

When does resistance to toxins evolve in animals?

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Well-known examples of ecological contexts underpinning toxin resistance. (A–C) predator resistance, where a predator is resistant to the toxins of its prey. (A) The mongoose is known to predate on true cobras. (B) The grasshopper mouse preys on bark scorpions. (C) Garter snakes prey on toxic newts. (D) Prey resistance is resistance of a prey species to the toxins of a predator and is exemplified here by rattlesnakes preying on North American ground squirrels. (E) Autoresistance is where an animal is resistant to its own toxins. The example shown here is of true cobras that show resistance to cobra α -neurotoxins. Credit:



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Does a snake die when it bites its lip? Why will a mongoose survive a scorpion's sting, but we humans perish? These questions occupied the minds of toxin-enthusiasts and Master's students in Biology Jory van Thiel and Roel Wouters. They collected information from many sources and published their findings in *Biological Reviews*.

"Some <u>animals</u> have <u>genetic adaptations</u>, which enable them to handle super <u>dangerous toxins</u>. They can eat poisonous animals, or survive after being bitten or stung," Van Thiel says. "But it was striking how often those genetic adaptations were exactly the same in unrelated animal groups. This is called <u>convergent evolution</u>, and we investigated this for all kinds of toxins and <u>animal species</u>."

All types of toxin resistance in one model

The publication is a review, a large summary of research and theories. "The exceptional part of our work is that there has never been an overview for all toxic animals," Wouters states. To achieve this feat, they asked for the aid and opinions of renowned scientists in the toxins field, such as their supervisor Michael Richardson, Nick Casewell, and the Netherlands' best-known biologist, Freek Vonk.

Balance of resistance and a working body

Van Thiel and Wouters propose several hypotheses on how convergent evolution came about. The concept of functional constraints proved to be essential. This means that resistance to the toxins must not come at the expense of processes in your body, such as the blood circulatory system



or controlling the nervous system.

Van Thiel explains: "Receptors bind signal transmitters, and in that way direct biological processes. It makes it possible to contract our muscles, for example. Toxins are like these transmitters and also bind to these receptors, but block the biological process. Thus, it paralyzes the muscles. Resistance occurs when the receptor-DNA changes, which alters the shape of the receptor and makes it impossible for toxins to bind. However, the principle of functional constraints then becomes important, as their ability to transport signal transmitters should continue to function."

Wouters adds: "You can't change the receptor endlessly. Only small adjustments work without the receptor losing its proper function, and so you see this changes happen in the same way all kinds of animal groups, from mammals to reptiles and insects. Especially if they are co-existing with toxic animals for millions of years, and if there is a chance that they get caught. That answers the question of why a mongoose can survive a scorpion's sting, but humans can't."

Immune to your own toxins

Additionally, the students reviewed many other theories related to convergent evolution. They also discuss auto-resistance—being resistant to your own venom. They hypothesize that auto-resistance made it possible for animals to become increasingly venomous or poisonous. "The origin of their venom often lies in another source. An example of that is the Pitohui bird of Papua New Guinea," Wouters says. "The bird is poisonous because it eats toxic beetles, but it is resistant. Therefore, it can accumulate higher levels of toxins in their body and eventually becomes venomous itself. Examples like this you see all over the animal kingdom."



The next project

Will the gentlemen relax after their second successful publication? "Not really," Van Thiel shrugs. "I am now doing an internship in Liverpool with one of the largest snake venom groups, and look at <u>toxin</u> variation. Roel is investigating the personality of snakes at the IBL, in collaboration with Serpo Zoo. And we are looking at the indirect effects of snake venom with an ophthalmologist. So if a snake bites your foot, what happens in your eye? More information on that will follow soon."

More information: Jory Thiel et al, Convergent evolution of toxin resistance in animals, *Biological Reviews* (2022). DOI: 10.1111/brv.12865

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