TECH TALK - Insect Growth Regulators (Part I Juvenile Hormone Analogues)

An introduction to how IGRs function

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Looking at Insect Growth Regulators (more commonly called 'IGRs') brings me in a full circle on my career as an entomologist. After first working in Veterinary Investigation with cestodes, I moved up the Phylla to become a Research Scientist at the then Ministry of Agriculture, Farming and Fisheries (MAFF), Pest Infestation Control Laboratories in Slough, UK. In this position I worked with juvenile hormones with a range of insects including Pharaoh's ants, house flies, German cockroaches and my specialisation, which resulted in my first paper, 'Cross-resistance to Juvenile Hormone Analogues in a Multi-resistant Strain of *Tribolium castaneum* TC-14'. This was pretty cutting edge at the time, since this was 1974, and juvenile hormone itself had only been identified in 1965. So it's fun to be back here looking at these unique insecticides.

Essentially there are two types of insect growth regulators in urban pest markets, Juvenile Hormone Analogues (JHA) and Chitin Synthesis Inhibitors (CSI). In this issue we will focus on the Juvenile Hormone Analogues. JHAs are synthetic chemicals that work by mimicking the naturally occurring juvenile hormone in insects. So let's start by looking at what juvenile hormone is and what it does.

Juvenile hormone (JH) controls reproduction and maintains the insect in the juvenile state. When juvenile hormone is present in the insect, it promotes larva-to-larva moults. When reduced levels occur, it promotes pupation, and in the complete absence of JH, the insect moults through to the adult stage.

Juvenile Hormone Analogue insecticides work by mimicking the presence of natural JH. They do not kill adult insects. So JHA treated larvae are unable to successfully change from pupae to the adult insects. This breaks the biological life cycle of the insect and prevents recurring infestation.

JH has been isolated and chemically identified as a *sesquiterpenoid*. Four have been identified, but only JH-III (the trimethyl form) is present in all insects, (JH-0, JH-I and JH-II have only been identified in Lepidoptera). Whilst a great deal of progress has been made over the past 50+ years,

knowledge of how JH works at the molecular level remains elusive. JH regulates an unusually large diversity of processes during post-embryonic development and adult reproduction. It is a long-standing conundrum in insect developmental physiology as to how one hormone can have such diverse effects.

It was first discovered as the hormone that represses metamorphosis, hence its name of juvenile hormone, and then later in stimulating aspects of reproduction. Since then, its many actions in reproductive processes have been noted, and in many species it is known to be the primary co-ordinator of reproductive processes, including the production of eggs in female insects. From an evolutionary perspective, its role in reproduction probably preceded its metamorphic role.

Juvenile hormone ensures the growth of insect larvae, while preventing metamorphosis. It is secreted by two endocrine glands behind the insect brain known as the *corpora allata*.

Juvenile hormone (JH), as the name suggests, maintains the insect in the juvenile state. The level of JH found in the haemolymph gradually decreases during the development of the insect, allowing it to proceed to successive instars with each moult. For an insect to moult to the next stage (instar), the correct ratio of JH and *ecdysone* must be present. Ecdysone is a primary moulting hormone that is necessary for insects to go from the larval to pupal stage.

In essence, when JH is present, ecdysone promotes larva-to-larva moults. When reduced levels of JH occur, ecdysone promotes pupation, and in the complete absence of JH the insect moults through to the adult stage. Ecdysone is a steroidal pro-hormone of the major insect moulting hormone, 20-hydroxyecdysone, which is secreted from the prothoracic glands.

JH is degraded (broken down) by the enzymes *Juvenile-hormone esterase* (JHE) or *juvenile hormone epoxide hydrolase* (JHEH). JHE and JHEH both lead to suppression of JH signalling and response.

Juvenile Hormone Analogues (JHAs) are designed to mimic the effects of JH and disrupt these endocrine-regulated processes that are relatively unique to insects. Consequently these insecticides tend to be very low toxic to non-target organisms.

The main examples found in the urban pest market are pyriproxyfen, fenoxycarb and s-methoprene. Typically these products are used for the developmental control of mosquitoes, fleas, flies, and cockroaches.

The mechanism of toxicity of JHAs is still in question. They do not kill adult insects. Thus, with fleas and mosquitoes, these products work by mimicking the presence of natural juvenile hormone. As mentioned above, JH must be absent for a pupa to moult to an adult, so JHA treated larvae are unable to successfully emerge from the pupal form, to the adult insect. This breaks the biological life-cycle of the insect, thus preventing recurring infestation.

In cockroaches, where there is no pupal form, the high level of JHA in the larval stage causes deformations when the insects moult, which usually lead to death.

JHAs also affect egg production. The mode of this differs depending on the compound. In one study, when adult fleas were exposed to residues of pyriproxyfen, they produced eggs devoid of yolk, frequently with collapsed walls after oviposition; and there was no blastoderm formed (the layer of cells from which the embryo develops). In contrast, eggs laid by methoprene treated fleas showed no gross morphological effects, though the eggs either did not hatch, or the larvae died within hours after hatching. Histological examination revealed most of the eggs contained segmented embryos, which apparently died during blastokinesis (a bending of the embryo in the process of embryonic development). ■

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