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Corticosteroid responses of snakes to toxins from toads (bufadienolides) and plants (cardenolides) reflect differences in dietary specializations

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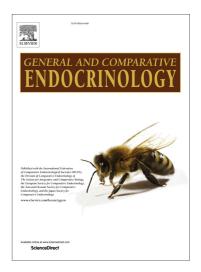
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ACCEPTED MANUSCRIPT

Corticosteroid responses of snakes to toxins from toads (bufadienolides) 1 and plants (cardenolides) reflect differences in dietary specializations 2 3 Shabnam Mohammadi^{a,b*}, Susannah S. French^{a,b}, Lorin A. Neuman-Lee^a, Susan L. 4 Durham^b, Yosuke Kojima^c, Akira Mori^c, Edmund D. Brodie, Jr. ^{a,b}, Alan H. Savitzkv^{a,b} 5 6 7 ^aDepartment of Biology, Utah State University, 5305 Old Main Hill, Logan, UT 84322-5305, United States 8 ^bEcology Center, Utah State University, 5205 Old Main Hill, Logan, UT 84322-5305, United States 9 10 ^cDepartment of Zoology, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan 11 12 *Corresponding author at: Department of Biology & Ecology Center, Utah State University, Logan, UT 84322, USA. E-mail address: shab.mohammadi@gmail.com (S. Mohammadi). 13 14 HIGHLIGHTS 15 Snake corticosteroid responses to toxins vary with dietary specialization and sex. 16 Snakes of the genus *Thamnophis* have high stress response to cardenolides. Male Rhabdophis tigrinus have higher corticosteroid responses than females. 17 18 ABSTRACT 19 Toads are chemically defended by cardiotonic steroids known as bufadienolides. Resistance to the acute effects of bufadienolides in snakes that prey on toads is conferred 20 by target-site insensitivity of the toxin's target enzyme, the Na⁺/K⁺-ATPase. Previous 21 22 studies have focused largely on the molecular mechanisms of resistance but have not 23 investigated the physiological mechanisms or consequences of exposure to the toxins. 24 Adrenal enlargement in snakes often is associated with specialization on a diet of toads. 25 These endocrine glands are partly composed of interrenal tissue, which produces the 26 corticosteroids corticosterone and aldosterone. Corticosterone is the main hormone 27 released in response to stress in reptiles, and aldosterone plays an important role in 28 maintaining ion balance through upregulation of Na⁺/K⁺-ATPase. We tested the 29 endocrine response of select species of snakes to acute cardiotonic steroid exposure by 30 measuring circulating aldosterone and corticosterone concentrations. We found that

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