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COMPARISON OF TWO HIGHLY TOXIC AUSTRALIAN SNAKE VENOMS: THE TAIPAN (*OXYURANUS S. SCUTELLATUS*) AND THE FIERCE SNAKE (*PARADEMANSIA MICROLEPIDOTUS*)

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THE TAIPAN was first described by Peters in 1867 as *Pseudechis scutellatus* (PETERS, 1867). Kinghorn re-examined the snake and called it *Oxyuranus maclennani* (KINGHORN, 1923). The present name, *Oxyuranus s. scutellatus,* was suggested by Thomson (THOMSON, 1933). The fierce snake was described in 1879 by McCoy, who called it *Diemenia microlepidata,* or small-scaled brown snake (McCOY, 1879). In 1882 Macleay described the same snake under the name *Diemenia ferox* (MACLEAY, 1882). Kinghorn regarded ferox as a synonym for microlepidotus and proposed the genus *Parademansia* (KINGHORN, 1956). Worrell considered *P. microlepidotus* and *O. scutellatus* to be the same species (WORRELL, 1963*a, b*). BOULENGER (1896) classified both as belonging to the same genus (*Pseudechis*). Most recently, COVACEVICH and WOMBEY (1976) have argued that *Parademansia microlepidotus* belongs to a distinct genus and this is also the opinion of Cogger (COGGER, 1975). Comparison of the venom of this disputed species with that of the taipan sheds new light on the issue.

Venom from the only known live specimen of *P. microlepidotus* was kindly provided by C. Tanner, who has also provided us with taipan venom. The venom was fractionated as described earlier for taipan venom (FOHLMAN *et al.,* 1976) by gel filtration on Sephadex G-75 and the patterns are compared in Fig. 1. Evidently the venoms are very similar, but the relative proportions of the fractions differ. The first peak in both chromatograms accounts for 7 and 21% of the total protein in the fierce snake and taipan venoms, respectively, and contains direct prothrombin activity in both cases. The taipoxin-analog paradoxin, which accounts for 12% of the venom protein, was fractionated further. The bulk of the protein in both venoms elutes in the third peak, which contains phospholipases. A retarded non-protein peak containing nucleosides is also shown.

Taipoxin was previously shown to be composed of three subunits α, β and γ (FOHLMAN *et al.,* 1976). All are homologs of pancreatic phospholipases A2. The complete amino acid sequence of the γ-subunit has been reported (FOHLMAN *et al.,* 1977). Paradoxin behaves like taipoxin upon gel filtration in 6 M guanidine hydrochloride on Sepharose 6B; namely, the γ-component elutes alone ahead of the α and β components, which were then separated by column zone electrophoresis at pH 1·9. The amino acid compositions given for the neurotoxin subunits in Table 1 further illustrate the strong similarity between paradoxin and taipoxin. The similarity of the gel filtration patterns, the occurrence of a direct prothrombin activator and a presynaptic neurotoxin with three subunits make

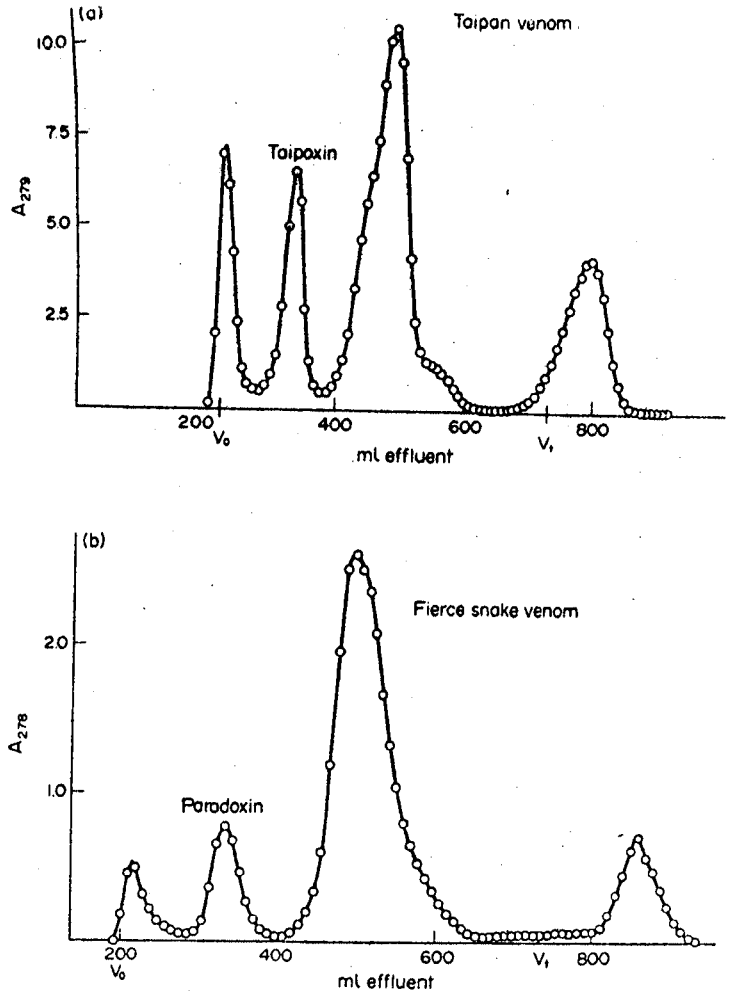

FIG. 1. GEL FILTRATION PATTERNS OF CRUDE TAIPAN (a) AND FIERCE SNAKE (b) VENOM.

these two venoms unique among those examined so far. This pattern is not found in tiger snake venom (EAKER *et al.*, 1976). These three are the only Australian snake venoms that have been compared by our approach. The clinical effects of other Australian venoms are different, with the possible exception of *Pseudechis papuanus*, the papuan black snake (CAMPBELL, 1967). Therefore, the fierce snake and the taipan appear to be very closely related with regard to the types of proteins present. The data presented here support the classification suggested by Worrell on morphological grounds and by Boulenger, i.e. that the two snakes are congeneric. The name *Oxyuranus microlepidotus* would then seem appropriate.

The lethality of the crude venom was not investigated in this study, but Sutherland has determined the LD_{50} to be 20 and 65 μg/kg for the fierce snake and the taipan, respectively, by the subcutaneous route (Sutherland, personal communication). MORGAN (1956) pointed out that the subcutaneous LD_{50} of taipan venom was 7 times the i.v. value, and this probably is due to the high molecular weight of taipoxin. For notexin the subcutaneous i.v. ratio appears to be less than 2. A higher content of notexin-like molecules (peak III

TABLE 1. AMINO ACID ANALYSIS OF TAIPOXIN, PARADOXIN AND THEIR SUBUNITS. PARADOXIN AND SUBUNITS 24 hr HYDROLYSIS, NO DERIVATIZATION. TAIPOXIN VALUES FROM FOHLMAN *et al.* (1976). VALUES ARE CALCULATED AS RESIDUES PER MOLECULE

	Taipoxin	Paradoxin	α-Taipoxin	α Paradoxin	β-Taipoxin	β-Paradoxin	γ-Taipoxin from sequence	γ-Paradoxin
Aspartic acid	50	49	13·0	12·7	13·9	14·0	22	22·0
Threonine	20	20	6·0	6·4	6·5	7·0	7	7·0
Serine	19	21	5·2	5·6	3·6	2·5	9	10·6
Glutamic acid	35	34	7·7	8·9	13·1	11·3	14	15·1
Proline	16	18	4·9	5·5	4·5	4·2	7	6·8
Glycine	29	27	9·4	9·9	9·1	8·3	10	11·8
Alanine	28	30	9·0	8·7	10·1	11	8	8·5
Half-cystine	44	(44)	13·9	(14)	14·1	(14)	16	(16)
Valine	12	12	4·7	4·0	5 9	4·9	2	2·3
Methionine	8	7	2·0	1·4	2·0	1·6	3	1·5
Isoleucine	13	13	2·1	2·1	3·0	2·9	7	5·8
Leucine	17	21	4·0	4·4	5·7	7·9	7	6·4
Tyrosine	21	22	7·8	7·8	6·1	5·7	8	7·1
Phenylalanine	12	15	4·7	4·8	4·8	4·8	4	3·6
Glucosamine*	5	6	—	—	—	—	4·9	4·6
Histidine	7	9	1·9	1·7	3·4	3·6	2	2·1
Lysine	16	17	6·2	5·4	5·6	5·1	5	5·0
Tryptophan	5	(5)	3		1		0	
Arginine	22	23	12·7	14·9	6·6	8·8	2	2·3
Sum	374	379	119	120	121	119	133	135

*Not included in the sum.

in Fig. 1) might thus explain the relatively higher toxicity of fierce snake venom by the subcutaneous route. Paradoxin has the same i.v. mouse LD_{50} as taipoxin, 2 μg/kg.

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