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Insect Hormone Activity of p-(1,5-Dimethylhexyl)benzoic Acid Derivatives in *Dysdercus* species

Abstract. Derivatives of p-(1,5-dimethylhexyl)benzoic acid are juvenile hormone analogs with selective action on the hemipteran insects of the family Pyrrhocoridae. Their juvenile hormone activity is constant on five species of *Dysdercus*; it is about ten times lower on *Pyrrhocoris*, and no activity has been detected on hemipterans of some other families. Absence of profound species-specific variations in the activity suggests that the most active compounds of this type can be used as selective pesticides against all species of *Dysdercus*.

Substances with juvenile hormone activity on Pyrrhocoridae occur in the wood of certain evergreen trees (1). They have been identified as the terpenes juvabione (2) and dehydrojuva-

bione (3). We have described the juvenile hormone effects of p-(1,5-dimethylhexyl)benzoic acid derivatives which are structurally related to dehydrojuvabione, and contain an aromatic

ring in the molecule (4). Some of these synthetic derivatives are about 100 times more active than the original natural products, retaining their specific action on Pyrrhocorid bugs.

We have prepared some new derivatives and tested them, in addition to those mentioned previously (4), for species-specific variations in juvenile hormone activity in *Dysdercus*. The experiments were performed on larvae of African species *Dysdercus* (*Neodysdercus*) *intermedius* Distant and *Dysdercus* (*Dysdercus*) *superstitiosus* (Fabr.); South American species *Dysdercus* (*Dysdercus*) *fulvoniger discolor* (Walker) and *Dysdercus* (*Dysdercus*) *chaquensis* Freiberg; and an Indian species *Dysdercus* (*Paradysdercus*) *cingulatus* (Fabr.). They were reared in glass jars at 25°C with an 18-hour light, 6-hour dark cycle, and fed with cottonseeds, and drinking water in cotton-plugged vials.

The juvenile hormone activity was tested by topical assay of freshly moulted larvae of the last instar (5). Test substances were applied on abdominal tergites as acetone solutions in 1- μ l drops. Hormone activity was evaluated from the degree of morphogenetical change induced. The effects are expressed in activity units indicating the amount of the substance in micrograms per specimen which caused formation of a half-larval, half-adult intermediate. Dose-response experiments on large numbers of larvae suggest that the range of juvenile hormone effect from zero (formation of perfect normal adults) to the maximum activity (formation of perfect supernumerary giant larvae) corresponded approximately to a tenfold change in concentration (5). For example, when the activity unit is 0.05 μ g per specimen, the substance will show first signs of activity when applied at approximately 0.01 μ g per specimen, medium activity at 0.05 μ g per specimen, and maximum activity when more than 0.1 μ g per specimen is applied.

Initially, we determined the range of activity of each compound by testing it in a series of tenfold dilutions on five or ten specimens at each concentration. The most active concentrations were then utilized to determine the activity unit more precisely.

Preparation of the compounds (Fig. 1) has been described (4). Purity of the compounds was checked by elemental analysis and infrared spectroscopy.

The most active compounds are the

Table 1. Juvenile hormone activity units of test substances on several species of *Dysdercus*. The unit value is the amount of the substance in micrograms per specimen that caused formation of half-larval, half-adult intermediates after topical application to freshly moulted last-instar larvae. Structural formulas of the compounds I through XII are shown in Fig. 1.

Compound	Activity units				
	<i>D. intermedius</i>	<i>D. discolor</i>	<i>D. chaquensis</i>	<i>D. cingulatus</i>	<i>D. superstitiosus</i>
I	0.3	0.05	0.05	0.1	0.3
II	3	.5	.5	1	
III	0.7	.4	.3	0.5	
IV	.8	.8	.4	.8	
V	.08	.08	.08	.08	
VI	.3	.4	.1	.1	0.4
VII	.05	.02	.01	.04	.05
VIII	.05	.06	.01	.06	
IX	.05	.03	.007	.04	
X	20.0			7.0	
XI	100.0			30.0	
XII	4.0			4.0	
Juvabione	5.0	0.5	1.0	0.5	1.0
Dehydrojuvabione	3.0	.1	0.5	.5	0.8

Table 2. Average juvenile hormone activity units for compounds I to IX (Table 1) in several species of *Dysdercus* and in *Pyrrhocoris apterus* L.

Species	Average unit per specimen (μ g)	Freshly moulted last-instar larvae (mg)	Average unit per gram of larvae
<i>D. intermedius</i>	0.59	38.8	15.2
<i>D. discolor</i>	.26	17.5	14.9
<i>D. chaquensis</i>	.16	15.7	10.2
<i>D. cingulatus</i>	.30	26.9	11.2
<i>P. apterus</i>	1.57	16.0	98.0

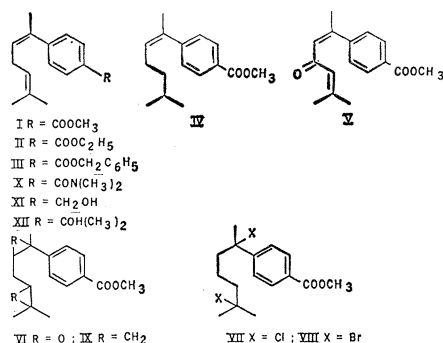


Fig. 1. Structural formulae of synthetic juvenile hormone analogs with specificity for *Dysdercus* spp.

dihalo derivatives VII and VIII, and the compound IX (Table 1). The unit values for the juvenile hormone activity of these compounds range from 0.01 to 0.1 μ g per specimen. The least active compounds are X, XI, and XII, in which the carbomethoxy group of the benzene ring is replaced by alcohol or dimethyl amido groups. Their unit values range from 4 to 100 μ g per specimen.

There is a close parallel in the juvenile hormone effects of each compound among the species of *Dysdercus* tested. There is less than a tenfold variation in the activity of a given compound from species to species. Variations in activity of different compounds on the same species differ by several orders of magnitude. This indicates that the structural changes of the molecule have much more pronounced effect on the activity than do endogenous factors of species specificity.

The most sensitive species is *D. chaquensis*, and the least sensitive is *D. intermedius*. Their average unit values differ by about 3.7-fold; however, there is about a 2.5-fold difference in size of the last-instar larvae of these species. For this reason we have calculated an average juvenile hormone activity unit on the basis of micrograms of substance per gram of larval weight, and this unit more precisely indicates the sensitivity of individual species (Table 2). Thus, the actual sensitivity of *Dysdercus* species to the juvenile hormone analogs decreases in the following manner: *D. chaquensis*, *D. cingulatus*, *D. discolor*, *D. superstitiosus*, and *D. intermedius*. Small variations in the activity units suggest that there are no profound species-specific differences in the sensitivity of *Dysdercus* bugs to the juvenile hormone analogs tested.

Earlier we determined the juvenile hormone activity of compounds I to IX on *Pyrrhocoris apterus* L. (4). The average juvenile hormone unit per gram of larval weight was about ten times larger than those found for the *Dysdercus* species (Table 2). All these compounds have been found inactive when tested on *Graphosoma italicum* Müll. of the family Pentatomidae. Thus, we expect that changes in insect sensitivity to these juvenile hormone analogs are rather insignificant at the species level, becoming more pronounced at the genus level, and extreme at the family level and higher. Similar relationships have also been found with other juvenile hormone analogs, for example farnesenic acid derivatives (6).

The compounds with the lowest unit values are potential pesticides with which it would be possible to prevent *Dysdercus* larvae from becoming sexually mature adults, or to sterilize adult females (1). So far as we know, these compounds are not toxic to insects in general and are specific for Pyrrhocorid bugs. They show no juvenile hormone activity on some representatives of Lepidoptera, Coleoptera, Diptera, or Hymenoptera. The low differences in their activity on these five *Dysdercus* species suggests that the compounds could be used against any

Dysdercus species. The high juvenile hormone activity of these materials in topical assays indicates their superiority to the paper or wood extracts used in earlier experiments (8).

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Maintenance of Responding by Fixed-Interval Schedule of Electric Shock Presentation in Squirrel Monkeys

Abstract. After stabilization of response rates engendered by a free-operant avoidance contingency, the lever-pressing of two squirrel monkeys was maintained for several months by a fixed-interval schedule of electric shock presentation. Initially, response-contingent shocks produced substantial increases in response rates. Continued exposure to the schedule resulted in a reduced overall rate accompanied by a change in the temporal patterning of responses. There was a pause in responding after most shock deliveries; the rate of responding then increased during the interval to reach a terminal value preceding shock presentation. Omission of shocks for part of the daily session led to higher rates of responding; the reintroduction of response-contingent shocks produced a lower overall rate and reinstated the temporal patterning of responding characteristic of the fixed-interval schedule.

Punishment is usually defined as a procedure in which a noxious stimulus, such as a loud noise (1) or an intense electric shock (2), is made contingent on the occurrence of a specific response. There is some uncertainty, however, regarding the behavioral effects of a punishing stimulus. Although most experiments show that punishment decreases the future likelihood of a re-

sponse, others indicate that response suppression is a temporary phenomenon or that a punishing stimulus may sometimes exert the paradoxical effect of maintaining a response which it follows in time (3). However, a noxious stimulus has been shown to affect (4, 5) patterns of responding differently depending upon the manner in which the stimulus is scheduled to occur and