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Denmotoxin: A three-finger toxin from colubrid snake *Boiga Dendrophila* (mangrove catsnake) with bird-specific activity

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Boiga dendrophila (Mangrove Catsnake) is a rear-fanged colubrid snake, which lives in Southeast Asian lowland rainforests and mangrove swamps, and which preys primarily on birds. We have isolated, purified and sequenced a novel toxin from its venom, which we named denmotoxin. It is a monomeric polypeptide of 77 amino acid residues and five disulphide bridges. In organ bath experiments it displayed potent postsynaptic neuromuscular activity and irreversibly inhibits the indirectly stimulated twitches in chick biventer cervicis nerve-muscle preparations. In contrast, it induced much smaller and readily-reversible inhibition of the electrically evoked twitches in mouse hemidiaphragm nerve-muscle preparations. More precisely, the chick $\alpha_1\beta\gamma\delta$ muscle nicotinic acetylcholine receptor is 100-fold more susceptible as compared to mice. These data indicate that denmotoxin has a bird-specific postsynaptic activity. We chemically synthesized denmotoxin, crystallized it, and solved its crystal structure at 1.9 Å by molecular replacement method. The toxin structure adopts a non-conventional three-finger fold with an additional (fifth) disulphide bond in the first loop, and seven additional residues at its NH₂-terminus, which is blocked by a pyroglutamic acid residue. This is the first crystal structure of a three-finger toxin from colubrid snake venom and the first fully characterized bird-specific toxin. Denmotoxin illustrates the relationship between toxin specificity and the primary prey type that constitutes the snake's diet.