Spider physiology and Behaviour: Physiology.
Venom Composition and Strategies in Spiders: Is Everything Possible?

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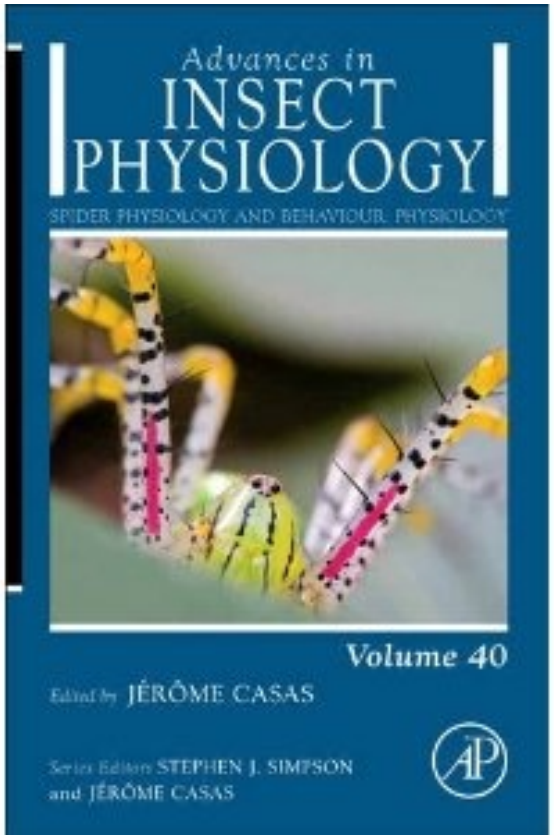

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クモ毒への興味

- セアカゴケグモの毒素にはセキツイ動物に対するαラトロトキシン (神経毒, Caチャネル開放,MV13万のタンパク質　アミノ酸1401個)
- 昆虫に対するαラトロインセクトトキシン (神経毒, タンパク質)
- 機能不明なラトロディクティン　88個
- 甲殻類に対するラトロクラスタトキシン (神経毒, タンパク質) がある。

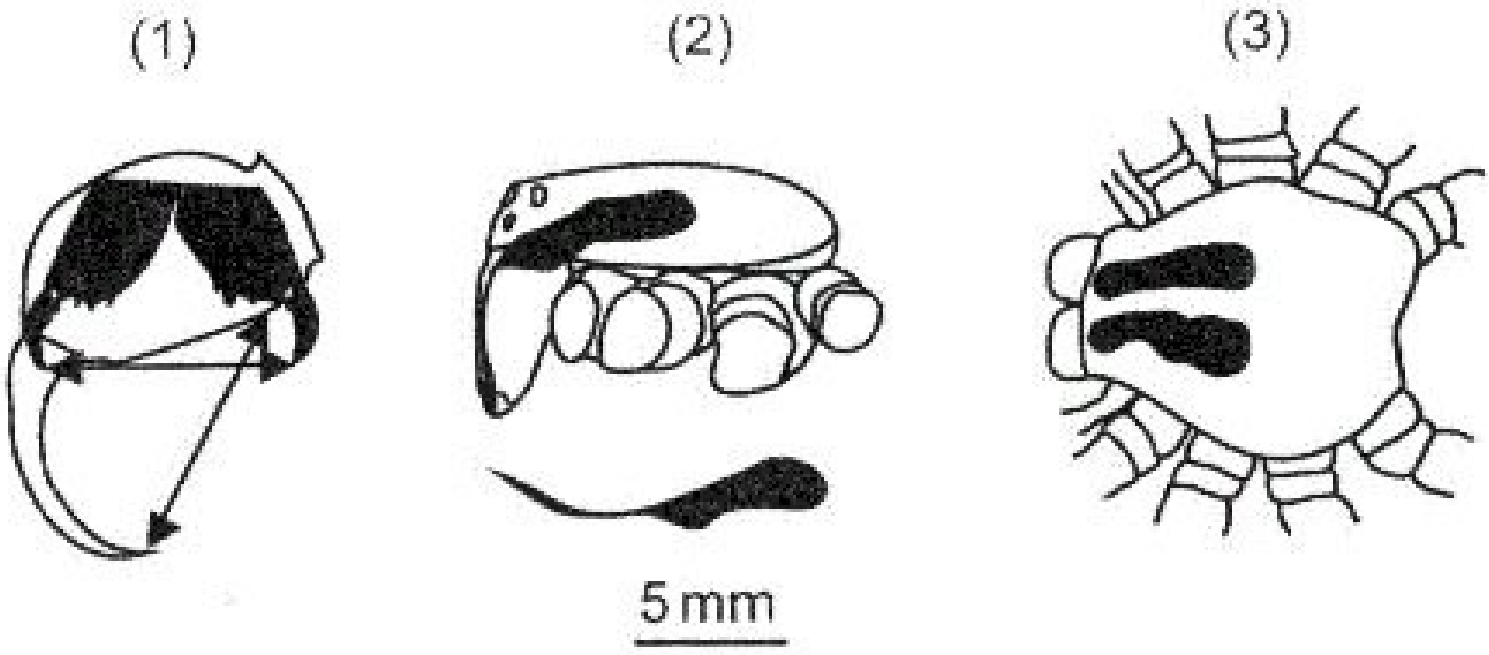
クモ毒の進化

- 餌の広汎な利用という観点からすると、

  甲殻類
  昆虫類
  セキツイ動物

  と毒は進化した？

顎のサイズとクモの毒腺の位置



Labidognath spider(black)
Orthognath spider (white)

Cupiennius salei

174種，1618論文を調査

TABLE 1
Number of compounds known from spider venom reviewed in this study

Substance group	Number of records	Number of species	Number of families
Low molecular mass compounds	259	85	26
Acylpolyamines	176	20	8
Linear peptides	102	17	8
Mini-proteins	965	60	20
Large proteins	11	7	1
Enzymes	105	49	14
Total	1618	174	32

primary literature and included finally 344 references. In total we aggregated 1618 data sets on venom compounds of spiders (Table 1). Since our literature records comprise more than 50 years in which spider taxonomy made considerable advances, we checked all spider names with Platnick's catalogue (Platnick, 2011), the authoritative taxonomic on-line catalogue for spiders. We consequently use only currently valid names of species but add a compilation of those species that appeared in the venom literature under older (invalid) names (Table 2).

研究された種数

TABLE 3

Spider species occurring worldwide per family (species worldwide, all families with > 500 species included) and species included into this study (species investigated), arranged per family, decreasing order according to number of species known worldwide

Family	Species worldwide	Species investigated	Family	Species worldwide	Species investigated
Salticidae	5337	4	Oxyopidae	430	3
Linyphiidae	4378	0	Nemesiidae	353	2
Araneidae	3006	15	Miturgidae	348	2
Lycosidae	2374	13	Pisauridae	333	4
Theridiidae	2310	8	Amaurobiidae	276	2
Thomisidae	2146	3	Lamponidae	192	1
Gnaphosidae	2111	1	Desidae	182	1
Agelenidae	1146	7	Cyrtaucheniidae	134	2
Pholcidae	1111	0	Palpimanidae	131	1
Sparassidae	1109	10	Ctenizidae	125	1
Corinnidae	962	0	Sicariidae	124	19
Tetragnathidae	951	0	Filistatidae	113	1
Zodariidae	942	1	Segestriidae	111	3
Theraphosidae	933	39	Eresidae	96	3
Oonopidae	684	0	Hexathelidae	86	10
Clubionidae	570	0	Nephilidae	58	6
Dictynidae	565	0	Titanoecidae	49	1
Philodromidae	536	1	Actinopodidae	40	1
Anyphaenidae	514	0	Plectreuridae	30	1
Ctenidae	475	7	Diguetidae	15	1

Data on species abundance worldwide according to Platnick (2011).

毒の構造による系統

Jocque &
Dippenaar –Schoeman
(2006) and
Kuntner et. al., (2008)

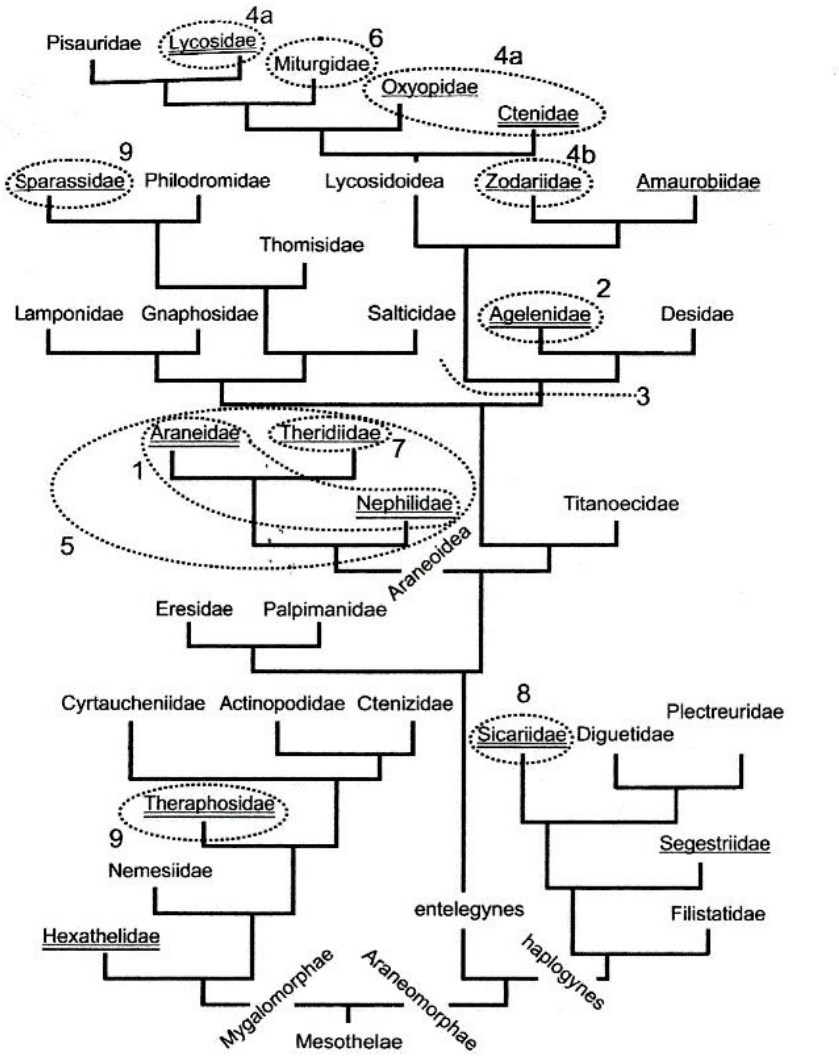


FIG. 2 Phylogenetic tree of the 32 spider families (out of a total of 109 families) from which at least one publication on a structurally elucidated venom compound is available. Modified from Jocqué and Dippenaar-Schoeman (2006) and Kuntner *et al.* (2008). *Underlined* family names refer to groups with > 10 entries (i.e. compounds and/or species) in our databases, *doubly underlined* families refer to groups with > 50 entries. (1) Exclusive presence of amino acid acylpolyamines, (2) non-amino acid acylpolyamines very common, (3) appearance of linear peptides, (4) presence of short and long cationic linear peptides (4a α-SCPs, 4b α-SCPs and α-LCPs), (5) absence of mini-proteins/cysteine-knotted peptides, (6) changed function of modified mini-proteins/cysteine-knotted peptides, (7) large proteins, (8) phospholipases D (PLDs) and (9) various neurotransmitter substances very common.

低分子のクモ毒の化学構造

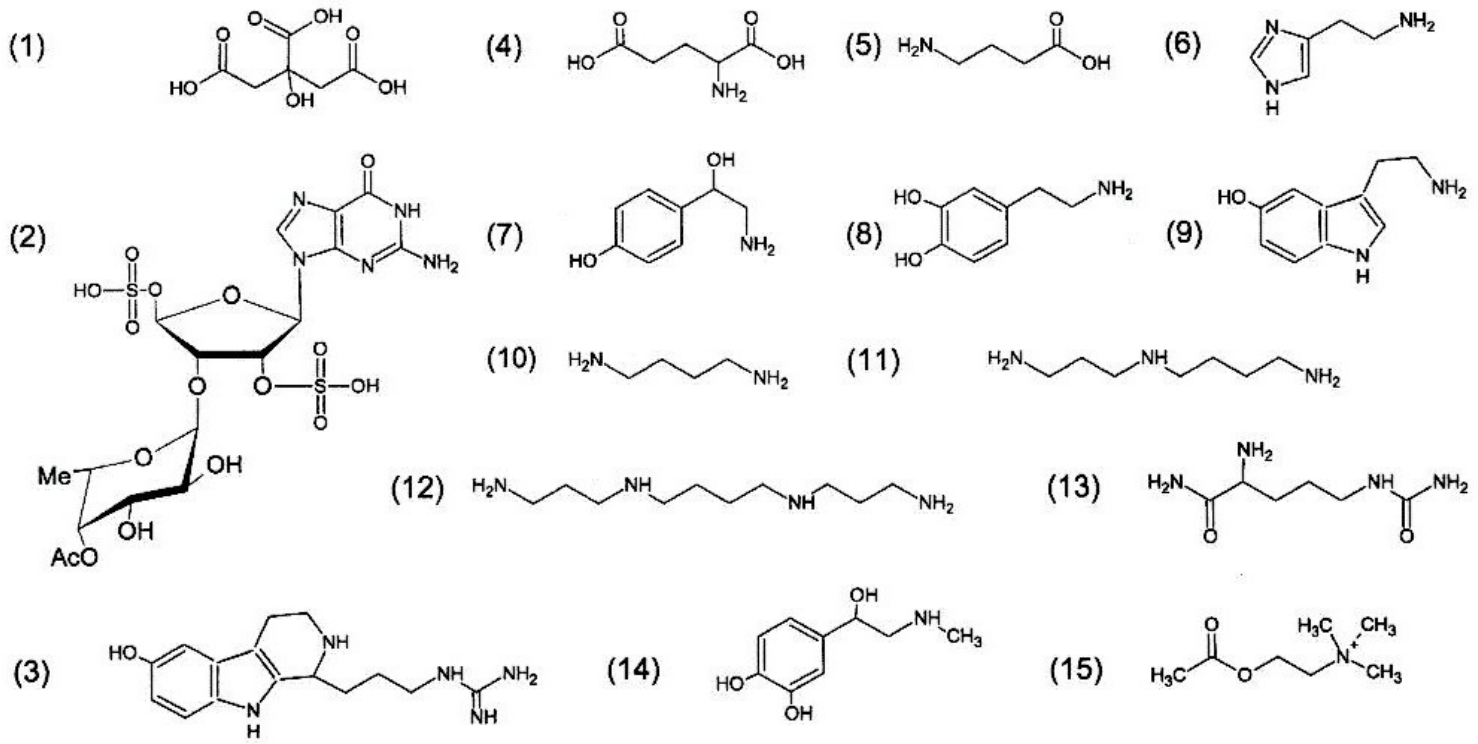


FIG. 3 Chemical structures of low molecular mass substances identified in the venom of spiders: (1) citric acid, (2) HF-7 (Taggi *et al.*, 2004), (3) PwTx-I (Cesar *et al.*, 2005b), (4) glutamic acid, (5) γ-aminobutyric acid, (6), histamine, (7) octopamine, (8) dopamine, (9) serotonin, (10) putrescine, (11) spermidine, (12) spermine, (13) FrPbAII (Gelfuso *et al.*, 2007), (14) adrenaline and (15) acetylcholine.

クモ毒液中のアシルポリアミン毒

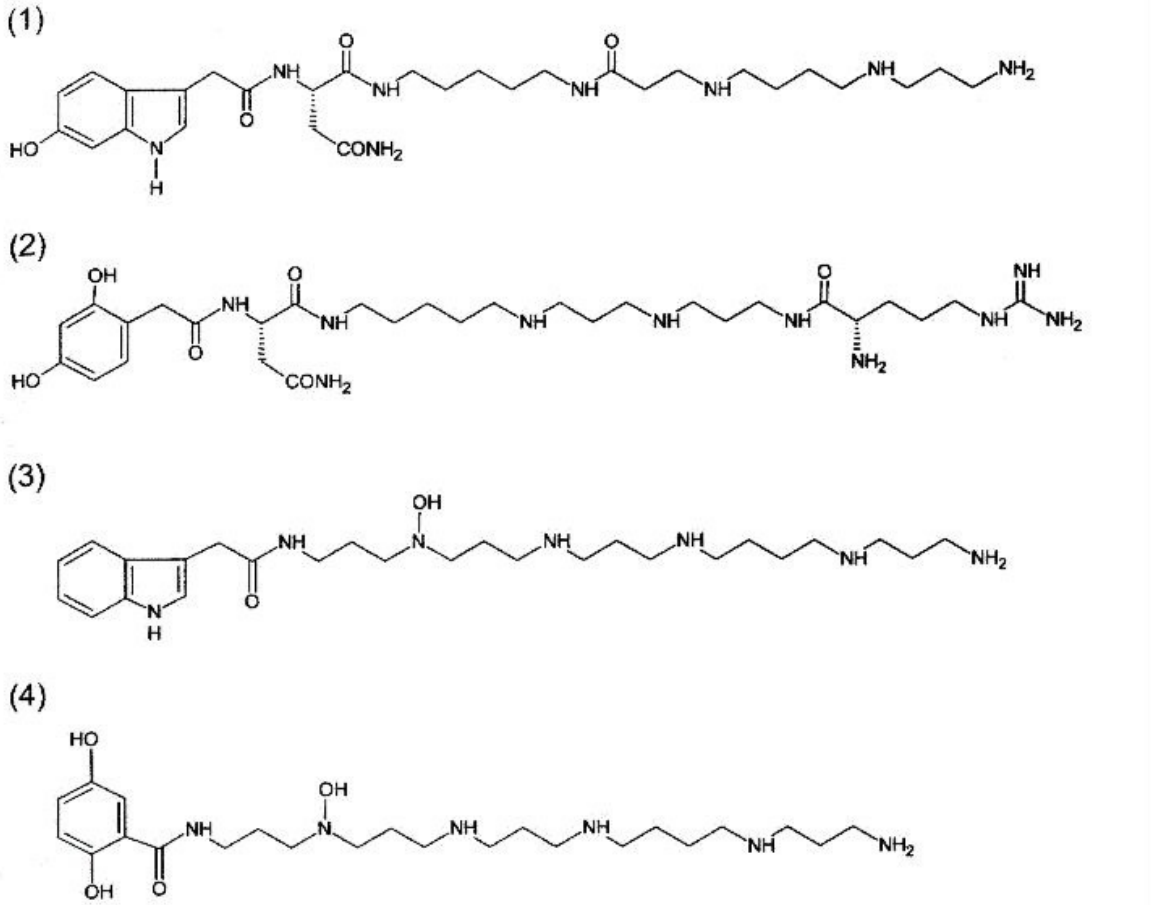


FIG. 4 Characteristic acylpolyamine toxins from spider venom. (1) Amino acid-containing acylpolyamines exhibiting an indolic NPTX-1 (Toki *et al.*, 1988) or phenolic end group (2) Argiopine (Grishin *et al.*, 1989), connected via asparagine to the polyamine chain; and (3) non-amino acid-containing acylpolyamines exhibiting an indolic AGEL 489 or phenolic end group (4) AGEL 468 (Jasys *et al.*, 1990) connected to the polyamine chain

アミノ酸と非アミノ酸のAPAの分子量

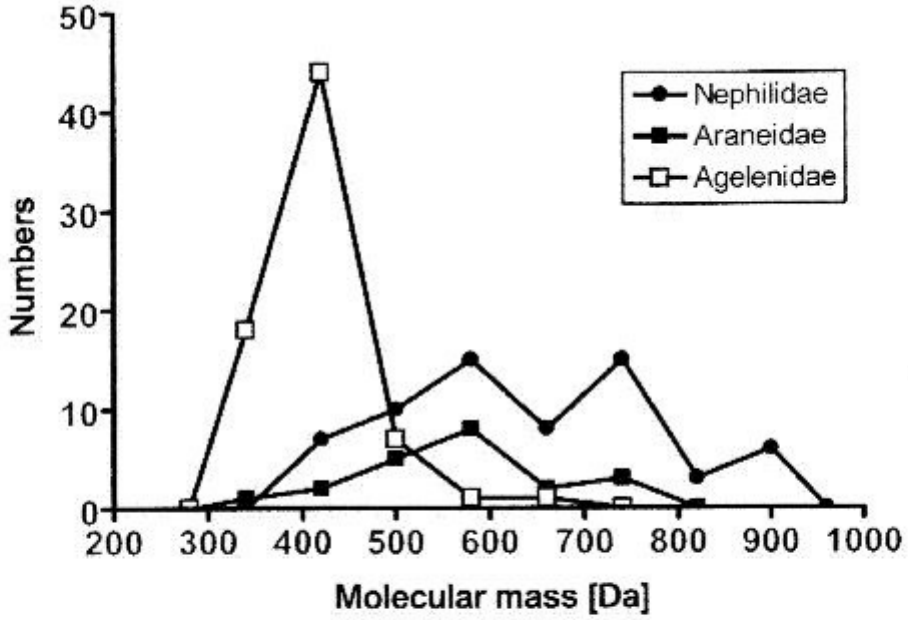


FIG. 5 Molecular mass distribution of amino acid-containing acylpolyamines (Nephilidae, Araneidae) and non-amino acid-containing acylpolyamines (Agelenidae) in three spider families (see Section 3.3).

クモ毒液中の細胞破壊ペプチド

TABLE 5

Spiders which possess cytolytic peptides (α-SCPs and α-LCPs) in their venom

Family	Genus	Species	Evidence		
Agelenidae	*Agelena*	*labyrinthica*			Weak
Araneidae	*Eriophora*	*edax*			Weak
	Neoscona	*arabesca*			Weak
Ctenidae	*Cupiennius*	*salei*	Strong		
Lycosidae	*Geolycosa*	*riograndae*	Strong		
	Hogna	*carolinensis*	Strong		
	Hogna	*helluo*		Probable	
	Lycosa	*erythrognatha*	Strong		
	Lycosa	*singoriensis*	Strong		
	Trochosa	sp.		Probable	
Oxyopidae	*Oxyopes*	*takobius*	Strong		
	Peucetia	*viridans*		Probable	
Salticidae	*Phidippus*	*ardens*			Weak
	Phidippus	*johnsoni*			Weak
	Phidippus	*octopunctatus*			Weak
Theridiidae	*Latrodectus*	*hesperus*			Weak
Zodariidae	*Lachesana*	*tarabaevi*	Strong		

The evidence for the existence of cytolytic peptides is *strong* (compound isolated, sequence known, tests performed or plausible due to sequence homology), *probable* (no compound isolated but cytolytic peptides are known from the same family) or *weak* (sequence not isolated, tests include only crude venom in cell culture)

細胞破壊ペプチドの分子量

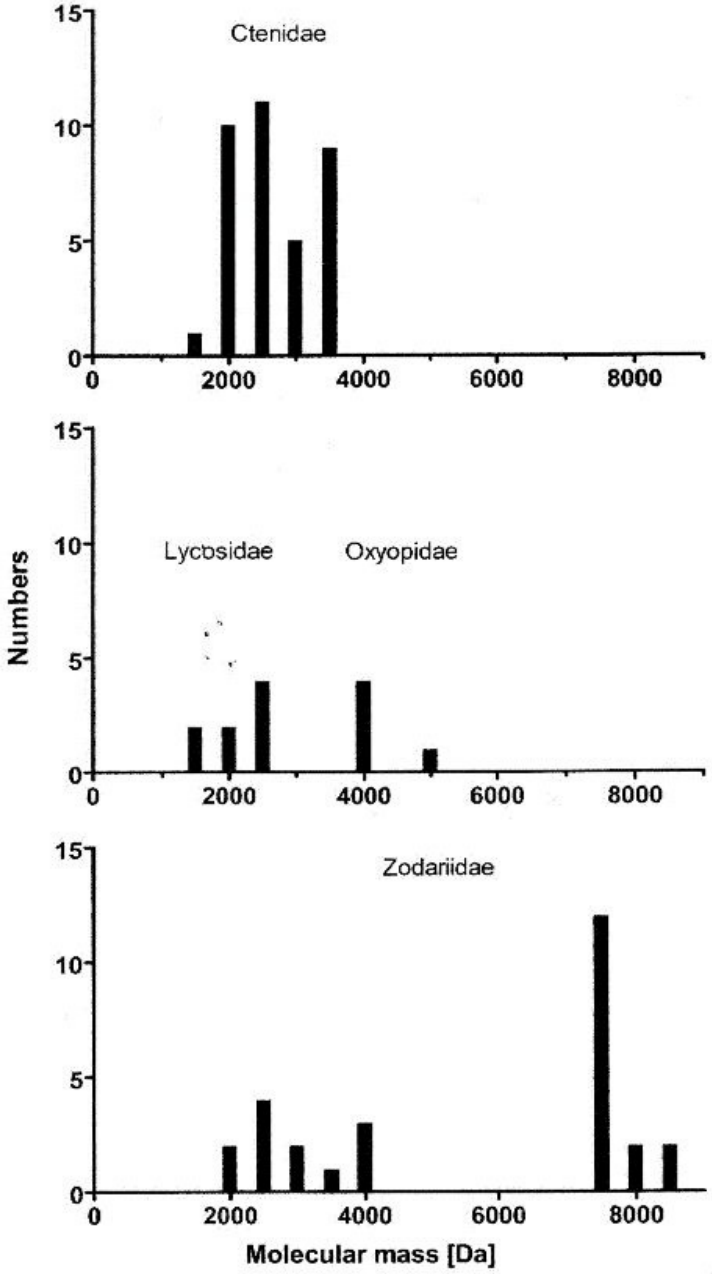


FIG. 6 Molecular mass distribution of cytolytic peptides in Lycosoidea (Ctenidae (*Cupiennius salei*), Lycosidae, Oxyopidae) and Zodariidae (*Lachesana tarabaevi*).

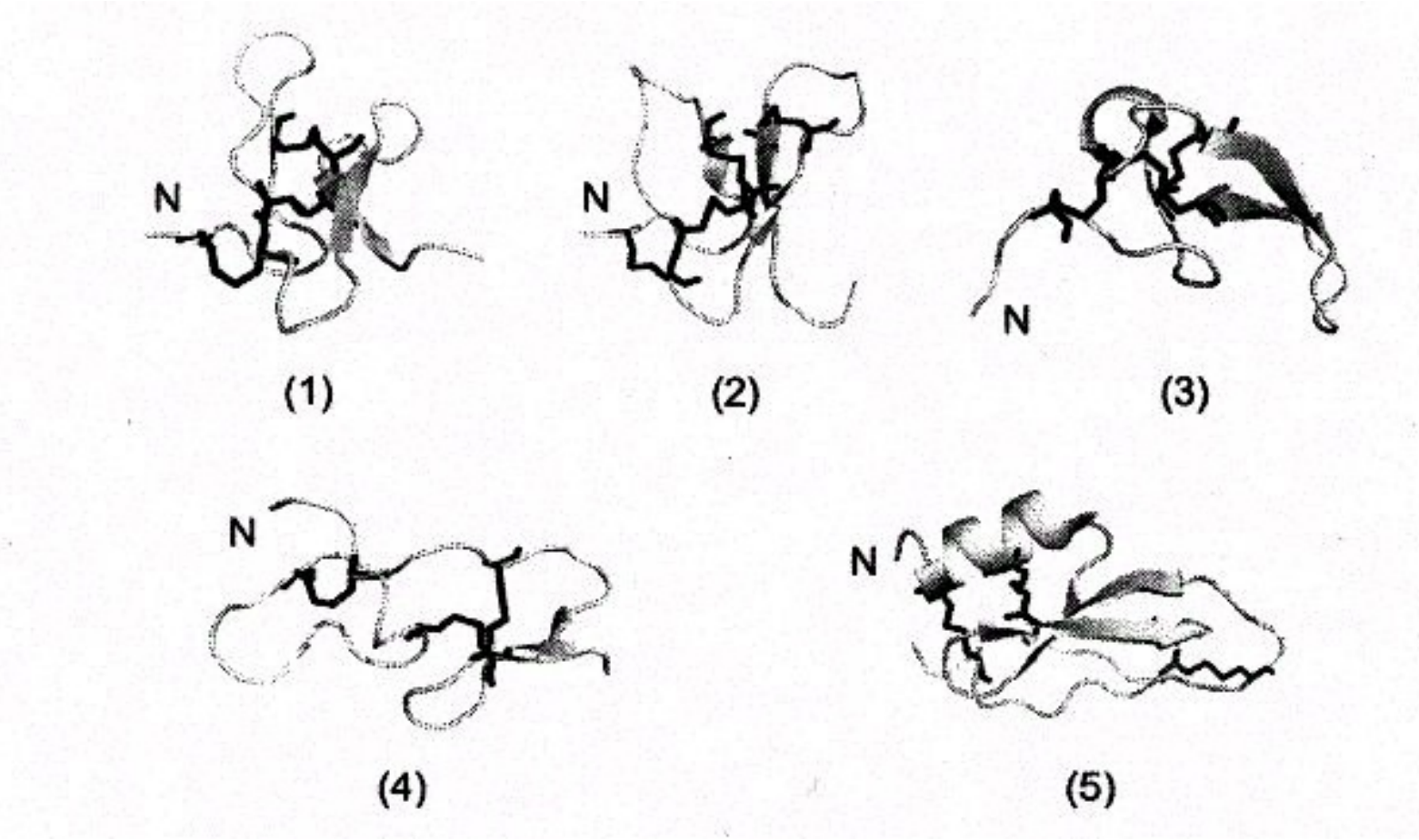
分子量とアミノ酸配列データ

TABLE 6
Characteristics of cytolytic peptides from four spider families

Family	Number of cytolytic peptides	Average molecular mass (Da ± SD)	Average number of		
			Amino acids	Lysines	Arginines
Ctenidae	36	2875 ± 605	25.9 ± 6.6	6.1 ± 1.8	0.5 ± 0.9
Lycosidae	9	2809 ± 501	24.3 ± 3.7	6.0 ± 2.6	0.2 ± 0.4
Oxyopidae	5	4343 ± 492	39.2 ± 4.9	8.4 ± 0.5	2.0 ± 0.7
Zodariidae SCPs	12	3303 ± 691	27.5 ± 5.5	6.5 ± 1.2	1.6 ± 1.2
Zodariidae LCPs	16	8031 ± 245	70.0 ± 2.1	19.0 ± 0.5	1.3 ± 0.4

Ctenidae, Lycosidae and Oxyopidae constitute the Lycosoidea superfamily which is the sister group to Zodariidae

ミニ･タンパク毒の立体構造



3次元分子構造

(1)
Cupiennin 1a [2K38]

GFGALF FLA VA TVA QAAQG A YVVN QME

(2)
Latarcin 1 [2PCO]

SMWSGMW L L NAL L GE

(3)
Latarcin 2a [2G9P]

GLFG LI FG AISYAV A G H

FIG. 7 Amino acid sequences and three-dimensional structures of (1) short cationic α-helical peptides from the ctenid *Cupiennius salei* and (2 and 3) the zodariid *Lachesana tarabaevi*. Positively charged amino acids in the amino acid sequences are given in grey. In the spatial structure of the peptides charged/polar residues are shown in black and hydrophobic amino acids in grey. The Protein Data Bank codes are given in brackets. The structures were calculated using PyMOL (DeLano, 2002).

ミニ･タンパク毒のアミノ酸配列

TABLE 7
Structure of mini-proteins with six cysteines (C1–C6) and no amino acid between C3 and C4

	Number of mini-proteins	Molecular mass (Da)	Number of amino acids						
			N-terminal	C1–C2	C2–C3	C4–C5	C5–C6	C-terminal	Total
Hexathelidae	61	4124	2.6	5.9	5.0	4.1	8.5	7.4	33.4
Theraphosidae	122	4017	1.3	6.0	5.5	4.2	6.3	5.5	28.9
Agelenidae	25	3997	2.0	6.8	6.5	3.9	8.9	1.5	30.2
Sparassidae	7	3705	1.9	6.0	5.1	4.0	4.9	4.4	27.7
Ctenidae	14	3903	1.9	5.9	5.1	4.4	7.8	3.4	26.3

Average molecular masses, number of amino acids between neighbouring cysteines and total number of cysteines are given for five spider families.

ミニ・タンパク毒の作用

TABLE 8

Activity descriptors and biological function of mini-proteins, nomenclature according to King *et al.* (2008), and the number of known occurrences in spiders

Target ion channel	Descriptor	Function	Number of mini-proteins
Ca^{2+}	ω (omega)	Inhibits voltage-activated calcium (Ca_v) channels	111
K^+	κ (kappa)	Inhibits voltage-activated potassium (K_v) channels	75
Na^+	β (beta)	Shifts voltage dependence of Na_v channels activation	48
	δ (delta)	Delays inactivation of voltage-activated Na_v channels	50
	μ (mu)	Inhibits voltage-activated sodium (Na_v) channels	37
others	γ (gamma)	Targets hyperpolarisation-activated, cyclic nucleotide-gated nonspecific cation channels	1
	π (pi)	Targets acid-sensing ion channels	1
	τ (tau)	Targets transient receptor potential channel	3

ミニ･タンパク毒の分子量

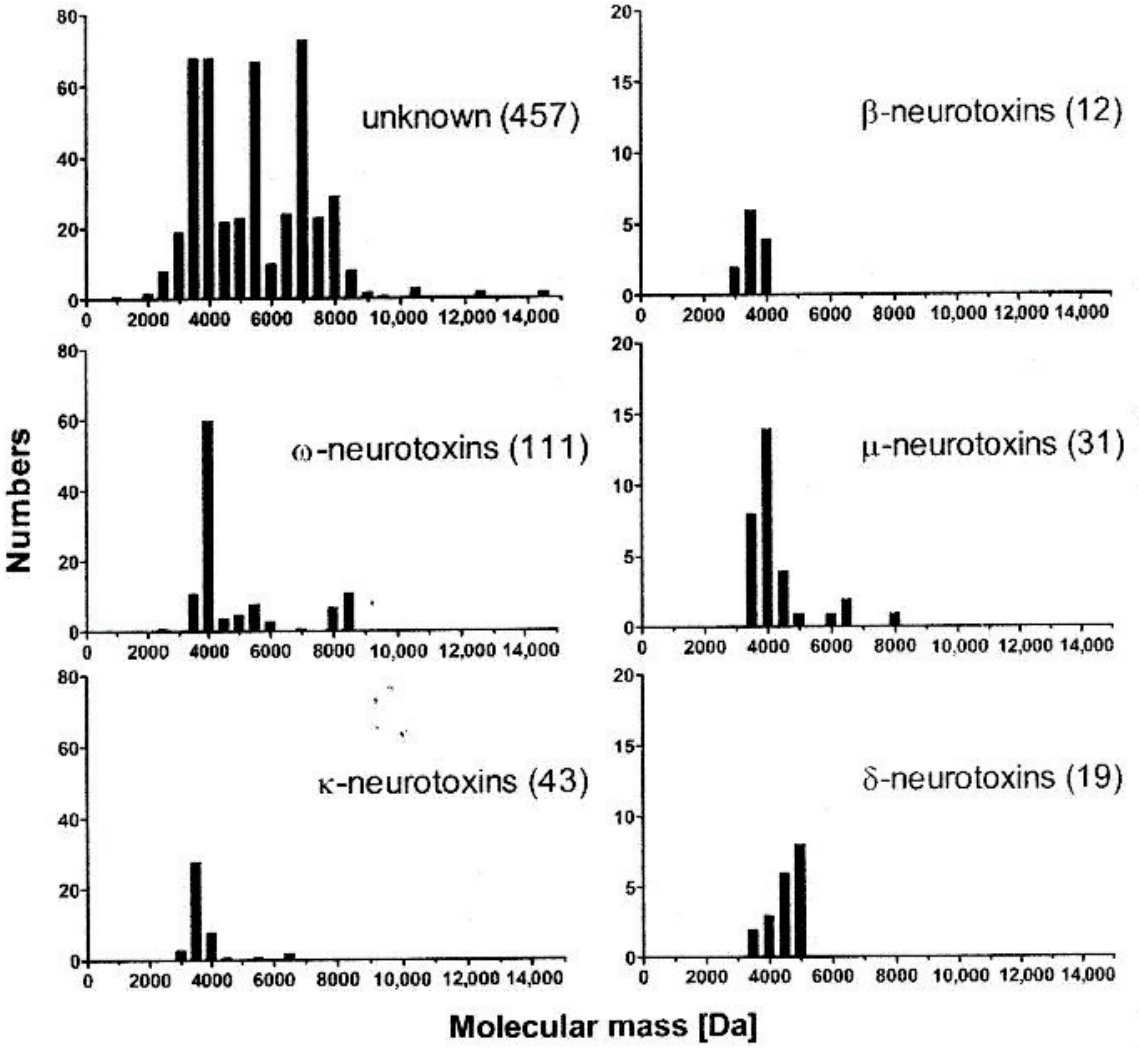


FIG. 9 Molecular mass distribution of mini-proteins/cysteine-knotted peptides from spider venom with respect to their function as ω-, κ-, β, μ- and δ-toxins. For most toxins, however, the exact mode of action remains unknown. Numbers in brackets refer to the number of records.

分子量とシスティン数

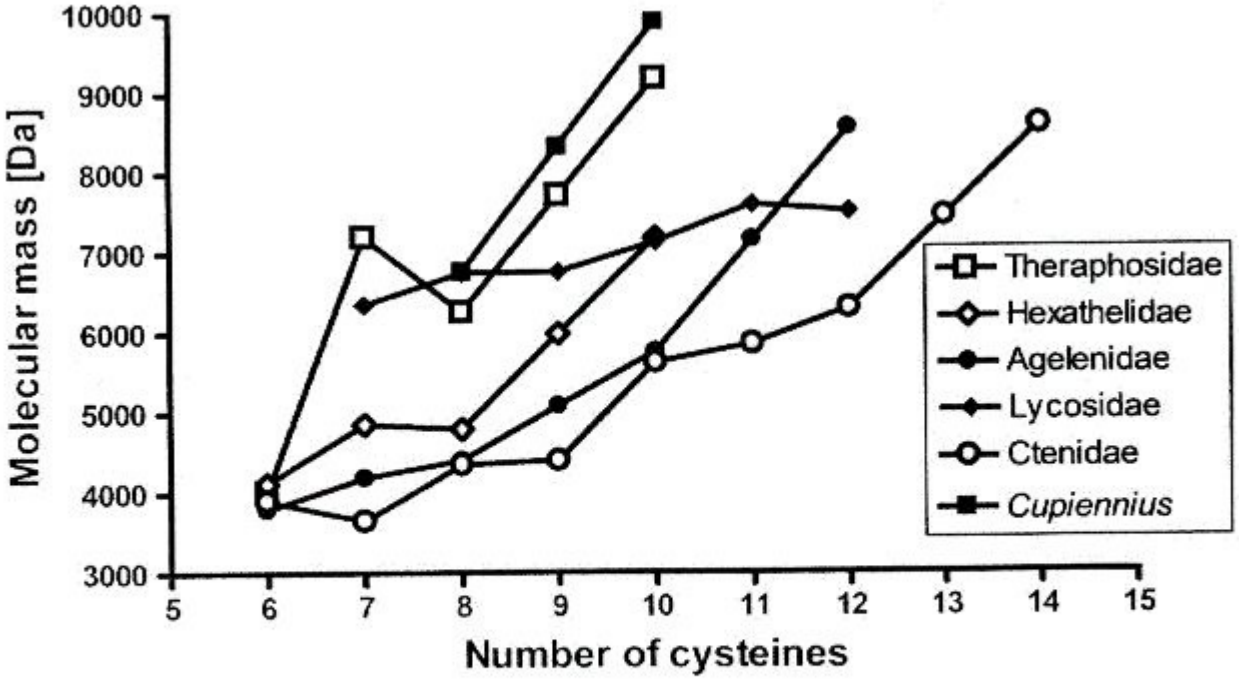


FIG. 10 Molecular mass of neurotoxic peptides depending on the number of cysteines for six spider families (Ctenidae without *Cupiennius*) and *Cupiennius salei*.

タランチュラ毒の比較

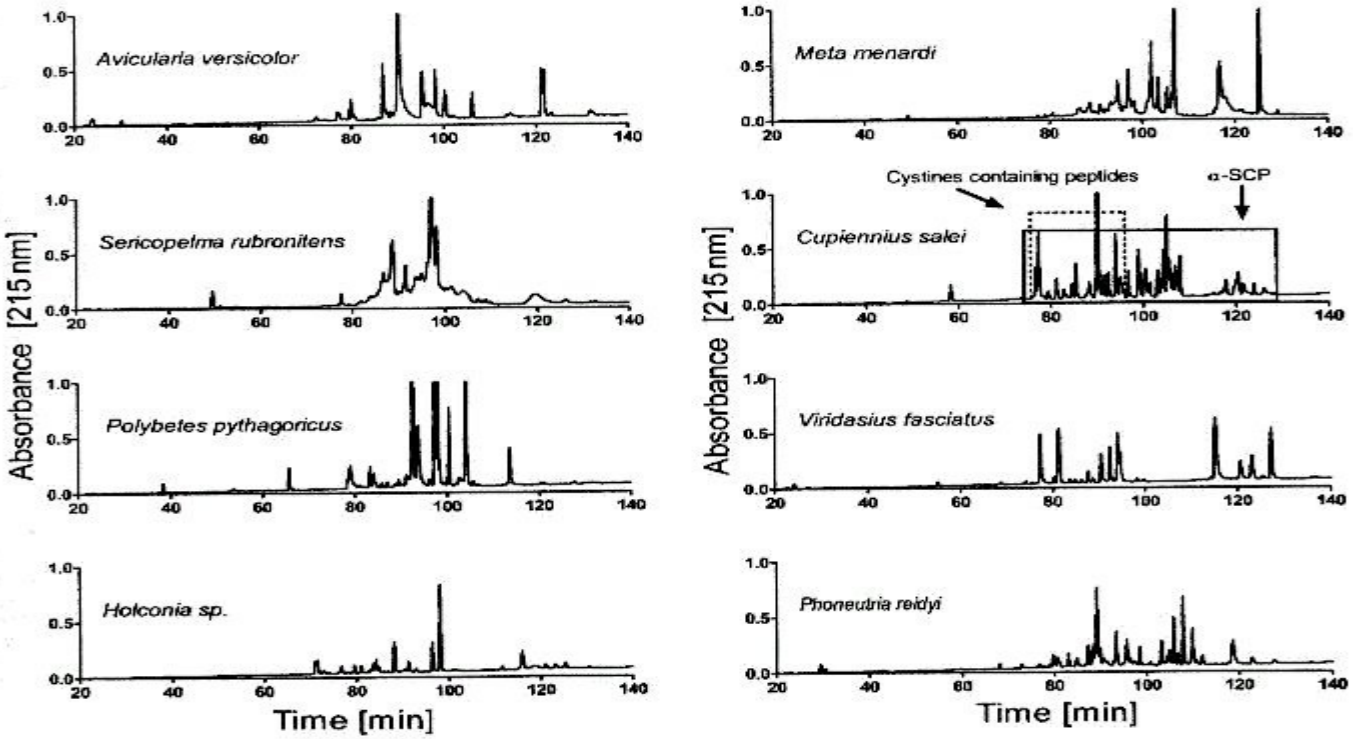


FIG. 11 RP-HPLC-chromatograms produced under comparable conditions for venoms of the theraphosids *Avicularia versicolor* and *Sericopelma rubronitens*, the sparassids *Polybetes pythagoricus* and *Holconia* sp., the tetragnathid *Meta menardi*, and the ctenids *Cupiennius salei*, *Viridasius fasciatus* and *Phoneutria reidyi*. The separation was done on a NUCLEOSIL 100-5 C_{18} column (Macherey & Nagel, 250/4 mm) using solvent A (0.1% trifluoroacetic acid in double distilled water) from 0 to 10 min, followed from 10 to 150 min by a gradient (0–60%) of solvent B (0.1% trifluoroacetic acid in acetonitrile).

ゴキブリに対する LD_{50} 比較

TABLE 11

LD_{50} (ng dry venom/mg insect) of crude venom of various spider species, measured in a bioassay with the cockroach *Blatta orientalis*

Family	Spider species	LD_{50}
Agelenidae	*Tegenaria atrica*	92.6
Amaurobiidae	*Amaurobius* sp.	542.9
Ctenidae	*Cupiennius salei*	26.0
Filistatidae	*Kukulcania* sp.	0.3
Hexathelidae	*Atrax robustus* female	9.7
	Atrax robustus male	20.0
Lycosidae	*Lycosa* sp.	45.1
Plectreuridae	*Plectreurys tristis*	1.2
Salticidae	*Phidippus johnsonii*	2.6
Sicariidae	*Loxosceles deserta*	5.1
	Loxosceles gaucho	20.6
Sparassidae	*Olios* sp.	5.9
Theraphosidae	*Brachypelma albopilosum*	50.3
	Avicularia metallica	10.0
Theridiidae	*Latrodectus hesperus*	0.9

Data from Friedel and Nentwig (1989) and Nentwig *et al.* (1992).

than three orders of magnitude. In other words, the variation among spider venom toxicities varies as much as the sensitivity of the main prey taxa to these venoms. This may explain why the venom of a given spider species does not necessarily have to be more toxic than the venom of another species, especially when ecological circumstances are different.