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Comparative Biochemistry and Physiology – Part B: Biochemistry & Molecular Biology

# Snakes exhibit tissue-specific variation in cardiotonic steroid sensitivity of $Na^+/K^+$-ATPase

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## ABSTRACT

Toads are among several groups of organisms chemically defended with lethal concentrations of cardiotonic steroids. As a result, most predators that prey on amphibians avoid toads. However, several species of snakes have gained resistance-conferring mutations of $Na^+/K^+$-ATPase, the molecular target of cardiotonic steroids, and can feed on toads readily. Despite recent advances in our understanding of this adaptation at the genetic level, we have lacked functional evidence for how mutations of $Na^+/K^+$-ATPase account for cardiotonic steroid resistance in snake tissues. To address this issue, it is necessary to determine how the $Na^+/K^+$-ATPases of snakes react to the toxins. Some tissues might have $Na^+/K^+$-ATPases that are more susceptible than others and can thus provide clues about how the toxins influence organismal function. Here we provide a mechanistic link between observed $Na^+/K^+$-ATPase substitutions and observed resistance