

Mulder R & Gijswijt M J. The laboratory evaluation of two promising new insecticides which interfere with cuticle deposition. *Pestic. Sci.* 4:737-45, 1973. [Research Laboratories Philips-Duphar BV, Boekestejn, 's-Graveland, The Netherlands]

The paper gives information on insecticidal properties of some benzoylureas, as well as the mode of action of these compounds. Failure of chitin deposition in larval cuticles appeared to be the cause of the insecticidal effect. [The SC<sup>1</sup>® indicates that this paper has been cited in over 145 publications, making it the most-cited paper ever published in this journal.]

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Two aspects of the development of a new insecticide were discussed in this paper. The efficacy of two representatives of the benzoylureas was appraised by the senior author (RM), who was at that time head of the insecticide department at Duphar BV. This part of the paper appears to have been of interest particularly to applied entomologists. The second part, which was my domain as second author, focused on the mode of action of these compounds. Changes in tissues of larvae that were treated with these compounds could be made visible with plain histological methods. The nature of these changes led me to develop a hypothesis of the mode of action of benzoylureas in general. It is this part of the paper that is often cited by other researchers.

In the 1960s the then current idea of activating latent viruses in insects by chemicals made me search for apparently diseased caterpillars in the screening procedures for insecticides. Benzoylureas induced symptoms that

were reminiscent of a virus infection. However, in our treated caterpillars, no virus could be detected. Histological sections, made from dying specimens, showed animals that were deprived of adipose tissue, a symptom of starvation.

The breakthrough came when a distinct symptom could be seen in a developmental stage in between two molts in larvae that had behaved up to that point as healthy specimens. What I saw in the sections was the effect of blocking the formation of chitin in the cuticle. Due to insufficient rigidity, the newly formed skin was not resistant to muscle contractions, and, therefore, locomotion became impossible. The animals could not creep out of the remnants of their old skins at the time of molting, and they subsequently died.

Looking back, it is not so difficult to see why this discovery has been cited so often. At the time that we worked on these insecticides, insect cuticles had become a subject for study. The physiological and biochemical steps in the sclerotization process were discovered, but the formation of chitin still remained largely unexplored. We found a substance that inhibited one of the last and maybe the most specific step in the formation of chitin molecules. This fact and the easy way in which the effect could be made clear have contributed to its apparent popularity.

Moreover, environmental toxicology of pesticides became a highlight in biological science. Ecotoxicologists all over the world fell upon this new insecticide whose toxicity was specific to arthropods. They used it to check their newly developed methods: a run of investigators of all feathers came to ask for samples from Duphar BV, the pioneer firm.

A review of recent work will be published soon.<sup>1</sup>

1. Muzzarelli R A A, Jeuniaux C & Gooday G W, eds. *Chitin in nature and technology*. (In press.)