Poison frogs upgrade toxins from prey - Skin Chemistry

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For the first time, scientists have found a poisonous frog that takes up a toxin from its prey and then tweaks the chemical to make it a more deadly weapon.

At least three species of the 4-to-5-centimeter-long Dendrobates frogs of the New World tropics modify an alkaloid to create one that's about five times as poisonous, according to a team led by John W. Daly of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in Bethesda, Md. The souped-up poison, one of a class called pumiliotoxins, ends up as a protective agent in the frogs' skin, the researchers report in an upcoming Proceedings of the National Academy of Sciences.

"It's an important thing, showing how chemistry connects the life of one organism to another," comments chemical ecologist Jerrold Meinwald of Cornell University. Although scientists have found that some creatures other than frogs customize a basic toxin for various purposes, "I don't know of any other examples of improving a defensive weapon," Meinwald says.

The new work grows out of years of research that started with a puzzle regarding dart-poison frogs, which belong to the family that includes Dendrobates. Frogs in three other families in South America, Australia, and Madagascar also carry poisons in their skin. However, when zoos and aquariums raise these supposedly deadly creatures, frogs from all but one Australian genus grow up harmless.

Daly and his collaborators in the early 1990s proposed that the wild frogs must be picking up the toxins from food and storing them in their skins. Since then, the scientists have found that ants and other arthropods in the frogs' habitat carry most of the poisons that show up in frogs' skin.

The finding that some frogs change the toxins they have eaten came as an unexpected twist of a theoretical study. NIDDK chemists Jingyuan Ma and Herman Ziffer were working with an alkaloid called pumiliotoxin 251D, one of the skin toxins of the frog Dendrobates auratus. The scientists produced both the form of the alkaloid found in nature plus a mirror-image form.

Daly and Valerie Clark dusted these substances onto termites and fruit flies and fed the spiced prey to captive frogs. When Thomas F. Spande and another NIDDK chemist, H. Martin Garraffo, analyzed the skins of these frogs, some 80 percent of the natural form of 251D had been converted to another toxin, allopumiliotoxin 267A. It has an extra hydroxyl group on one of its two rings. The unnatural form of 251D, however, showed up unchanged in frog skin.

The frogs must have a specific enzyme that retrofits just one form, the researchers conclude. Two other Dendrobates species modified the natural form, but two species in related genera didn't.

When the scientists tested allopumiliotoxin 267A on mice, they found it a much more potent poison than its precursor.

"It's the first case found where a frog is clearly modifying one of the sequestered alkaloids," says Spande. "We were very surprised."