Combinatorial chemistry in toad: a protoxin self-resistance way to its own bufadienolide toxin

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Abstract

1. Toxin resistance in all taxa is important for their survival. Resistance to bufadienolide toxin is mediated by molecular changes to the sodium-potassium-pump. As for toads themselves, the parotid is consisted of extremely high concentration of bufadienolide toxin, it indicates toads need stronger resistance for self-protection than any other species involved in toad predation. Thus, besides the widespread convergence of Na+/K+-ATPase, toads may develop a unique self-resistance way for their accumulated bufadienolide toxin. 2. Our studies on invasive cane toads from Australia and common asiatic toads from China showed that toads store defensive venom in parotid as a combinatorial library composed of low-toxic protoxin (conjugated bufadienolides), which is characterized by two building blocks, i.e. high-toxic toxin (free bufadienolide) and the argininyl side chain contributed to toxin absorption promotion. This protoxin could be hydrolyzed to high-toxic toxin for defense immediately as it is discharged from parotid at the time when toad is attacked or stimulated by predators. 3. Our results revealed that toads indeed develop a unique protoxin self-resistance way to their own extremely high concentration of bufadienolide toxin for self-protection besides the widespread convergence of Na+/K+-ATPase. The revelation of this protoxin self-resistance way highlights the importance and ecological multifunctionality of the sophisticated combinatorial chemistry of nature and may partly account for the strong adaptability of toad as infamous ailing invaders. It completes the picture of self-resistance mechanism to their own bufadienolide toxin for toad or may even for many other venomous animals.

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