



A THREE-COMPARTMENT OPEN PHARMACOKINETIC MODEL CAN EXPLAIN VARIABLE TOXICITIES OF COBRA VENOMS AND THEIR ALPHA TOXINS

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M. Ismail, M. H. M. Aly, M. A. Abd-El salam and A. M. Morad. A three-compartment open pharmacokinetic model can explain variable toxicities of cobra venoms and their alpha toxins. *Toxicon* 34, 1011-1026, 1996.—The pharmacokinetic profiles of labelled *Naja melanoleuca*, *Naja nivea*, *Naja nigricollis* and *Naja haje* venoms and their alpha neurotoxins were determined following rapid i.v. injection into rabbits. The data obtained fitted a triexponential equation characteristic of a three-compartment open pharmacokinetic model comprising a central compartment 'blood', a rapidly equilibrating 'shallow' tissue compartment and a slowly equilibrating 'deep' tissue compartment. The distribution half-lives for the shallow compartment ranged from 3.2 to 5 min, reflecting the rapid uptake of venoms and toxins compared with 22-47 min for the deep tissue compartment denoting much slower uptake. The overall elimination half-lives, $t_{1/2\beta}$, ranged from 15 to 29 hr, indicating a slow body elimination. Peak tissue concentration was reached within 4-5-20 min in the shallow tissue compartment. The corresponding values for the deep tissue compartment were 120 min for *N. melanoleuca* and *N. nigricollis* venoms and their toxins and 240 min for *N. nivea* and *N. haje* venoms and their toxins. Steady-state distribution between the shallow tissue compartment and the blood gave values of 0.50 and 0.92 (*N. melanoleuca*), 1.64 and 1.05 (*N. nivea*), 0.78 and 0.92 (*N. nigricollis*) and 1.70 and 1.03 (*N. haje*) for the venoms and their toxins, respectively. The corresponding values for the deep tissue compartment gave ratios of 3.31 and 3.44 (*N. melanoleuca*), 2.99 and 1.68 (*N. nivea*), 3.74 and 3.79 (*N. nigricollis*) and 1.39 and 2.46 (*N. haje*) for the venoms and their toxins, respectively. Ratios lower than unity indicate lower venom and toxin concentrations in the tissues than in the blood, while larger ratios denote higher tissue concentrations. The values thus reflect a higher affinity of the venoms and their toxins for the central than the shallow tissue compartment and for the deep tissue than the central compartment. The

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