University of Basel

The Resistant Mosquito

Video Transcript

How do insecticides work?

If you want to control malaria vectors, you need to understand how insecticides function. Therefore, I would like to introduce you to some concepts that are important to know if you work with insecticides. Let us start with a term which is often used in the context of pest control agents.

The Mode of Action defines the process of how an insecticide works at a molecular level. Now, why is it helpful to know the Mode of Action of an insecticide? Knowing the Mode of Action is key to managing insecticide resistance. Insecticide resistance is a long-standing and increasing problem for insect pest control in both agriculture and public health.

Insecticide Modes of Action can be divided into major classes: There are those that affect the insect's 'nerve and muscle', those affecting 'growth and development', those acting on 'respiration', those acting on the insect 'midgut', and those whose Mode of Action is unknown or non-specific.

Now let us take a closer look at how insecticides work at a molecular level. Insecticides generally bind to key functional proteins that fall under the major classes just mentioned. These target proteins regulate vital processes within the insect.

Let's look at an example: this small molecule insecticide binds to a specific site or so-called 'binding pocket' at its molecular target in the insect nervous system to alter its function and ultimately the biological response. You can picture this interaction like a key fitting into a lock.

To deepen your understanding, I am going to show you a poster with all current Insecticide Modes of Action depicted. You will find the link to it attached to this step. We are not going into detail, important is, that you get the general sense.

I would like for you to picture each one of these boxes as a different lock, referred to as a Mode of Action Group. The yellow hexagons represent the keys or insecticides that fit that lock. The colour of the box indicates what major class the insecticide belongs to. Each box, or Mode of Action Group is assigned a number: Group 1, 2, 3 and so on. In cases, where the 'keys' or insecticides look different enough, but fit the same 'lock', subgroups may be assigned by adding a letter to the number such as Group 1A and

Group 1B. Whilst all the Mode of Action Groups are used in agriculture, only a subset have the right properties to be used for mosquito control.

To understand why these grouping of Modes of Action is so important for resistance management, let's take a closer look at how insecticide resistance can occur, how an insecticide might lose its effectiveness. The culprits are small differences in the insect's genetic material: just like your DNA and my DNA are not 100% identical, individual insects' DNA is not either. Natural selection by an insecticide allows insects with initially rare, naturally occurring resistance genes to survive.

Coming back to our picture of the insecticide as the key and the molecular target site as the lock, resistance genes can affect either of the two. The lock can be changed so the key does not fit anymore, or the key for example gets broken down easily and does not fit into to the lock anymore.

These resistance genes can get passed on to future generations and eventually entire populations of insects can become resistant to the insecticide. Proactive resistance management and insecticide stewardship are therefore critical.

This brings me to the Insecticide Resistance Action Committee, IRAC, and its mission. IRAC is part of CropLife and provides a coordinated industry response to prevent or delay resistance development in insects. IRAC operates at both the global and the country level. IRAC promotes development and implementation of resistance management strategies to support sustainable agriculture and improved public health.

The IRAC Mode of Action Team, which I am a part of, is responsible for keeping the Mode of Action Classification up to date. This includes the review of new insecticide submissions based on best available evidence. Is it a key that fits into an existing lock (or Mode of Action Group) or does it work on a new lock that gets a new Group number? Does the key look different enough from other Group members, that it might not be degraded as quickly, warranting a new subgroup? These are questions the IRAC Mode of Action Team tries to decide.

I hope I was able to tell you in a nutshell how insecticides work, how they fall into Modes of Action Groups and why that knowledge is crucial for resistance management.