TECH TALK - Insect Growth Regulators (Part II Chitin Synthesis Inhibtors)

An introduction to how IGRs function

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We previously discussed that there are two types of insect growth regulators used in the urban pest market, Juvenile Hormone Analogues (JHAs) and Chitin Synthesis Inhibitors (CSIs). In this issue, we will focus on the Chitin Synthesis Inhibitors.

Chitin Synthesis Inhibitors interfere with enzymes that stimulate the synthesis and formation of chitin, an essential structural component in the insect's exoskeleton. Without chitin, the insect dies in the immature stage, or grows into a sterile adult. This, combined with the ability of CSIs to stop normal embryonic (egg) development, makes them effective at all stages of an insect's life.

The cuticle, or outer exoskeleton, is the external structure of the insect. It needs to be waterproof for protection, soft and flexible to allow movement, extensible in between segments for increases during feeding and growth, and rigid to provide firm points of attachment for muscles, mandibles, and claws. The cuticle is secreted by a single underlying layer of epidermal cells and itself consists of different layers of which the thick *procuticle* contains *chitin*, the major component of the insect cuticle (30 – 60%). Technically, chitin is a β-1,4-linked aminopolysaccharide homopolymer of *N–acetylglucosamine* (GlcNAc), a glucose derivative. It is by far one of the most abundant biological materials on earth. Chitin is also present in the insect gut, trachea, reproductive tract and peritrophic matrix, where it also provides structural support.

> Chitin synthesis inhibitors stop the formation of chitin, an amino-polysaccharide compound needed in the insect's exoskeleton. Once affected, the insect will grow normally until it moults. It is then unable to form a new exoskeleton properly and dies. Death may be quick, or take up to several days, depending on the species and the nature of the IGR. Chitin synthesis inhibitors also disrupt the normal development of eggs.

The cuticle forms a protective matrix, consisting of a chitin microfiber–protein complex. Chitin biosynthesis is a multifaceted process, and not fully understood, but it seems to consist of a series of enzymatic steps beginning with a glucose molecule. This molecule is converted to N–acetylglucosamine, that then links with

uracil triphosphate (UTP) and dolichol phosphate. The resultant monomers are combined, through polymerisation, into chitin. This is then embedded within proteins to form chitin strands (microfibrils) in the cuticle. The entire process is catalysed by the enzyme *chitin synthase*.

CSIs generally alter cuticle composition by inhibiting the formation of the N–acetylglucosamine, leading to reduced levels of chitin in the cuticle. Cuticular elasticity and firmness are directly affected. The imperfections in the cuticle are most evident at moulting (ecdysis) and lead to abortive moulting. Several potential modes of action have been discussed, but most evidence points to inhibition of the chitin synthase enzyme.

The main CSI products in the market are all *benzyl phenyl urea* compounds (BPUs). They act mainly after ingestion, and are also effective as ovicides, reducing the egg-laying rate or inhibiting embryonic development. In most cases, the embryo fully develops, but the larvae fail to hatch.

The first Chitin Synthesis Inhibitor, *diflubenzuron*, was discovered by scientists at Philips-Duphar in the Netherlands. Diflubenzuron is widely used around the world as a public health insecticide, and in the United States and Europe in termite baits.

Within the FAOPMA regions, CSIs are mainly used in termite baits and dusts; these include hexaflumuron (Corteva), chlorfluazuron (Ensystex), bistrifluron (Sumitomo) and triflumuron (Bayer).

These products are particularly effective as termite baits. In addition to its effects on the termite at time of moult, chlorfluazuron also has a significant effect on the termite's peritrophic matrix. The peritrophic matrix is a semi-permeable, non-cellular structure which surrounds the food bolus in an insect's *mesenteron* (midgut). The peritrophic matrix serves several functions, including improvement of digestion, protection against mechanical and chemical damage and serves as a barrier to infection by pathogens. In all insects, the peritrophic matrix is continuously being synthesised, and excreted with the faecal matter.

The peritrophic membrane largely consists of γ-chitin. In termites the peritrophic matrix is a Type II single uniform layer synthesised by a group of cells in the front of the mesenteron.

Studies have shown significant damage to the peritrophic matrix of termites after ingestion of chlorfluazuron. Loss of the peritrophic matrix can have drastic consequences on the ability of termites to digest their food and resist disease. The lack of peritrophic matrix in actively feeding termite workers seems to contribute to the loss of epithelial cells in the inner mesenteron, probably caused by abrasion due to direct contact with wood particles. This may contribute to the premature death of termite workers by reducing food assimilation efficiency and inducing nutritional deficiency. This mechanism can also affect reproductive castes of termites by inducing nutritional deficiency, potentially affecting their reproductive capacity, tolerance to pathogens, and longevity.

The chitin synthesis inhibitory action of CSIs is generally quite specific towards insects. Related biochemical processes, such as chitin synthesis in fungi, and biosynthesis of hyaluronic acid and other mucopolysaccharides in chickens, mice, and rats, are not affected. CSIs do have varying degrees of effects on crustaceans, requiring that they be used with care around aquatic environments.

Another important feature of these compounds is that they are not degraded by insects, which further enhances their retention and longevity in the insect's system and consequent effectiveness.

And finally, what of the future for Insect Growth Regulators? One of the more exciting aspects of the IGR field is the likely discovery of new agents with novel sites of action on the insect integumental, endocrine or other biological systems. Such compounds hold out the hope of possessing even more properties of the ideal insecticide. ■

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