Non-mutagenicity of fenvalerate in Drosophila

M. Batiste-Alentorn, N. Xamena, A. Velázquez, A. Creus and R. Marcos

Divisió de Genètica, Departament de Genètica i Microbiologia, Universitat Autònoma de Barcelona, Bellaterra, Spain

1To whom correspondence should be addressed

The induction of genetic damage in germ cells of Drosophila melanogaster by the pyrethroid insecticide fenvalerate was studied. Adult feeding, larval feeding and adult injection were the routes of administration used. Our results indicate that, under the conditions of testing, fenvalerate is unable to induce sex-linked recessive lethals, sex-chromosome losses and non-disjunction.

Introduction

At the 1973 British Crop Protection Conference, Elliott and his co-workers reported the discovery of permethrin, a new pyrethroid possessing good photostability (Elliott et al., 1973). Since that time, new photostable pyrethroids have been developed to control a variety of pests, based on their high activity against insects, low mammalian toxicity and low plant residues (Papadopoulou-Mourkidou, 1983). For detailed information on the biological activity, mode of action, metabolism and toxicology of pyrethroid insecticides see International Congress of Pesticide Chemistry (IUPAC, 1982).

In recent years, information regarding fenvalerate’s acute toxicity in several species has been published (Verschoyle and Aldridge, 1980; Cagen et al., 1982; Bradbury and Coats, 1982; Rattner and Franson, 1984; Parker et al., 1984), but there is very little information available as to whether this pyrethroid possesses genotoxic properties. Thus far, fenvalerate has not been found to be carcinogenic in mice and rats (Parker et al., 1983, 1984) and it showed no detectable mutagenic activity in Salmonella typhimurium strains TA100 or TA98 and in V79 Chinese hamster cells (Pluijmen et al., 1984). However, chromosome aberrations and alterations of the mitotic index were observed after prolonged treatment of rats with low doses of fenvalerate (Chatterjee et al., 1982).

The increasing use of fenvalerate, together with the limited information concerning possible mutagenic effects, makes it necessary to screen this compound for mutagenicity in different screening systems.

The advantages of using Drosophila melanogaster in mutagenicity tests are many (Sobels, 1974) and there are good reasons to include a Drosophila assay in a minimal battery to evaluate in vivo the mutagenicity of chemicals (Sobels, 1980). In spite of the fact that insecticides would pose special difficulties for mutagenic assays with fruit flies (Valencia, 1981), several reports showed the applicability of the Drosophila screening system to testing of insecticides (Valencia, 1981; Woodruff et al., 1983; Velázquez et al., 1981, 1986).

Here we report the results found in the sex-linked recessive lethal (SLRL), sex-chromosome loss (SCL) and non-disjunction (ND) assays in D. melanogaster, following treatment with fenvalerate using different routes of administration: larval exposure, adult feeding and adult injection.

Materials and methods

Details on materials and methods are summarized in tabular form (Table I). For a full explanation of genetic symbols of mutant strains see Lindsley and Grell (1968).

Results and Discussion

In our experiments, fenvalerate showed a significant toxicity (i.e. after the exposure feeding of adult Berlin-K males to 50 p.p.m. and Ring-X males to 25 p.p.m. for 24 h, the mortality was ~ 100%).

The results obtained from different SLRL experiments with strain Berlin-K are summarized in Table II. We applied the Kastenbaum–Bowman significance test (Kastenbaum and Bowman, 1970), using a FORTRAN program developed by Würgler and Berchtold (1982). At the concentrations evaluated, the frequencies of lethal mutations in the exposed groups did not differ significantly from the control values, regardless of the male germ-cell stage treated and the route of administration used. The lack of mutagenicity of fenvalerate in the Drosophila SLRL assay is in good agreement with the negative results obtained by Pluijmen et al. (1984) in experiments with S. typhimurium strains TA100 or TA98 in the presence or absence of a rat liver activation system, using the plate incorporation assay and fluctuation tests, and in V79 Chinese hamster cells in the presence or absence of hepatocytes. It appears that fenvalerate showed no significant mutagenic activity in tests detecting gene mutations.

In another series of experiments, we tested whether it can induce chromosome damage. The detection of this kind of genetic damage is greatly facilitated when using a ring-shaped chromosome. We therefore used a Ring-X strain in the tests for total sex-chromosome loss (X or Y), partial Y-loss (YL or YS) and non-disjunction.

Tables III and IV show the results from sex-chromosome loss induction after adult feeding and injection, respectively. With the exception of the statistically significant increase in the frequency of complete losses after exposure to 5 p.p.m. in feeding experiments, analysis of the data led to the conclusion that fenvalerate is not able to produce clastogenic effects after adult exposure. In our opinion, the seemingly significant increases found may be due to chance, since ~ 1.5% loss represents a yield that is observed in controls.

The results of tests on SCL and ND after treatment of third instar larvae are presented in Table V. As can be seen, fenvalerate was also ineffective when pre-meiotic germ cell stages were treated.

Our negative results in the tests assaying for chromosome damage are not in accordance with the results obtained by Chatter-
Table I. Materials and methods for sex-linked recessive lethal mutations, sex-chromosome loss and non-disjunction tests

| 1. Strains | Berlin-K: a wild-type strain  
|            | Base: In(l) sc^{54} sc^{54} + S, sc^{54} sc^{54}  
|            | Ring-X: males with genotype R(1)2, yB/B5 y y  
|            | y sp: y w sp m; bw sp \  
| 2. Culture medium | Standard food medium enriched with living yeast  
| 3. Culturing temperature | Standard temperature (23–25°C)  
| 4. Compound | Fenvalerate \([\alpha\text{-cyano-3-phenoxybenzyl-2-(4-chlorophenyl)-3-methylbutyrate}](\text{purity 95%})\) was kindly provided by S.P.E. Shell S.A. (Madrid, Spain)  
| 5. Preparation of the test solution | Fenvalerate was dissolved in ethanol and then diluted in a 5% sucrose solution in distilled water, to give a final ethanol concentration of 5% and the desired insecticide concentration. In treatments by injection, fenvalerate was dissolved in cotton oil  
| 6. Route of administration | Adult feeding  
|            | Adult injection  
|            | Larval feeding  
| 7. Mating scheme | For adult treatment, males were mated with three new virgin females for each of three broods (3, 2 and 2 days). For larval treatment only one brood was performed  
| 8. Brooding scheme | For adult treatment, males were mated with new virgin females (5 Of 9 9) for each of two broods (3 and 2 days). For larval treatment only one brood was performed  
|            | For adult treatment, males were mated with new virgin females (5 \(\sigma\) \(\sigma\) \(\varpi\) \(\varpi\)) for each of two broods (3 and 2 days). For larval treatment only one brood was performed  
|            | As we treated larvae, only one brood was performed  

| Table II. Frequencies of sex-linked recessive lethals in \(D.\ melanogaster\) germ cells exposed to fenvalerate  
| Route of administration | Concentration (p.p.m.) | Number of lethals/number of chromosomes tested (%)  
|                        |                       | Brood 1 (3 days) | Brood 2 (2 days) | Brood 3 (2 days) | Total \(b\)  
| Adult feeding         | 0.0                  | 4/2608 (0.15)    | 8/2189 (0.36) | 3/1812 (0.16) | 15/6609 (0.23)  
|                       | 10.0                 | 2/1290 (0.15)    | 2/1304 (0.15) | 3/1087 (0.28) | 7/3681 (0.19)  
|                       | 20.0                 | 1/1066 (0.09)    | 2/1045 (0.19) | 5/1089 (0.46) | 8/3200 (0.25)  
| Adult injection       | 0.0                  | 2/1078 (0.18)    | 1/875 (0.11)  | 3/859 (0.35)  | 6/2812 (0.21)  
|                       | 20.0                 | 3/1183 (0.25)    | 1/712 (0.14)  | 1/733 (0.14)  | 5/2628 (0.19)  
| Larval feeding        | 0.0                  | 5/3205 (0.16)    |                   |                   |                   
|                       | 25.0                 | 4/1553 (0.26)    |                   |                   |                    

| Differences between treatments and controls are not significant (Kastenbaum–Bowman test).  
| Pooled data from three broods.  

| Table III. Frequencies of offspring resulting from sex-chromosome loss in male germ cells of \(D.\ melanogaster\) exposed to fenvalerate administered by adult feeding for 24 h  
| Experiment | Concentration (p.p.m.) | Brood | Regular offspring | Exceptional offspring | Other \(a\) | Total offspring  
|           |                       |       |                  | Complete losses | Partial losses |  
|           |                       |       |                  | No. | %  | No. | % |  
| I         | 0.0                  | 1     | 4941           | 50 | 1.00 | 1 | 0.02 | 10 | 5002  
|           | 2                   | 5375  |               | 69 | 1.26 | 4 | 0.07 | 8 | 5456  
|           | 5.0                 | 1     | 5754           | 88 | 1.50 \(b\) | 5 | 0.08 | 15 | 5862  
|           | 10.0                | 2     | 4939           | 73 | 1.45 | 4 | 0.08 | 6 | 5022  
|           | 2                   | 3207  |               | 51 | 1.56 | 1 | 0.03 | 6 | 3265  
| II        | 0.0                  | 1     | 4348           | 48 | 1.09 | 1 | 0.02 | 14 | 4411  
|           | 2                   | 5155  |               | 59 | 1.13 | 2 | 0.04 | 24 | 5240  
|           | 5.0                 | 1     | 5748           | 90 | 1.54 \(b\) | 5 | 0.08 | 11 | 5854  
|           | 2                   | 4355  |               | 49 | 1.11 | 0 |   | 16 | 4420  
|           | 10.0                | 2     | 2476           | 34 | 1.35 | 0 |   | 8 | 2518  
|           | 2                   | 3293  |               | 46 | 1.37 | 0 |   | 9 | 3348  

| Includes phenotypes corresponding to spontaneous non-disjunction and mosaics.  
| Significant at the 5% level (Kastenbaum–Bowman test).
jee et al. (1982). They reported that when fenvalerate was force-fed at low daily doses to Ratus norvegicus, in vivo, over a long period, some abnormalities representing chromosome breakage were found. It should be noted, however, that cumulative effects after prolonged treatment may be attributed in part to the action of the detoxification products of the pyrethroid, as Chatterjee et al. (1982) pointed out.

Taking into account that the SLRL assay records a broad mutation spectrum (point mutations, deletions and aberrations), and that the test for ring-X losses is a pertinent tool for estimating chromosome breakage, the repeated negative results obtained in this work testing different kinds of genetic damage following several routes of administration support the view that fenvalerate is not mutagenic in Drosophila, at least under the conditions of test.

Acknowledgements

We thank S.P.E.Shell S.A. for generously supplying the insecticide. This investigation was supported in part by the Spanish Ministry of Education and Science (Grant No. 0577/84 CAICYT). A.V. was supported during this work by a fellowship (F.P.I.) from the Ministry of Education and Science.

References


International Congress of Pesticide Chemistry (IUPAC) (1982) IX, Pyrethroid insecticides: Biological Activity, Mode of Action, Metabolism and Toxicology, Kyoto, Japan.


Received on 21 July 1986; accepted on 1 September 1986