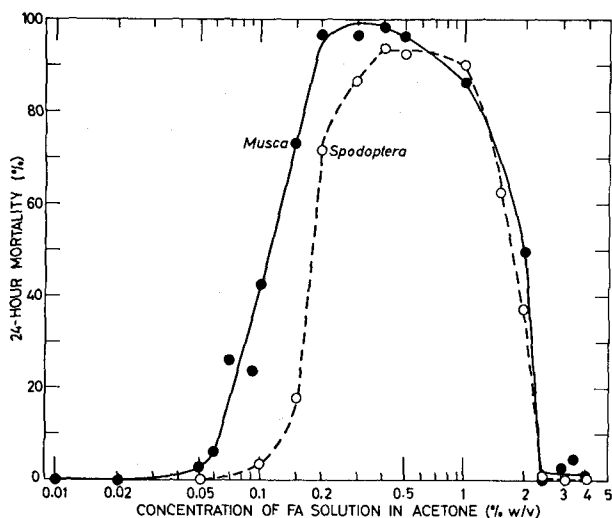
to remain in tarsal contact with the FA deposits for 45 min, counting from their recovery from the cold anaesthesia. They were then transferred to untreated jars which were closed with pieces of mosquito netting held in place with rubber bands; cotton wads moistened with sugar water were laid on the mosquito netting. Live, prostrate and dead flies were counted 24 h later. Analogous tests were carried out with 200 mg *Spodoptera littoralis* Boisd. larvae, which were exposed for 90 min to 1-day-old FA residues obtained by swirling to dryness 0.67 ml of FA acetone solutions in the lower halves of 9 cm-diam. Petri dishes (base area, 67 cm<sup>2</sup>). There were 5 larvae per dish and 140–170 larvae were employed for each concentration. The larvae were then transferred in groups of 10 into 700 ml glass jars containing alfalfa placed over sawdust, for 24 h mortality observations. All the experiments were conducted at 22–23°C.

The results (Figure) show that mortality in the houseflies exposed to FA residues rose gradually from zero at 0.02% to nearly 100% at 0.15% FA. It remained at this

level up to 0.5% FA; it then dropped, slowly at first and then rapidly until the zero level, which was reached at 2.5%. Results with *S. littoralis* (Figure) exhibited essentially the same trend.

No similar paradoxical effect (Table) was found in houseflies after 45-min tarsal contact with FA residues from ether (highly toxic at all the concentrations tested), ethanol and methanol (of intermediate to high toxicity), benzene (weakly toxic), or CCl<sub>4</sub>, CHCl<sub>3</sub> and 2-butanone (non-toxic).

It is known from Mössbauer and IR-spectra and molecular weight measurements that FA<sup>8</sup> (but not tricyclohexyltin acetate<sup>9</sup>) and some other triaryl- and trialkyltin carboxylates exist as polymers<sup>10</sup> in the solid and molten state and in concentrated solutions in non-polar solvents, but are monomeric in dilute solutions. Polymerization might be the cause of the biological inactivity of the vitreous, transparent FA residues obtained, e.g. from 1 to 4% CCl<sub>4</sub> and CHCl<sub>3</sub>. It is conceivable that such polymerization may perhaps occur also at specific FA concentrations of certain polar solvents, such as acetone. We conjecture that, in FA residues from acetone, it is the monomer which is toxic for insects. The monomer exists in dilute solutions and the rate of polymerization increases with concentration. The rapid evaporation of the solvent 'freezes' and retains in the residues the monomer state or only partial degree of polymerization which existed in the solution. Such residues from acetone solutions above 1.5% consist increasingly of the polymer, which we suppose to be non-toxic. It is of interest that a paradoxical effect observed in the curve of inhibition of human prostatic acid phosphatase by fluoride<sup>11</sup> is ascribed, too, to the formation a polymer, probably the tetramer (HF<sub>2</sub>)<sub>2</sub><sup>2-</sup>.



Percentage of 24-h mortality of insects after their exposure to 24-h-old fentin acetate (FA) residues on glass, which were obtained by evaporation of acetone solutions of various concentrations: ●—●, housefly females (45-min contact); ○---○, *Spodoptera littoralis* (90-min contact).

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<sup>9</sup> W. N. ALCOCK and R. E. TIMMS, J. chem. Soc. A 1968, 1876.

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