CHAPTER IV

PROTEOMIC AND ANTIVENOMICS ANALYSES OF WESTERN (WI), EASTERN (EI), AND SOUTHERN INDIA (SI) RVV SAMPLES AND CORRELATION OF VENOM COMPOSITION WITH *IN VITRO* BIOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF RVV AS WELL AS CLINICAL MANIFESTATIONS OF RV ENVENOMATION

4.1 Results

4.1.1 Determination of molecular mass of WI, EI, and SI RVV proteins

4.1.1.1 One dimensional SDS-PAGE analysis

The SDS-PAGE analyses of WI, EI, and SI RVVs suggested the presence of venom toxins in a molecular weight range of ~6 to 130 kDa (Figs. 4.1a-c).

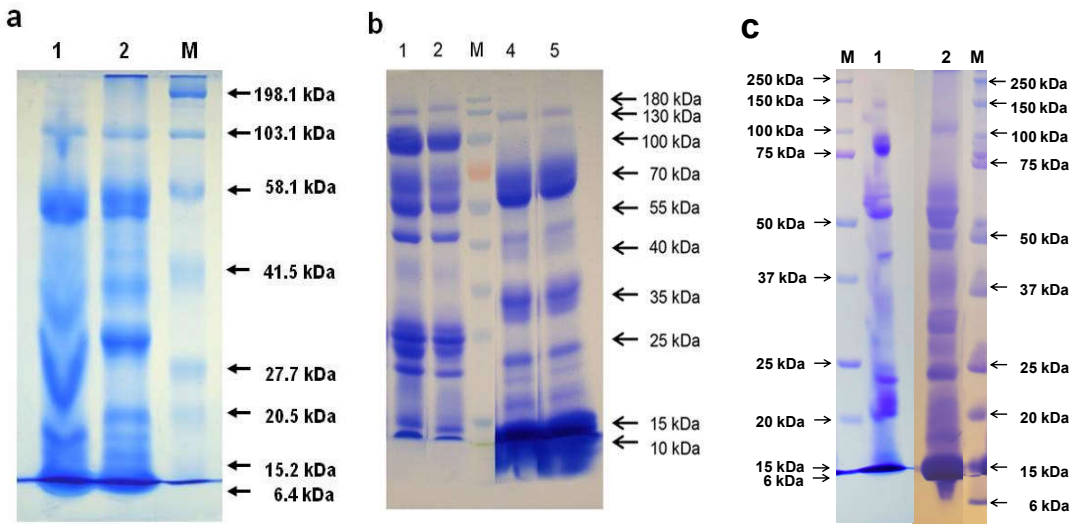


Fig. 4.1a. 12.5% SDS-PAGE analysis of crude WI RVV (50 µg) under non-reduced (lane 1) and reduced (lane 2) conditions. **b.** 12.5% SDS-PAGE analysis of crude EI RVV (B) and EI RVV (N) (80 µg) under non-reduced (lanes 1 and 2, respectively) and reduced (lane 4 and 5, respectively) conditions. **c.** 12.5% SDS-PAGE analysis of crude SI RVV (500 µg) under non-reduced (lane 1) and reduced (lane 2) conditions. Lane M contains protein molecular markers.

Densitometry analysis of the reduced RVV lanes suggested that the proteins in the mass range of ~6 to 22 kDa were predominate in WI (~56.1%), EI RVV (~57.4 to 60.7%), and SI RVV (~62.1%) samples (Table 4.1).

Table 4.1. Densitometry analysis of SDS-PAGs (reduced) of crude WI RVV, EI RVV (B and N), and SI RVV. The analysis was done using ImageQuant TL 8.1 software (GE Healthcare, Sweden).

Molecular weight range (kDa)	Relative SDS-PAGE band intensity (%)			
	WI RVV	EI RVV (B)	EI RVV (N)	SI RVV
6-22	56.1	57.4	60.7	62.1
23-45	16.4	18.6	18.1	20.1
>45	27.5	24.0	21.2	17.8

4.1.1.2 MALDI-TOF-MS analysis of WI, EI, and SI RVV samples

MALDI-TOF-MS analyses of crude RVV samples revealed the presence of 92 (*m/z* 5.3 to 195.9 kDa), 145 (*m/z* 6.5 to 123.8 kDa), 121 (*m/z* 6.2 to 147.7 kDa), and 142 distinct ions (*m/z* 8.6 to 150.0 kDa) in WI RVV, EI RVV (B), EI RVV (N), and SI RVV, respectively (Tables 4.2a-d). However, all of these ions may not be real gene products as at least some may be produced by the autocatalysis of RVV proteins.

Table 4.2a. List of ions detected in WI RVV by MALDI-TOF-MS analysis. The analysis was performed in the following three m/z ranges: 5 to 50 kDa, 50 to 100 kDa, and 100 to 200 kDa.

m/z ranges	m/z of the ions detected in WI RVV
5 - 50 kDa (61 entries)	5304.9, 5463.3, 5798.6, 6226.8, 7142.0, 7587.1, 8772.9, 9171.9, 10423.2, 11700.6, 11972.7, 12027.9, 12077.0, 12980.5, 13220.9, 13239.8, 13273.5, 14256.6, 14551.0, 15306.6, 15640.9, 15769.9, 16117.1, 17392.5, 17983.7, 18149.6, 19551.7, 20696.8, 21317.3, 21916.0, 21921.6, 22357.7, 22569.9, 22722.4, 22766.6, 24987.8, 26823.1, 29290.7, 30583.0, 30814.7, 30965.8, 31343.0, 32376.4, 32939.7, 33794.8, 35125.3, 35384.0, 35971.7, 37584.0, 37611.0, 38606.2, 39805.5, 39900.8, 42573.7, 43322.5, 44838.8, 45459.6, 45490.7, 48411.0, 49151.6, 49335.5
50 - 100 kDa (10 entries)	51211.6, 54670.8, 65432.0, 67019.8, 70944.4, 83041.0, 86706.0, 93780.9, 95098.4, 97857.3
> 100 kDa (21 entries)	101171.9, 107616.7, 111365.5, 114390.2, 115193.7, 121866.8, 127753.3, 128224.8, 133565.4, 137958.0, 142035.5, 143752.0, 146071.8, 148540.1, 152295.9, 158615.7, 162981.5, 170654.7, 184533.5, 188565.8, 195958.8

Table 4.2b. List of ions detected in EI RVV (B) by MALDI-TOF-MS analysis. The analysis was performed in the following three m/z ranges: 5 to 50 kDa, 50 to 100 kDa, and 100 to 200 kDa.

m/z ranges	m/z of the ions detected in EI RVV (B)
5 - 50 kDa (71 entries)	6593.9, 6738.1, 6851.7, 6982.9, 7105.6, 7217.7, 9668.2, 13121.2, 13233.5, 13353.6, 13475.5, 13599.2, 13719.8, 13884.2, 14001.1, 14113.4, 14228.6, 14350.7, 14468.2, 14582.4, 14703.4, 14845.4, 14976.5, 15088.8, 15248.2, 16789.4, 17447.8, 18171.4, 19929.5, 19940.1, 20087.4, 22081.2, 22920.4, 23677.8, 26417.4, 26606.6, 27553.8, 28384.0, 28597.9, 29716.3, 30772.7, 31042.1, 31359.3, 31932.7, 32046.1, 32454.1, 32759.4, 33926.9, 34073.0, 34552.7, 34769.1, 35581.9, 36596.1, 36971.2, 37716.9, 37881.3, 39766.7, 41020.7, 41892.8, 42120.4, 42763.2, 44030.3, 44319.3, 46119.0, 46631.7, 47193.2, 47607.9, 47873.8, 48361.3, 49331.9, 49909.5
50 - 100 kDa (58 entries)	51746.9, 51927.6, 53336.2, 53887.7, 54072.2, 54380.4, 55024.2, 55646.9, 56047.3, 56185.2, 56436.5, 56751.4, 57739.5, 58467.1, 59689.8, 60768.6, 61870.3, 63261.4, 63916.0, 64587.4, 65736.9, 66172.3, 66965.2, 67831.8, 68274.2, 70072.1, 70733.0, 70902.3, 71114.1, 71255.5, 72121.2, 72663.1, 74503.6, 74691.9, 75724.1, 77249.1, 79191.7, 79969.6, 81370.5, 81718.8, 82798.8, 83410.5, 84286.0, 84779.5, 86362.3, 86674.4, 87818.4, 89207.5, 89667.7, 90448.0, 92454.0, 92583.2, 93019.7, 95430.9, 96285.5, 97491.7, 98006.3, 98572.2
> 100 kDa (16 entries)	102817.8, 106581.0, 108479.6, 108619.6, 110695.3, 111261.7, 111687.4, 111936.1, 112274.1, 114187.1, 116370.2, 118354.6, 118574.2, 121409.5, 121891.5, 123866.8

Table 4.2c. List of ions detected in EI RVV (N) by MALDI-TOF-MS analysis. The analysis was performed in the following three m/z ranges: 5 to 50 kDa, 50 to 100 kDa, and 100 to 200 kDa.

m/z ranges	m/z of the ions detected in EI RVV (N)
5 - 50 kDa (56 entries)	6186.3, 6417.5, 6714.9, 7480.2, 7924.1, 9102.7, 9244.8, 10181.8, 11394.5, 13311.2, 13448.8, 13664.5, 13785.3, 13898.0, 14094.7, 14274.0, 14437.9, 14582.5, 14777.6, 15130.3, 15631.6, 18399.3, 20149.4, 20261.9, 21350.3, 22159.8, 22285.7, 22721.2, 22840.7, 23321.8, 25322.1, 25498.8, 27117.3, 29589.1, 32349.6, 32559.0, 33664.7, 34552.9, 35642.0, 36062.3, 36162.8, 36981.5, 39293.9, 39777.5, 42001.4, 42960.6, 43842.1, 44041.6, 44386.4, 44889.3, 45451.5, 46986.8, 47839.3, 48687.9, 49226.5, 49909.8
50 - 100 kDa (44 entries)	50324.4, 51075.1, 51506.6, 52133.2, 52946.0, 53397.6, 53618.0, 55684.7, 55872.2, 56286.0, 57320.7, 58186.0, 59496.3, 59793.7, 62068.4, 62730.0, 63903.0, 66145.4, 66910.7, 68316.1, 71709.4, 72777.9, 73164.5, 74113.9, 75011.4, 76646.5, 77588.8, 77751.4, 82372.5, 83487.6, 83886.5, 84024.8, 84147.9, 85244.0, 88149.4, 88275.5, 89208.0, 89319.0, 90193.4, 93961.4, 94629.7, 95447.9, 96764.3, 98622.7,

m/z ranges	m/z of the ions detected in EI RVV (N)
> 100 kDa (21 entries)	100381.2, 104528.3, 108060.7, 109655.6, 110802.0, 117461.1, 119326.4, 119712.2, 121929.3, 122971.0, 123886.2, 124354.4, 127068.9, 127961.3, 130407.7, 134024.0, 137039.7, 138303.0, 138936.8, 144991.1, 147678.4,

Table 4.2d. List of ions detected in SI RVV by MALDI-TOF-MS analysis. The analysis was performed in the following three m/z ranges: 5 to 50 kDa, 50 to 100 kDa, and 100 to 200 kDa.

m/z ranges	m/z of the ions detected in SI RVV
5 - 50 kDa (63 entries)	8627.8, 9632.5, 10224.8, 12970.2, 13227.9, 13368.7, 13504.1, 13619.4, 13733.8, 13850.0, 13980.4, 14105.1, 14234.1, 15038.9, 15972.0, 18445.3, 20584.8, 23881.2, 25161.0, 25279.9, 25777.6, 26976.6, 27159.0, 27604.7, 28204.6, 28355.6, 28508.7, 28658.7, 28864.8, 29001.3, 29134.6, 29270.0, 29432.9, 29578.0, 29714.5, 30043.2, 30226.6, 30364.5, 30530.4, 30696.8, 30863.6, 31462.3, 31574.9, 32833.9, 34121.8, 35293.4, 35549.9, 35751.6, 37103.4, 37266.5, 37399.3, 37817.3, 38002.6, 41944.4, 42599.3, 44141.3, 44439.2, 44654.0, 45776.1, 46119.0, 46355.1, 46608.8, 47986.7
50 - 100 kDa (55 entries)	50931.4, 53003.4, 53189.5, 53446.2, 53909.0, 56282.2, 56521.1, 56785.8, 57041.8, 57790.4, 57965.2, 58967.5, 59569.8, 60543.2, 61134.7, 61366.9, 63057.9, 63270.9, 64466.2, 64668.2, 65326.0, 65628.2, 66018.4, 66618.8, 68274.1, 68384.9, 69340.3, 69470.1, 69605.7, 70662.5, 71010.9, 71425.3, 72149.6, 72420.4, 72873.1, 73590.4, 73998.0, 75093.5, 75384.3, 75520.0, 75826.2, 75986.9, 76274.9, 77087.0, 77908.9, 79909.6, 80540.5, 81350.4, 81643.0, 91119.5, 92534.6, 93987.7, 97867.4, 98455.4, 99050.1
> 100 kDa (24 entries)	100178.8, 100930.4, 101714.0, 102375.5, 107397.5, 108129.9, 109373.6, 117387.5, 120595.8, 124053.9, 124710.1, 125454.6, 126424.5, 130003.9, 130541.4, 132141.1, 138797.1, 139392.4, 139849.6, 141946.7, 142098.5, 144787.6, 146840.1, 150059.7

4.1.2 De-complexation of WI, EI, and SI RVV samples

4.1.2.1 Fractionation of WI RVV by gel filtration (GF) followed by anion-exchange (AEX) chromatography

Fractionation of WI RVV through GFC resolved it into 10 peaks (Fig. 4.2). The total protein yield in the gel filtration fractions was 80.7% of the total WI RVV loaded to the column. Peak GF4 (16.0%) was characterized with highest protein content followed by GF6 (14.5%), GF7 (11.1%), GF5 (9.6%), GF3 (8.4%), GF1 (6.6%), GF9 (4.4%), GF2 (4.3%), and GF10 (4.0%), while GF8 (1.8%) contained the least protein.

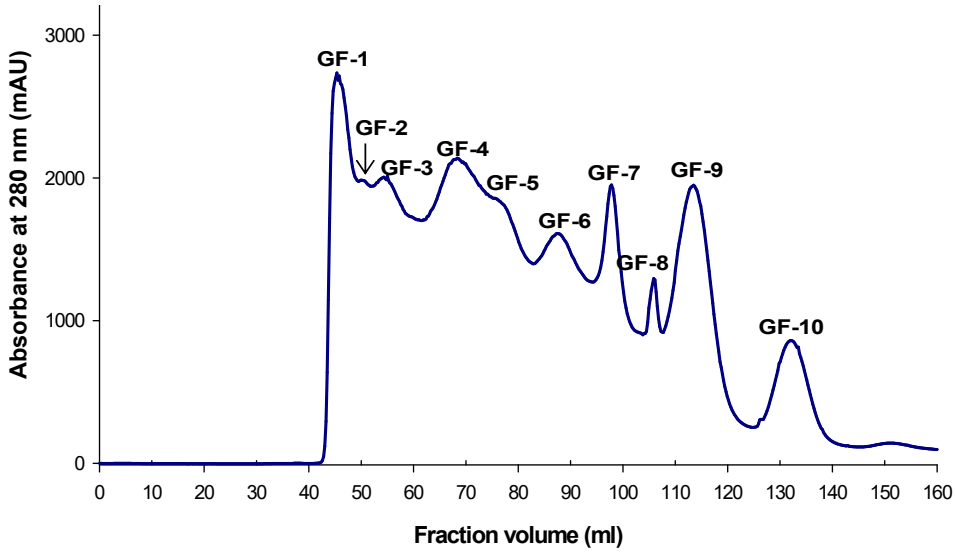
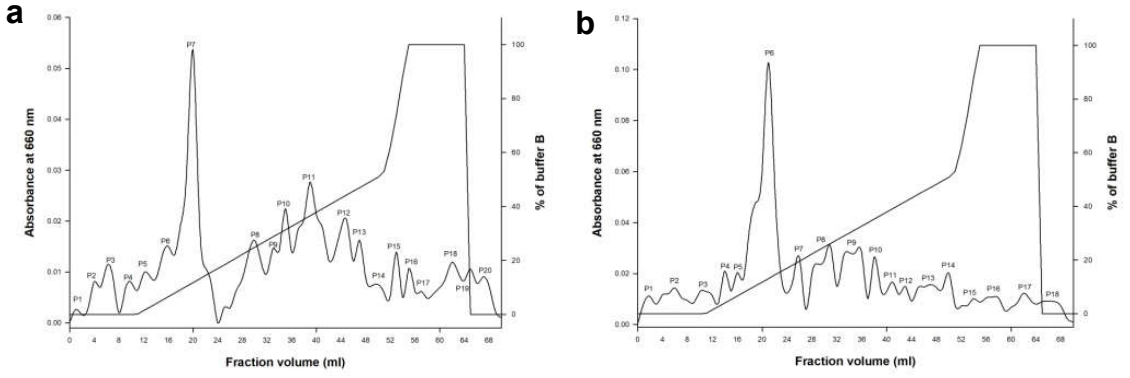
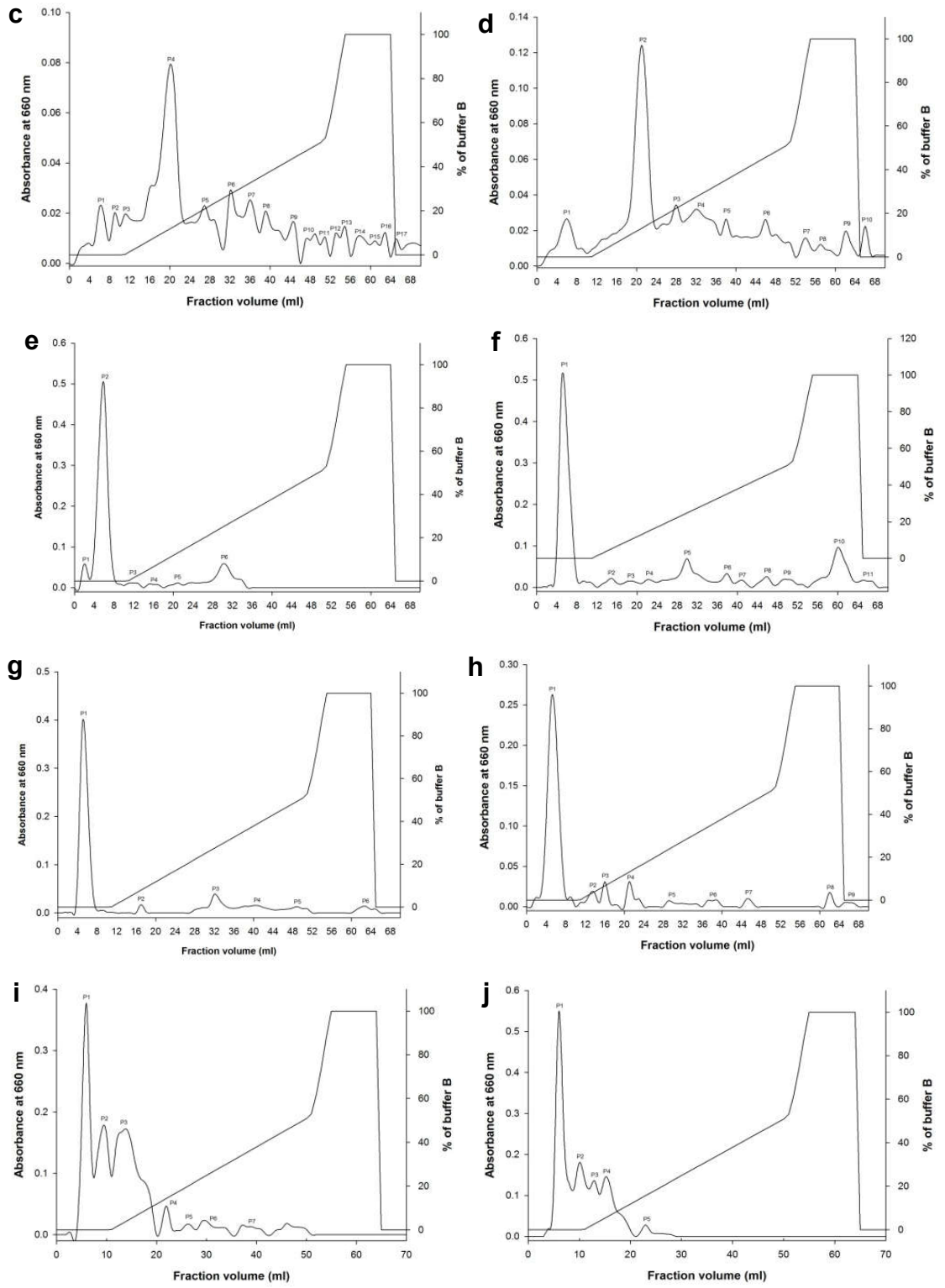


Fig. 4.2. Fractionation of WI RVV (200 mg dry weight) on a HiLoad 16/600 Superdex 75 pg GF column. The flow rate of buffer (25 mM HEPES containing 50 mM NaCl, pH 7.0) was maintained at 10 ml/h and fractions of 2.0 ml were collected. The fractionation was carried out at 4 °C.

AEX chromatography of all the 10 GF peaks resulted into a total of 137 AEX peaks (Figs. 4.3a-j) and the majority of WI RVV proteins (62.5%) were found to anionic at pH 7.4. Further, it was observed that the high molecular weight RVV proteins eluted through GF1 to GF4 were mostly anionic at pH 7.4, and thereafter, the percentage of anionic proteins in subsequent GF peaks decreased gradually (Fig. 4.4).



Figs. 4.3a,b. Fractionation of WI RVV GF1 and GF2 on an FPLC HiTrap Q FF anion-exchange column. The column was washed with two CV of buffer A (20 mM Tris-HCl, pH 7.4) to elute the unbound proteins and the bound proteins were eluted by a 0 to 50% linear gradient of buffer B (20 mM Tris-HCl, pH 7.4 containing 1.0 M NaCl) for 40 min at a flow rate of 1.0 ml/min.



Figs. 4.3c-j. Fractionation of WI RVV GF3 to GF10 on an FPLC HiTrap Q FF anion-exchange column. The column was washed with two CV of buffer A (20 mM Tris-HCl, pH 7.4) to elute the unbound proteins and the bound proteins were eluted by a 0 to 50% linear gradient of buffer B (20 mM Tris-HCl, pH 7.4 containing 1.0 M NaCl) for 40 min at a flow rate of 1.0 ml/min.

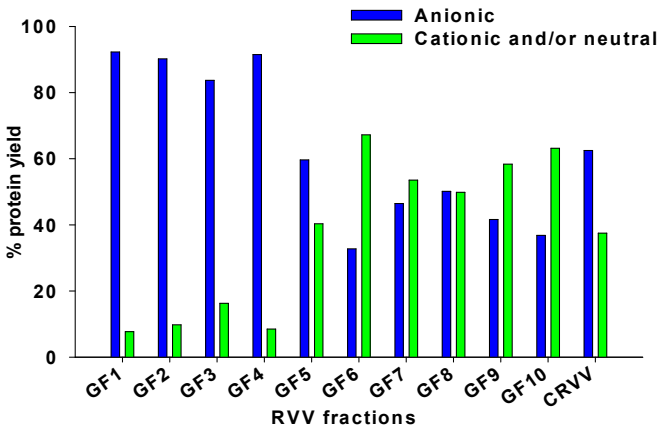


Fig. 4.4. Distribution of anionic, cationic and/or neutral proteins of WI RVV in its GF fractions. Data are from a typical experiment.

4.1.2.2 SDS-PAGE analysis of GF fractions of WI RVV

SDS-PAGE analysis under non-reduced conditions demonstrated the separation of WI RVV proteins in GF peaks according to their molecular mass (Fig. 4.5); however, the RVV proteins migrated with different molecular weight under reduced condition. In addition, presence of low molecular weight (<15 kDa) proteins were also observed along with high molecular weight (>50 kDa) proteins in the initial GF fractions under reduced condition (Fig. 4.5). Further, no proteins bands could be observed in the GF10 fractions of WI RVV, suggesting the elution of very low molecular mass peptides or degraded products of RVV in these fractions.

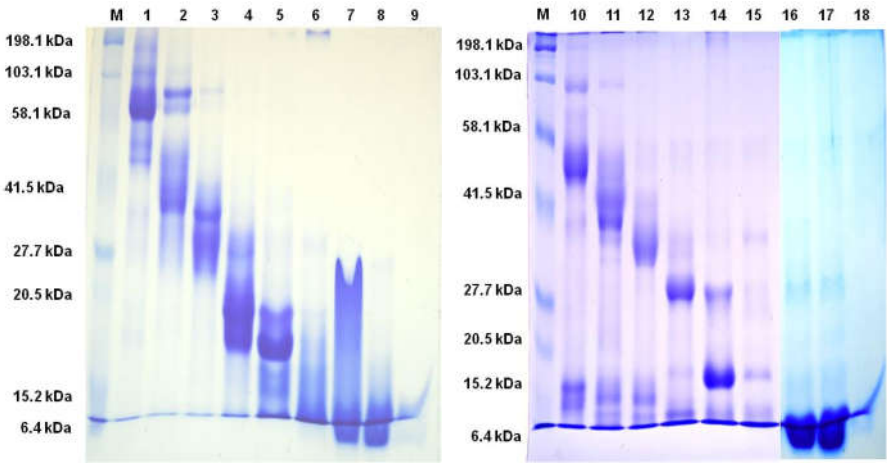


Fig. 4.5. 12.5% SDS-PAGE analysis of WI RVV GF fractions under non-reduced and reduced conditions. Lanes M represent protein molecular markers; lanes 1 to 9 and 10 to

18 represent fractions GF1 to GF9 (40 µg), under non reduced and reduced conditions, respectively.

4.1.2.3 Fractionation of EI RVV by GF chromatography

The EI RVVs (RVV B and RVV N) were resolved into 10 peaks each by GFC (Fig. 4.6). However, marked differences were observed in their chromatographic profiles in the context of peak intensities and elution times (Fig. 4.6). A comparison of the gel-filtration profiles for the two EI RVV samples revealed almost identical elution patterns, except for peak 8 of EI RVV (B) that was absent from EI RVV (N) and peak 10 of EI RVV (N) that was missing from the EI RVV (B) gel filtration profile (Fig. 4.6).

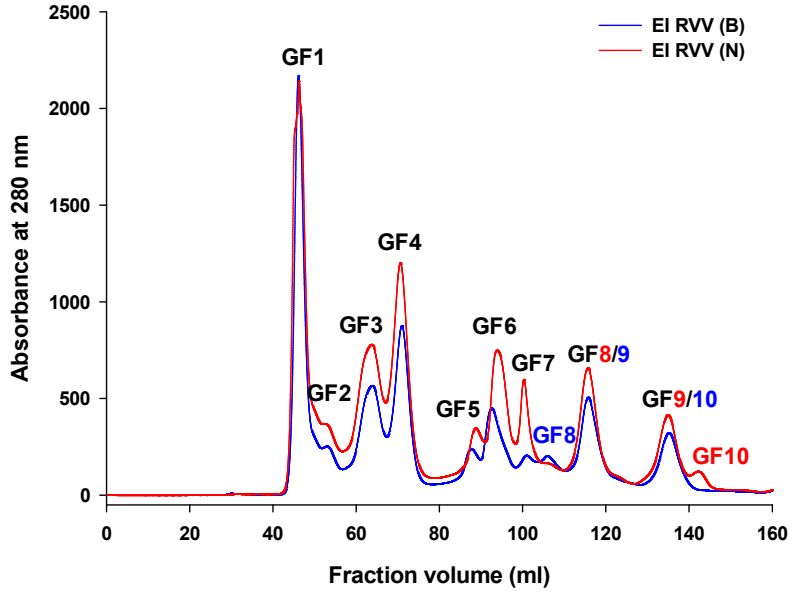


Fig. 4.6. Fractionation of EI RVV (B) and EI RVV (N) (35 mg protein) on a HiLoad 16/600 Superdex 75 pg GF column. The flow rate of buffer (25 mM HEPES containing 50 mM NaCl, pH 7.0) was maintained at 10 ml/h and fractions of 2.0 ml were collected. The fractionation was carried out at 4 °C.

4.1.2.4 SDS-PAGE analysis of GF fractions of EI RVVs

Similar to WI RVV, SDS-PAGE analysis under non-reduced conditions demonstrated the separation of EI RVV proteins in GF peaks according to their molecular mass (Figs. 4.7a,b); nevertheless, no proteins bands could be observed in the GF10 fractions. In addition, significant differences were observed in SDS-PAGs of the GF fractions of EI RVV (B) and EI RVV (N) under non-reduced and reduced

conditions, and these variations were more prominent from fractions GF5 to GF9 (Figs. 4.7a,b). In particular, the ~15 kDa band in GF8 of EI RVV (B) (reduced) was absent in EI RVV (N) under the same SDS-PAGE condition (Figs. 4.7a,b).

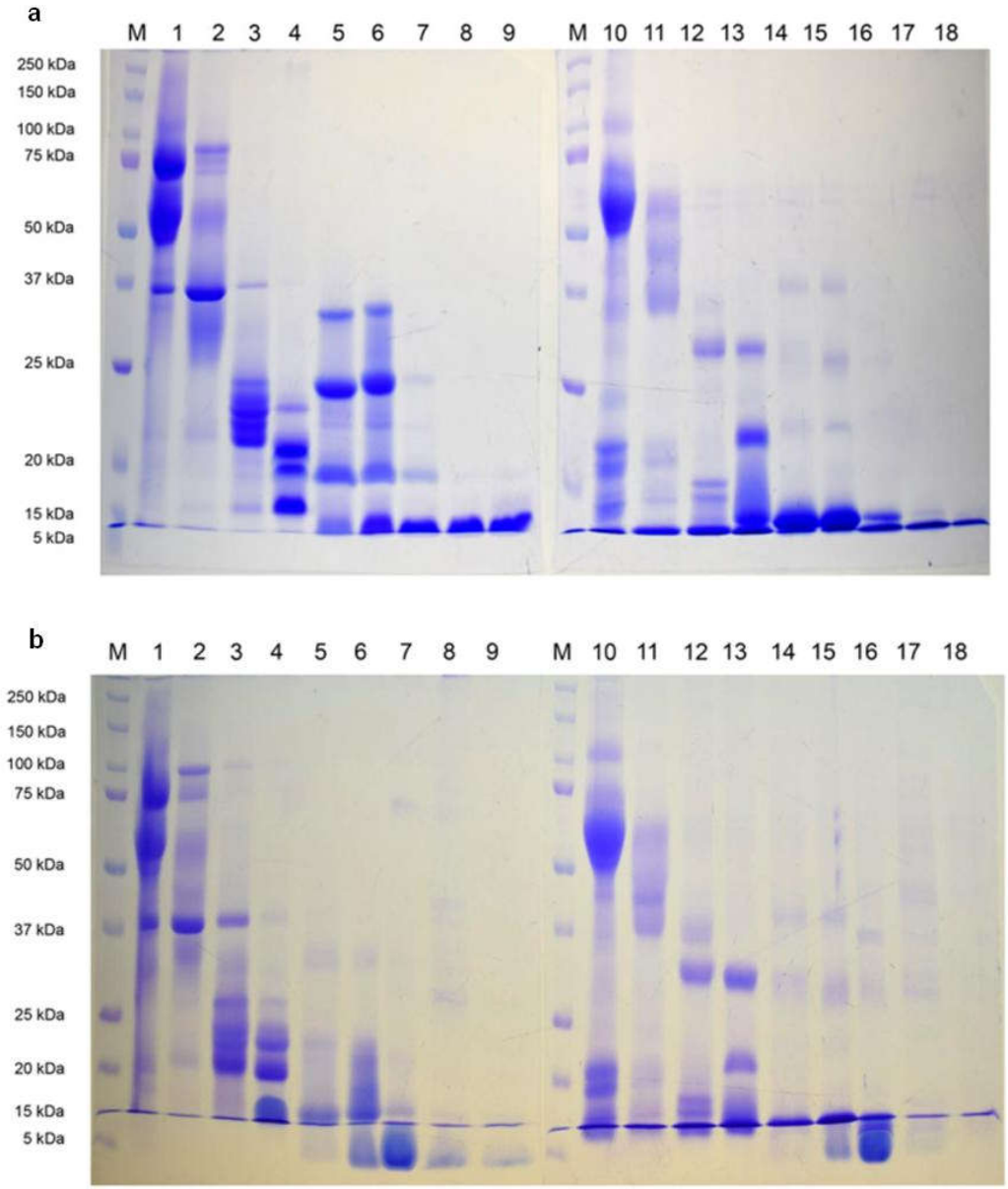


Fig. 4.7. 12.5% SDS-PAGE analysis of GF fractions of **a.** EI RVV (B) and **b.** EI RVV (N) under non-reduced and reduced conditions. Lanes M represent protein molecular markers; lanes 1 to 9 and 10 to 18 represent fractions GF1 to GF9 (40 µg), under non reduced and reduced conditions, respectively.

4.1.2.5 De-complexation of SI RVV by SDS-PAGE

SI RVV was de-complexed using 1D SDS-PAGE analysis under reduced conditions. The SI RVV proteins were distributed in the molecular weight range of ~6 kDa to 130 kDa. The lane was then divided into 10 gel sections (Fig. 4.8), which were excised, digested in-gel with trypsin and subjected to LC-MS/MS analysis (sections 3.2.1.5 to 3.2.1.7).

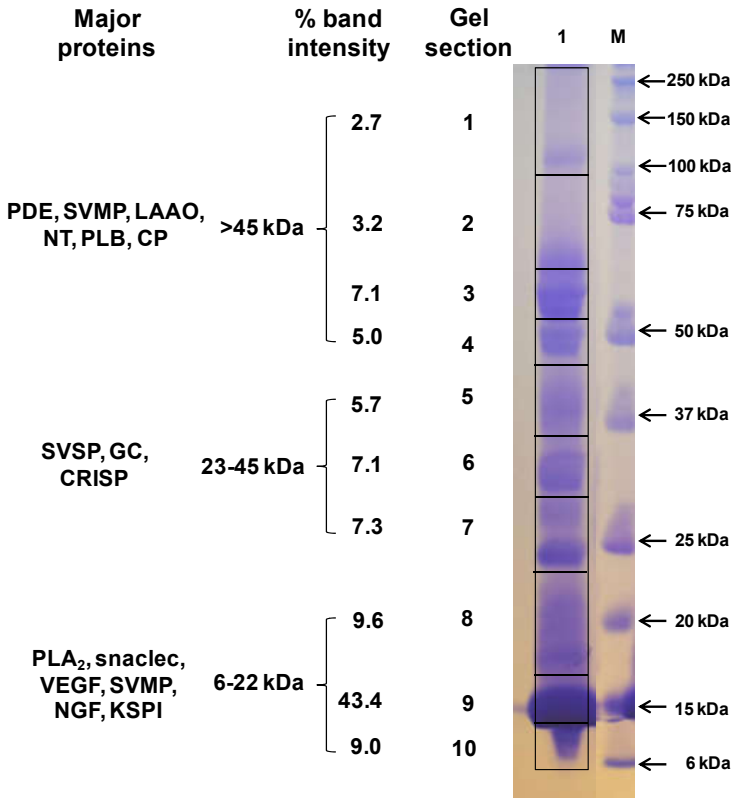


Fig. 4.8. 12.5% SDS-PAGE analysis of SI RVV (500 µg protein) under reduced condition (lane 1). Lanes M contain protein molecular markers. The gel sections were excised for ESI-LC-MS/MS analysis, the relative intensities of the excised bands were determined by densitometry analysis, the molecular mass range of the bands and the major protein families identified in each band by proteomic analysis are shown in the left side panel.

4.1.3 Proteomic analysis of WI, EI, and SI RVV samples

4.1.3.1 The proteome composition of WI RVV sample

ESI-LC-MS/MS analysis of the 137 AEX fractions of WI RVV against Viperidae protein entries of the NCBI database led to an initial identification of 1362

redundant protein entries. However, following the identification criteria mentioned in the Methods section (section 3.2.1.7), a total of 55 distinct enzymatic and non-enzymatic proteins belonging to 13 snake venom protein families were identified in WI RVV (Table 4.3a; Fig. 4.9a). The alignment of MS/MS-derived peptide sequences of WI RVV with the homologous proteins from the Viperidae entries of NCBI database is shown in Figure 4.9b. Further, all the identified peptide ions in WI RVV, their m/z, charge (z), the score for the ID, and ΔM (Da) are shown in Table 4.3b.

The enzymatic proteins identified in WI RVV include PLA_2 (32.5%), SVMP (24.8%), SVSP (8.0%), PDE (1.4%), NT (0.4%), LAAO (0.3%), and phospholipase B (PL B) (0.1%), while the non-enzymatic proteins were Kunitz-type serine protease inhibitor (KSPI) (12.5%), cysteine-rich secretory protein (CRISP) (6.8%), disintegrin (Dis) (4.9%), nerve growth factor (NGF) (4.8%), vascular endothelial growth factor (VEGF) (1.8%), and snake venom lectin-like proteins (snaclec) (1.8%) (Fig. 4.9a).

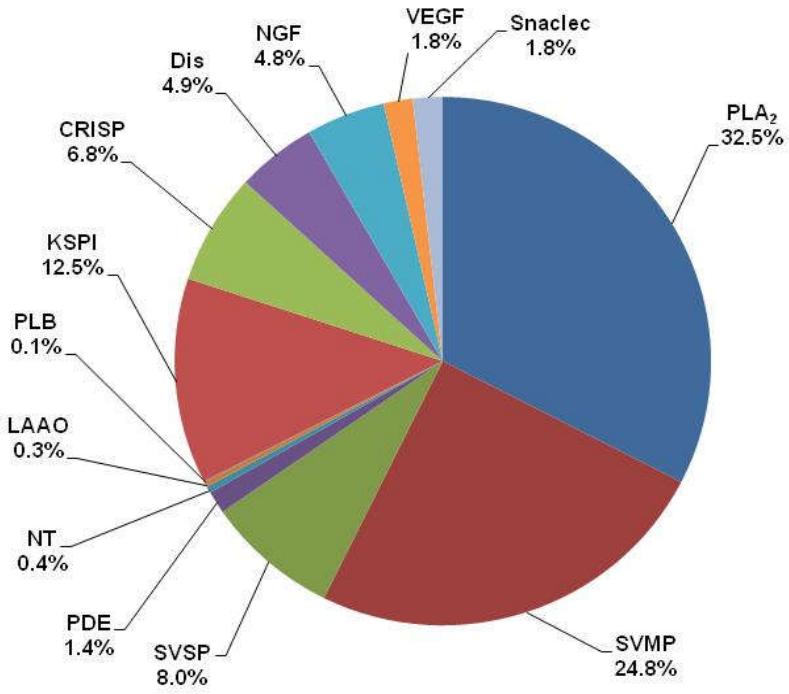


Fig. 4.9a. Protein family composition of WI RVV proteome. The pie chart represents the relative occurrence of different enzymatic and non-enzymatic protein families of WI RVV. Abbreviations: PLA_2, phospholipase A_2; SVMP, snake venom metalloprotease; SVSP, snake venom serine protease; PDE, phosphodiesterase; NT, nucleotidase; LAAO, L-amino acid oxidase; PLB, phospholipase B; KSPI, Kunitz-type serine protease inhibitor; CRISP, cysteine-rich secretory protein; Dis, disintegrin; NGF, nerve growth factor; VEGF, vascular endothelial growth factor.

Table 4.3a. Summary of the identified proteins in WI RVV by LC-MS/MS analysis followed by database search against the Viperidae family (taxid 8689) of proteins of the NCBI database.

Protein description	Accession no. (gi|)	Relative abundance (%)	Protein score	% Coverage	MW (kDa)	Source organism	GF peak(s)
Enzymatic proteins							
Phospholipase A_2							
Basic phospholipase A_2	71912223	0.4	11115.2	66.4	16.3	*D. russelii*	4
Basic phospholipase A_2 3	298351762	4.6	7409.7	76.0	13.7	*D. r. russelii*	1,2,3,4,5,6,7,9
Basic phospholipase A_2 RVV-VD	3914259	4.7	5514.4	57.0	13.6	*D. r. russelii*	1,2,3,4,6,8,9
Ammodytin I1(D) isoform	50874384	2.9	1203.5	43.5	15.4	*Vipera ammodytes montandoni*	3,5,6,7,9,10
Basic phospholipase A_2 homolog	27151648	0.5	704.1	20.5	13.9	*Gloydius halys*	5
Basic phospholipase A_2 VRV-PL-VIIIa	24638087	3.3	688.5	75.2	13.6	*D. r. russelii*	1,6,9
Acidic phospholipase A_2 DsM-A2/DsM-A2'	408407661	5.4	557.0	74.6	15.6	*D. siamensis*	3,5,6,7,8,9,10
Acidic phospholipase A_2 Cvv-E6b	82209451	2.9	544.0	10.1	15.4	*Crotalus viridis viridis*	5
Acidic phospholipase A_2 RV-7	400714	6.0	530.6	69.6	15.4	*D. siamensis*	1,2,3,5,6,7,8,9,10
Chain H, Structure Of D.toxin	149241831	0.3	460.3	34.4	14.0	*D. siamensis*	3,5,7,9
Acidic phospholipase A_2 Ts-A3	82201337	0.01	443.2	10.1	15.5	*Trimeresurus stejnegeri*	5

Protein description	Accession no. (gi|)	Relative abundance (%)	Protein score	% Coverage	MW (kDa)	Source organism	GF peak(s)
Acidic phospholipase A_2 homolog vipoxin A chain	2851544	0.1	312.1	45.1	13.6	*V. a. meridionalis*	3,5,6
Ammodytin I1(B') variant	50874310	0.4	307.8	48.6	15.4	*V. berus berus*	8,10
Ammodytin I1(F) isoform	50874356	0.2	278.8	47.8	15.4	*V. aspis atra*	9,10
Acidic phospholipase A_2 ammodytin I1	25453141	0.1	231.0	36.2	15.4	*V. a. ammodytes*	1,2,10
Vaspin acidic subunit (1) variant	50874232	0.5	150.4	39.9	15.5	*V. a. aspis*	3,5,9
Basic phospholipase A_2 RV-4	400713	0.01	97.6	23.9	15.5	*D. siamensis*	1,3
Snake venom metalloprotease							
Chain A, venom metalloproteinase	162329887	1.8	942.0	26.2	47.6	*D. siamensis*	2,5,6
Coagulation factor X activating enzyme light chain	251205	1.0	441.9	33.3	14.5	*D. russelii*	2,3
Factor X activator light chain 2	300079896	7.4	404.7	22.2	18.3	*D. r. russelii*	1,2
Coagulation factor X-activating enzyme beta-chain	73621140	2.9	375.4	23.4	18.3	*D. siamensis*	1
Factor X activator heavy chain	300079900	11.7	329.2	13.3	69.5	*D. r. russelii*	1,2,3,5,6,9
Snake venom serine protease							
Venom serine proteinase-like protein 2	13959655	1.9	484.9	8.9	28.9	*Macrovipera lebetina*	2

Protein description	Accession no. (gi|)	Relative abundance (%)	Protein score	% Coverage	MW (kDa)	Source organism	GF peak(s)
Serine protease, partial	297593758	0.3	222.9	12.7	28.8	*E. coloratus*	2
Beta-fibrinogenase-like	765684342	1.9	181.3	13.3	28.0	*D. siamensis*	2,3
Factor V activator RVV-V alpha	134129	2.8	161.4	20.3	26.2	*D. siamensis*	1,2,3
Serine protease VLSP-3	380875417	0.8	103.1	12.0	28.3	*M. lebetina*	2
Thrombin-like enzyme	38146946	0.3	59.2	5.9	26.5	*G. shedaoensis*	3
Phosphodiesterase							
Phosphodiesterase	586829527	1.38	964.4	17.4	96.1	*M. lebetina*	1, 2
5'-Nucleotidase							
Snake venom 5'-nucleotidase	395455152	0.2	151.3	6.8	64.4	*G. brevicaudus*	1
5'-nucleotidase, partial	586829529	0.2	121.4	11.5	45.0	*M. lebetina*	1
L-amino acid oxidase							
L-amino-acid oxidase	395406796	0.3	366.3	9.9	56.9	*D. r. russelii*	1,2
L-amino acid oxidase Lm29	704043548	0.01	54.4	3.7	58.5	*Lachesis muta*	1
Phospholipase B							
Phospholipase B	727360709	0.05	161.9	6.5	64.5	*E. coloratus*	1

Protein description	Accession no. (gi|)	Relative abundance (%)	Protein score	% Coverage	MW (kDa)	Source organism	GF peak(s)
Non-enzymatic proteins							
Kunitz-type serine protease inhibitor							
Kunitz-type protease inhibitor	379647506	0.4	2751.7	51.1	10.4	*D. russelii*	4
Kunitz protease inhibitor-II	87130864	0.1	1635.1	25.0	9.9	*D. r. russelii*	4
Kunitz-type serine protease inhibitor B2	239977248	0.9	1311.9	34.5	9.3	*D. siamensis*	1,2,3,6,7,8,9
Kunitz-type serine protease inhibitor 4	123913154	3.2	719.1	52.4	9.5	*D. r. russelii*	4,5,6,7,8
Kunitz-type serine protease inhibitor B1	239977245	3.0	423.7	48.8	9.3	*D. siamensis*	6,7
Kunitz-type serine protease inhibitor B4	239977254	3.0	351.9	39.3	9.4	*D. siamensis*	5,6,7,8,9
Kunitz-type serine protease inhibitor C6	239977259	0.1	223.0	43.8	10.3	*D. siamensis*	6
Kunitz-type serine protease inhibitor C3	239977252	1.8	161.0	41.7	9.4	*D. siamensis*	3,5,6,7,8,9
Cysteine rich secretory protein							
Cysteine-rich secretory protein Dr-CRPK	190195321	6.7	160.1	30.1	26.7	*D. russelii*	1,2,3,4,5,9
Cysteine-rich secretory protein Ch-CRPKa, partial	190195307	0.1	147.5	12.2	24.7	*C. horridus*	2,3,5,6
Disintegrin							
Jerdostatin	292659514	4.9	183.4	45.7	4.9	*Protobothrops jerdonii*	6,7,8,9

Protein description	Accession no. (gi|)	Relative abundance (%)	Protein score	% Coverage	MW (kDa)	Source organism	GF peak(s)
Nerve growth factor							
Venom nerve growth factor	400499	4.8	128.5	31.6	13.3	*D. r. russelii*	1,2,3,4,5,6
Vascular endothelial growth factor							
Snake venom vascular endothelial growth factor toxin VR-1	327478537	1.7	650.9	34.0	16.3	*D. r. russelii*	1,2,3,4,5
Vascular endothelial growth factor A	327488518	0.01	55.7	9.4	22.4	*V. a. ammodytes*	6
Snaclec							
Dabocetin alpha subunit	300490462	0.01	1659.6	36.4	17.9	*D. r. russelii*	4,5
P68 alpha subunit	300490470	0.2	1090.2	61.4	18.0	*D. siamensis*	3,5,6,8
Snaclec 3	73620111	0.6	900.4	46.0	16.9	*D. siamensis*	1,2,3,5
Dabocetin beta subunit	300490464	0.04	756.2	26.7	18.0	*D. r. russelii*	3,4,5
Snaclec 4	73620112	0.9	443.1	49.3	16.8	*D. siamensis*	1,2,3,9
P31 beta subunit	300490488	0.01	113.2	16.0	17.4	*D. r. russelii*	3
P31 alpha subunit	300490478	0.01	111.8	34.5	18.2	*D. r. limitis*	3

Fig. 4.9b. Alignment of tryptic and semi-tryptic peptide sequences identified in WI RVV with Viperidae proteins from NCBI database. The protein alignment was done using Clustal Omega programme (https://www.ebi.ac.uk/Tools/msa/clustalo/). The number of proteins in each protein classes is shown in parenthesis. The distinct peptides obtained for each of the following proteins is highlighted in green or yellow (two colours have been used in case of adjacent distinct peptides). The amino acid substitutions within the overlapping distinct peptides obtained from MS/MS are highlighted in red colour. The LC-MS/MS identified peptides other than distinct peptides are shown in blue or red colour.

Phospholipase A_2 [17]

```
gi|24638087   ----------------SLLEFGKMILEETGKLAIPSYSSYGCYCGWGGKGTPKDATDRCCFVHDCCYGNLPDCNPKSDRYKYKRVNGAIVCEKGTSCENRICECDKAAAICFRQNL
gi|298351762  ----------------SLLEFGMMILEETGKLAVPFYSSYGCYCGWGGKATPKDATDRCCFVHDCCYGNLPDCNPKSDRYKYKRVNGAIVCEQGTSCENRICECDKAAAICFRRNL
gi|82209451   MRTLWILAVLLLGVEGNLVQFELLIMKVAKRSGLLSYSAYGCYCGWGGYGRPQDATDRCCFVHDCCYGKVTDCNPKTASYTYSEENGEIVCGGDDPCKKQVCECDRVAAICFRDNI
gi|82201337   MRTLWIMAVLLLGVEGSLIQFETLIMKVAKKSGMFSYSAYGCYCGWGGQGQPQDATDRCCFVHDCCYGKVTGCDPKMDIYTYSEENGDIVCGGDDPCRKAVCECDKAAAICFRDNK
gi|149241831  ----------------NLFQFARLIDAKQEAFSFFKYISYGCYCGWGGQGTPKDATDRCCFVHDCCYARVKGCNPKLVEYSYSYRTGKIVCGGDDPCLRAVCECDRVAAICFRENM
gi|408407661  MRTLWIVAVCLIGVEGNLYQFGEMINQKTGNFGLLSYVYYGCYCGWGGKGKPQDATDRCCFVHDCCYGRVKGCDPKTATYSYSFENGDIVCGGDDPCLRAVCECDRVAAICFRENM
gi|50874356   MRILWIVAVCLIGAEGHLSQFGDMINKKTGIFGIMSYIYYGCYCGWGGKGKPLDATDRCCFVHDCCYGRVNGCDPKLSTYSYSFENGDIVCGGDDPCLRAVCECDRVAAICFGENM
gi|50874310   MRTLWIVAVCLIGAEGNLSQFGDMINKKTGIFGIMSYIYYGCYCGWGGKGKPLDATDRCCFVHDCCYGRVKGCDPKMGTYSYSFQNGAIVCGGDDPCLRAVCECDRVAAICFGENM
gi|25453141   MRILWIVAVCLIGAEGHLSQFGDMINKKTGIFGIMSYIYYGCYCGWGGKGKPLDATDRCCFVHDCCYGRVNGCDPKMGTYSYSFQNGDIVCGGDDPCLRAVCECDRVAAICFGENM
gi|50874384   MRILWIVAVCLIGAEGHLSQFGDMINKKTGIFGIMSYIYYGCYCGWGGKGKPLDATDRCCFVHDCCYGRVNGCDPKMGTYSYSFENGDIVCGGDDPCLRAVCECDRVAAICFGENM
gi|27151648   ----------------NLIQFKKMIKKMTGKEPVVSYAFYGCYCGSGGRGKPKDATDRCCFVHNCCYEKVTGCDPKWDDYTYSWKNGTIVCGGDDPCKKEVCECDKAAAICFRDNL
gi|71912223   MRTLWIVAVCLIGVEGNLLQFGRMIFRMTAKNPLSSYSNYGCYCGWGGKGKPQDATDRCCFVHDCCYEKVNDCNPKTATYSYSFENGGIVCGDRDPCKRAVCECDRVAATCFRDNL
gi|3914259    ----------------NLFQFAEMIVKMTGKNPLSSYSDYGCYCGWGGKGKPQDATDRCCFVHDCCYEKVKSCKPKLSLYSYSFQNGGIVCGDNHSCKRAVCECDRVAATCFRDNL
gi|400713     MRTLWIVAVCLIGVEGNLYQFARMINGKLGAFSVWNYISYGCYCGWGGQGTPKDATDRCCFVHDCCYGGVKGCNPKLAIYSYSFQFGNIVCGRNNGCLRTICECDRVAANCFHQNK
gi|400714     MRTLWIVAVCLIGVEGNLFQFGEMILEKTGKEVVHSYAIYGCYCGWGGQGRAQDATDRCCFVHDCCYGTVNDCNPKTATYSYSFENGDIVCGDNDLCLRTVCECDRAAAICLGQNV
gi|2851544    ----------------NLFQFGDMILQKTGKEAVHSYAIYGCYCGWGGQGRAQDATDRCCFAQDCCYGRVNDCNPKTATYTYSFENGDIVCGDNDLCLRAVCECDRAAAICLGENV
gi|50874232   MRTLWIVAVCLIGVEGNLFQFGDMILQKTGKEAVHSYAIYGRYCGWGGQGRAQDATDRCCFAQDCCYGRVNDCNPKMATYTYSFENGDIVCGDNDLCLRAVCECDRAAAICLGENV
```

```
gi|24638087    NTYSK-KYMLYPDFLCKGEL-KC
gi|298351762   NTYSK-IYMLYPDFLCKGEL-KC
gi|82209451    PSYDN-KYIQFPAKNCQEKPEPC
gi|82201337    DTYDWKKYWRFPTKNCQESV-PC
gi|149241831   NTYDK-KYMLYSIFDCKEESDQC
gi|408407661   NTYDK-KYMLYSIFDCKEESDQC
gi|50874356    NTYDK-KYMLYSLLDCKEESDQC
gi|50874310    NTYDK-KYMLYSLFDCKEESEQC
gi|25453141    NTYDK-KYMLYSLFDCKEESEQC
gi|50874384    NTYDK-KYMLYSLFDCKEESEQC
gi|27151648    KTYKK-RYMTYPNILCSSKSEKC
gi|71912223    NTYDK-KYRKYPPSQCTGTE-QC
gi|3914259     NTYDK-KYHNYPPSQCTGTE-QC
gi|400713      NTYNK-EYKFLSSSKCRQRSEQC
gi|400714      NTYDK-NYEYYSISHCTEESEQC
gi|2851544     NTYDK-NYEYYSISHCTEESEQC
gi|50874232    NTYDK-NYEYYSISHCTEESEQC
```

Snake venom metalloprotease [5]

```
gi|300079900   MMQVLLVTISLAVFPYQGSSIILESGNVNDYEVVYPQKVTAMPKGAVKQPEQKYEDTMQYEFEVNGEPVVLHLEKNKILFSEDYSETHYYPDGREITTNPPVEDHCYYHGHIQNDG
gi|162329887   ------------------------------------------------------------------------------------------------------------------------
gi|251205      ------------------------------------------------------------------------------------------------------------------------
gi|300079896   ------------------------------------------------------------------------------------------------------------------------
gi|73621140    ------------------------------------------------------------------------------------------------------------------------

gi|300079900   HSSASISACNGLKGHFKLRGEMYFIEPLKLSNNEAHAVYKYENIEKEDETPKMCGVTQTNWESDKPIKKASQLVSTSAQFNKAFIELIIIVDHSMAKKCNSTATNTKIYEIVNSAN
gi|162329887   ------------------------------------------------------------------------LVSTSAQFNKIFIELVIIVDHSMAKKCNSTATNTKIYEIVNSAN
gi|251205      ------------------------------------------------------------------------------------------------------------------------
```

```
gi|300079896  ------------------------------------------------------------------------------------------------------------MGR
gi|73621140   ------------------------------------------------------------------------------------------------------------MGR

gi|300079900  EIFNP---LNIHVTLIGV--EFWCDRDLINVTSSADETLDSFGEWRASDLMTRKSHDNALLFTDMRFDLNTLGITFLAGMCQAYRSVGIVQVQGNRNFKTAVIMAHELSHNLGM--
gi|162329887  EIFNP---LNIHVTLIGV--EFWCDRDLINVTSSADETLNSFGEWRASDLMTRKSHDNALLFTDMRFDLNTLGITFLAGMCQAYRSVGIVQEQGNRNFKTAVIMAHELSHNLGM--
gi|251205     --------------------VLDCPSGWLSYEQHCYKGFNDLKNWTDAEKFCTEQKKGSHLVSLHS--------------------------------REEEEFVVNLISENLEY--
gi|300079896  FIFVSFGLLAVFLSLSGTGAGLDCPPDSSPYRYFCYRVFKLRKSWEAAERFCMEHPNNGHLVSIES--------------------------------MEEAEFVAKLLSNTTGKFI
gi|73621140   FISVSFGLLVVFLSLSGTGAGLDCPPDSSLYRYFCYRVFKEHKTWEAAERFCMEHPNNGHLVSIES--------------------------------MEEAEFVAKLLSNTTGKFI

gi|300079900  ---------YHDGKNCICNDSSCVMSPVLSDQPSKLFSNCSIHDYQRYLTRYKPKCILYPPLRKDIVSPPVCGNEIWEEGEECDCGSPADCQNPCCDAATCKLKPGAECGNGLCCY
gi|162329887  ---------YHDGKNCICNDSSCVMSPVLSDQPSKLFSNCSIHDYQRYLTRYKPKCIFNPPLRKDIVSPPVCGNEIWEEGEECDCGSPANCQNPCCDAATCKLKPGAECGNGLCCY
gi|251205     PATWIGLG--NMWKDCRM---------EWSDRGNVKYKALAEES------------------YCLIM----ITHEKEWKSM-TCNFIAPVVCKF-----------------------
gi|300079896  THFWIGLRIKDKEQECSS---------EWSDGSSVSYDNLGKEE------------------FRKCFVLQKESGYRMWFNH-KCEEEYPFVCKVP----------P-----------
gi|73621140   THFWIGLMIKDKEQECSS---------EWSDGSSVSYDKLGKQE------------------FRKCFVLEKESGYRMWFNR-NCEERYLFVCKVP----------P-----------

gi|300079900  QCKIKTAGTVCR--RARNECDVPEHCTGQSAECPRDQLQQNGQPCQNNRGYCYNGDCPIMRNQCISLFGSRATVAKDSCFQENLKGSYYGYCRKENGRKIPCAPQDVKCGRLFCLN
gi|162329887  QCKIKTAGTVCR--RARDECDVPEHCTGQSAECPRDQLQQNGKPCQNNRGYCYNGDCPIMRNQCISLFGSRANVAKDSCFQENLKGSYYGYCRKENGRKIPCAPQDVKCGRLFCLN
gi|251205     ------------------------------------------------------------------------------------------------------------
gi|300079896  ------------------------EC--------------------------------------------------------------------------------
gi|73621140   ------------------------EC--------------------------------------------------------------------------------

gi|300079900  NSPRNKNPCNMHYSCMDQHKGMVDPGTKCEDGKVCNNKRQCVDVNTAYQSTTGFSQI
gi|162329887  NSPRNKNPCNMHYSCMDQHKGMVDPGTKCEDGKVCNNKRQCVDVNTAYQSTTG----
gi|251205     ------------------------------------------------------
gi|300079896  ------------------------------------------------------
gi|73621140   ------------------------------------------------------
```

Snake venom serine protease [6]

```
gi|765684342  MVLIKVLANLLVLQLSYAQKSSELVVGGDECNINEHRSLVFLYNN---SFGCSGTLINQQWVLSAVHCDMENVRIYLGVHNLTLRNNA-EIRLPEERFFCLSNKNYTKWDKDIMLI
gi|380875417  MVLIRVLANLLVLQLSYAQKSSELVIGGDECNINEHRSLVYLYND--SNFQCGGTLINQEWVLSAAHCDMENMEIYLGVHNLSLPNKDQKRRDPKEKFFCLSSKNYTKWDKDIMLI
gi|38146946   ------------------------MVIGGDECNINEHRFLVALYTSRFRTLFCGGTLINQEWVLTAAHCDRKNFRIKLGIHSKKVPNEDEQTRVPKEKFFCLSSKNYTLWDKDIMLI
gi|13959655   MVLIRVLANLLVLQLSYAQKSSELVIGGDECNINEHPFPVALHTARSKRFYCAGTLINQEWVLTAARCDRKNIRITLGVHSKNVPNEDQQIRVPKEKFFCLSSKTYTRWDKDIMLI
gi|297593758  MVLIRVLANLLVLQLSYAQRSSELVTGGAECDINEHPFLVALHTARSKRFHCTGTLIDNQWVLTAARCDRKNIRIKVGVHNKNKRNKDEMMRVPAEKFFCASSKTYTRWDKDIMLI
gi|134129     ------------------------VVGGDECNINEHPFLVALYTSTSSTIHCGGALINREWVLTAAHCDRRNIRIKLGMHSKNIRNEDEQIRVPRGKYFCLNTKFPNGLDKDIMLI

gi|765684342  KLDRPVKTSTYIAPLSLPSSPPRVGSVCRIMGWGAITSPNETFPGVTHCANINILPYSVCRAAYKG--LPAQSRTLCGGILEGGIGSCMGDSGGPLICNGEMHGIVAWGDDTCAQP
gi|380875417  KLNRPVKTSTHIAPLSLPSSPPSVGSVCRIMGWGTVTSPNETLLDVPHCANINILNYTVCRAASPR--LPTQSRTLCAGILQGGIDACKGDSGGPLICNGQIQGIVSWGNHPCAQP
gi|38146946   RLDSPVKNSTHIAPFSLPSSPPSVGSVCRIMGWGRISPTEETYPDVPHCVNINLLEYEMCRVPYPEFGLPATSRTLCAGILEGGKDTCRGDSGGPLICNGQFQGIASWGDDPCAQP
gi|13959655   RLKKPVNDSTHIVPLSLPSSPPSVGSVCRIMGWGTITTTKVTYPDVPHCANINMFDYSVCRKVYRK--LPEKSRTLCAGILQGGIDSCKVDNGGPLICNGQIQGIVSWGGHPCAQP
gi|297593758  RLKRPVNGSTHIAPLSLPSNPASVDSECRIMGWGTITTTKVTYPDVPHCANIKIFDYSVCREAYRK--LPEKSRTLCAGILEGGIDSCKADTGGPLICNGQFQGIASWGGKPCAQP
gi|134129     RLRRPVTYSTHIAPVSLPSRSRGVGSRCRIMGWGKISTTEDTYPDVPHCTNIFIVKHKWCEPLYPW--VPADSRTLCAGILKGGRDTCHGDSGGPLICNGQIQGIVAGGSEPCGQH

gi|765684342  HKPVHYTKVYDYTDWIQSIIAGNTAATCPP
gi|380875417  LKPGHYTHVFDYTDWIQSIIAGNTTATCPP
gi|38146946   HKPAAYTKVFDHLDWIKSIIAGNTDASCPP
gi|13959655   HKPALYTNVFDYTDWIQSIIAGNITATCPP
gi|297593758  LKPALYTNVFDYNDWIKSIIAGNTDATCPP
gi|134129     LKPAVYTKVFDYNNWIQNIIAGNRTVTCPP
```

Phosphodiesterase [1]

```
gi|586829527  MIQQKVLFISLVAVALGLGLGLGLKESVEPQVSCRYRCNETFSKMASGCSCDDKCTERQACCQDYEDTCVLPTQSWSCSKLRCSEKRMANVLCSCSEDCLEKKDCCTDYKSICKGE
gi|586829527  TSWLKDQCASSSAAQCPSGFEQSPLILFSMDGFRAGYLETWDSLMPNINKLKTCGTHAKYMRAVYPTKTFVNHYTIVTGLYPESHGIIDNNIYDVTLNLNFSLSAPTMTNPAWWGG
gi|586829527  QPIWHTVTYQGLKAATYFWPGSEVKINGSYPTIYKVYNKSIPFEARVTEVLKWLDLPKAERPDFVTLYIEEPDTTGHKFGPVSGEIIMALQMADRTLGMLMEGLKQRNLHNCVNLI
gi|586829527  LLADHGMEQISCNRLEYMTDYFDKVDFFMYEGPAPRIRSKNVPKDFYTFDSEGIVRNLTCQKPKQYFKAYLAKDLPKRLHYVNNIRIDKVNLMVDQQWMAVRNKNYNRCNGGTHGY
gi|586829527  DNEFKSMQAIFLAHGPGFKGKNEVTSFENIEVYNLMCDLLKLKPAPNNGTHGSLNHLLKNPFYNPSPAKEQTSPLSCPFGPVPSPDVSGCKCSSITDLGKVNERLNLNNQAKTESE
```

```
gi|586829527  AHNLPYGRPQVLQNHSKYCLLHQAKYISAYSQDVLMPLWSSYTINKSPPTSVPPSASDCLRLDVRIPAAQSQTCSNYQPDLTITPGFLYPPNFGSSNFEQYDALITSNLVPMFKGF
gi|586829527  TRLWNYFHGTLLPKYARERNGLNVISGPIFDYNYDGHFDSYDTIKEYVNDTKIPIPTHFFVVLTSCENQINTPLNCPGSLKVLSFILPHRPDNSESCADTSPDNLWVEERIQTHTA
gi|586829527  RVRDVELLTGLNFYSGLKQPLPETLQLKTFLPIFVNPVN
```

5'-Nucleotidase [2]

```
gi|395455152  MQTPKRRRGAQGCPRSSPSPPLLLLVGAVWFCAALSVAAGSFELTILHTNDVHARVEQTSRDSGKCTGQDCYGGVARRATKIRELRANHSHVLLLDAGDQYQGTIWFSFFKGREVV
gi|586829529  ------------------------------------------------------------------------------------------------------------

gi|395455152  KFMNSLGYDAMALGNHEFDNGLAGLLDPLLKHANFPILSANIRPKGSIASNISGYILPYKIINVGSEKVGIIGYTTKETPVLSNPGPYLEFRDEVEELQKHANKLTTLGVNKIIAL
gi|586829529  ------------------------------------------------------------AREKVGIIGYTTKETPVLSNPGPYLEFRDEVEELQIHANKLTTLGVNKIIAL

gi|395455152  GHSGFFEDQRIARKVKGVDVVVGGHTNTFLYTGSPPSTEVAAGNYPFMVKSDDGRQVPVVQAYAFGKYLGYLNVIFDDKGNVIKSSGNPILLNKNISEDQDVKAEVNKMKIQLHNY
gi|586829529  GHSGFFEDQRIARKVKGVDVVVGGHTNTFLYTGSPPSTEVPAGNYPFMVQSDDGRQVPVVQAYAFGKYLGYLNVVFNDKGNVIKASGNPILLNKDIPEDQVVKAQVNKMKIQLQNY

gi|395455152  SSQEIGKTIVYLNGTTQACRFHECNLGNLICDAVIYNNVRHPDYNEWNHVSMCIVNGGGIRSPIDERANNGTITLEELTAVLPFGGTFDLLQIKGCALKQAFEHSVHRHGQGMGEL
gi|586829529  YSQEIGKTIVYLNGTTQACRFHECNLGNLICDAVIYNNLRHPDDNEWNHVSMCIVNGGGIRSPIDERANNGIITLEELTSVLPFGGTFDLLQIKGSALKQAFEHSVHRHGQGTGEL

gi|395455152  LQVSGIKVVYDLSRKPGSRVVSLNVLCTECRVPTYVPLEKEKTYKLLLPSFLAGGGDGYHMLKGDSSNHSSGNLDISIVGDYIKRMGKVFPAVEGRVIFSAGTLFQAQLFLTWGLC
gi|586829529  LQVSGIKVVYDLSQKPGSRVVSLNVLCTKCRVPTYVPLEMEKTYKVLLPSFLATGGDGYHMLKGDSSNHNSGDLDISIVGDYIKRMEKVFPAVEGRVTFLDGTLFQAQLFLTWGLC

gi|395455152 ISLLYFIL
gi|586829529 ISLLFFIL
```

L-amino acid oxidase [2]

```
gi|395406796  MNVFFMFSLLFLATLGSCADDKNPLEECFREDDYEEFLEIAKNGLKKTSNPKHIVIVGAGMSGLSAAYVLAGAGHKVTVLEASERPGGRVRTHRNVKEGWYANLGPMRVPEKHRII
gi|704043548  MNVFFMFSLLFLAALGSCADDRNPLGECFRETDYEEFLEIAKNGLRATSNPKHVVIVGAGMSGLSAAYVLAEAGHQVTVLEASERAGGRVRTYRNDKEGWYANLGPMRLPEKHRIV
```

```
gi|395406796  REYIRKFGLKLNEFVQETENGWYFIKNIRKRVGEVKKDPGLLKYPVKPSEAGKSAGQLYQESLGKAVEELKRTNCSYILNKYDTYSTKEYLIKEGNLSPGAVDMIGDLLNEDSGYY
gi|704043548  REYIRKFGLQLNEFHQENDNAWHFIKNIRKRVGEVKEDPGLLQYPVKPSEEGKSAGQLYEESLGKVAEELKRTNCSYILNKYDTYSTKEYLLKEGNLSPGAVDMIGDLLNEDSGYY

gi|395406796  VSFIESLKHDDIFAYEKRFDEIVGGMDQLPTSMYRAIEESVHFKARVIKIQQNAEKVTVTYQTTQKNLLLETADYVIVCTTSRAARRITFKPPLPPKKAHALRSVHYRSGTKIFLT
gi|704043548  VSFIESLKHDDIFGYEKRFDEIVDGMDKLPTSMYQAIKEKVRFNARVIKIQQNDREVTVTYQTSANEMSPVTADYVIVCTTSRATRRITFEPPLPPKKAHALRSVHYRSGTKIFLT

gi|395406796  CTKKFWEDDGIQGGKSTTDLPSRFIYYPNHNFTTGVGVIIAYGIGDDANFFQALNLNECADIVFNDLSSIHQLPKKDLQTFCYPSIIQKWSLDKYAMGAITTFTPYQFQHFSEALT
gi|704043548  CTKKFWEDDGIRGGKSTTDLPSRFIYYPNHNFTSGVGVIIAYGIGDDANFFQALDFKDCGDIVINDLSLIHQLPKKDIQTFCYPSMIQRWSLDKYAMGGITTFTPYQFQHFSEALT

gi|395406796  APVGRIFFAGEYTANAHGWIDSTIKSGLTAARDVNRASEL------------
gi|704043548  APFKRIYFAGEYTAQFHGWIDSTIKSGLTAARDVNRASENPSGIHLSNDNEL
```

Phospholipase B [1]

```
gi|727360709  MIRFGNRSSSDKRRQRCWSWYWVGLLLLWAVAETRADIHYATVYWLEAEKSFQIQDVLDRNGDAYGYYNDTIQSTGWGILEIKAGYGNQHISNEILMYAAGFLEGYLTASHMSDHF
gi|727360709  ANLFPLMIKNVIIEQKVKDFIQKQDEWTRQQIKNNMDDPFWRNAGYVIAQLDGLYMGNVEWAKRQKRTPLNDFEINFLNALGDLLDLTTAFDSQLRKSDFLSMPDVSRIYQWDMGH
gi|727360709  CSALIKVLPGYENIYFAHSSWFTYAATLRIYKHWDFKITDPQTKTGRASFSSYPGLLVSLDDFYILGSGLIMLQTTNSVFNLFLLKQVVPESLFAWERVRIANMMADSGKTWAQIF
gi|727360709  EKENSGTYNNQYMILDTKKIKLQRSLEDGTLYIIEQIPKLVKYSDQTEVLRHGYWPSYNIPFHKVIYNMSGYTEYVQKLGLEFSYEMAPRAKIFRRDQGKVTDMESMKHIMRYNNY
gi|727360709  KEDPYTKHNPCNTICCRQDLSRKTPVPAGCYDSKISDISMAAKFTTYAINGPPVEKDLPVFSWVHFNQTKHQSLPESYNFDFVTMKPVL
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Kunitz-type serine protease inhibitor [8]

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gi|87130864   MSSGGLLLLLGLLTLWAEPTPISGQDRPKFCFLRPDFGRYGHPRPRFYYNPATNQCQGFLAQRSRENTNNFDTRDKCRQTCGRK------------
gi|239977252  MSSGGLLLLLGLLTLWAELTPISGHDRPKFCYLPADPGECMAYIRSFYYDSESKKCKEFIYGGCHGNANNFPTRDKCRQTCRGK------------
gi|239977245  MSSGGLLLLLGLLTLWAELTPISGHDRPKFCYLPADPGECLAHMRSFYYDSESKKCKEFIYGGCHGNANKFPSRDKCRQTCGGK------------
gi|379647506  MSSGGLLLLLGLLTLWAELTPISGQDRPKFCNLAPESGRCRGHLRRIYYNPDSNKCEVFFYGGCGGNDNNFETRKKCRQTCGAPFKGRPT------
gi|239977248  MSSGGLLLLLGLLTLWAELTPISGHDRPTFCNLAPESGRCRGHLRRIYYNLESNKCNVFFYGGCGGNDNNFETRDECRQTCGGK------------
gi|239977254  MSSGGLLLLLGLLTLWAELTPISGHDRPTFCNLAPESGRCRGHLRRIYYNLESNKCEVFFYGGCGGNDNNFSTWDECRHTCVGK------------
gi|123913154  MSSGGLLLLLGLLTLWAELTPISGQDRPKFCHLPVDSGICRAHIPRFYYNPASNQCQGFIYGGCGGNANNFETRDQCRHTCGGK------------
gi|239977259  MSSGGLLLLLGFLTLWAELTPISGQNRPMFCHLPADSGRCKAHIPRFYYNPASNQCQGFTYGGCGGNANNFETRDQCRHTCGASGNVGPRPRIASN
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Cysteine rich secretory protein [2]

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gi|190195321  MIAFIVLPILAAVLQQSSGSVDFDSESPRRPEIQNEIVDLHNSLRRSVTPTASNMLKMEWYPEAAANAERWAFRCILNHSPYNSRVIGGIKCGENIYMSPYPMKWTAIIHEWHKEK
gi|190195307  --------------------SVDFDSESPRKPEIQNEIVDLHNSLRRSVNPTASNMLKMEWYPEAAANAERWAYRCIESHSPRDSRVLEGIKCGENIYMSPVPIKWTEIIHGWHGEN

gi|190195321  KDFVYGQGASPANAVVGHYTQIVWYKSYRSGCAAAYCPSSEYNYFYVCQYCPAGNIIGKIATPYTSGPPCGDCPSACDNGLCTNPCSHHDEFTNCKDLVKQ-GCHSNYLKTKCPAS
gi|190195307  KNFKYGIGAEPSNAVTGHFTQIVWYKSYRVGCAAAYCPSSKYSYFYVCQYCPAGNIRGKTATPYKSGPPCGDCPSACDNGLCTNPCTKEDKYTNCKSLVQQAGCEDKQIQSDCSAI

gi|190195321  CFCHNEII
gi|190195307  CFCQNKII
```

Disintegrin [1]

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gi|292659514  AMDCTTGPCCRQCKLKPAGTTCWRTSVSSHYCTGRSCECPSYPGNG
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Nerve growth factor [1]

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gi|400499     HPVHNQGEFSVCDSVSVWVANKTTATDMRGNVVTVMVDVNLNNNVYKQYFFETKCKNPNPVPSGCRGIDAKHWNSYCTTTDTFVRALTMERNQASWRFIRINTACVCVISRKNDNFG
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Vascular endothelial growth factor [2]

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gi|327488518  MNFLLSWIHWGLAALLYFHNAKVLQAAPAQGDGDRQQGEVISFLTVYERSACRPVETMVDIFQEYPDEVEYIFKPSCVALMRCGGCCNDEALECVPTEVYNVTMEIMKLKPFQ-SQ
gi|327478537  -----------MA--AYLLAVAILFCI-QGWPSGTVQGQVRPFLDVYERSACQTRETLVSILQEHPDEISDIFRPSCVAVLRCSGCCTDESMKCTPVGKHTADIQIMRMNPRTHSS

gi|327488518  HIHPMSFQQHSKCECRPKKEVRIRQENHCEPCSERRKHLYKQDPLTCKCSCKFTDSRCKSKQLELNERTCRCEKPRR
gi|327478537  KMEVMKFMEHTACECRPRWKQGEPE----GPKEPRRGGVRAKFPFD--------------------------------
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Snaclec [7]

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gi|300490470  MGRFISVSFGLLVVFLSLSGTRADFDCPSGWSAHDQHCYKAFDEPKRSGDAETFCTEQANSGHLVSIESVEEAEFVAQLISENIKTPADYVWIGLRNQRKAQYCISKWTDGSSVIY
gi|300490478  MGRFISVSFGLLVVFLSLSGIGADLDCPSGWSAYDQHCYQAVDEPKSWADAEKFCTEQANSGHLVSIKSVGEANFVAQLASGFMQKDGIYVWIGLRDRRKEQQCRSEWTDGSKIIY
gi|300490488  MGRFISVSFSSLVVFLSLSGTEAGFSCPNGWSSFGQHCYKVIEPLKNWTDAEKFCREQHKGSHLASIHSSEEEAFVSKVASKVLKFG--SVRIGLNDPWH--NCNWEWSDNARFDY
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gi|300490464  MGRFISVGFGLLVVFLSLSGTGAKQDCLSDWSFYEGYCYKVFNEKKTWEDAEKFCNEQVNGGYLVSFRSSEEMDFVIRMTFPIFRFD--FFWIGLRDFWR--DCYWRWSDGVNLDY
gi|73620112   MGRFISISFGLLVVFLSLSGTEAAFCCPSGWSAYDQNCYKVFTEEMNWADAEKFCTEQKKGSHLVSLHSREEEKFVVNLISENLEYP--ATWIGLGNMWK--DCRMEWSDRGNVKY
gi|73620111   MGRFISVSFGLLVVFLSLSGTEAAFCCPSGWSAYDQNCYKVFTEEMNWADAEKFCTEQHKGSHLLSLHNIAEADFVLKKTLAMLKDG--VIWMGLNDVWN--ECNWGWTDGAKLDY
gi|300490462  MGRFISVSFGLLVVFLSLSGTGA--DCPSDWSSHEGHCYKVFKLLKTWEDAEKFCTQQANGWHLASIESVEEANFVAQLASETLTKSKYHAWIGLRDQSQRQQCSSHWTDGSAVSY

gi|300490470  KNVIERFIKNCFGLEKESDYRTWFNLSCGDDYPFVCKFPPRC
gi|300490478  VNWKEGESKMCQGLAKWTYFHKWDYVNCAEHYRFVCKFPPQY
gi|300490488  KAMTR--RPYCTVMVLKPDRIFWFNRGCEKFVSFVCKFLA--
gi|300490464  KAWSR--EPNCFVSKT--TDNQWLRWNCNDPRYFVCKSRVSC
gi|73620112   KALAE--ESYCLIMIT--HEKVWKSMTCNFIAPVVCKF----
gi|73620111   KAWNE--GTNCFVFKI--AKNHWSHMDCSSTHNFVCKFRV--
gi|300490462  ETVTK--YTKCFGLNKETKYHEWITLPCGDKNPFICKSWVLH
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Table 4.3b. List of all the proteins identified by LC-MS/MS analysis of anion-exchange fractions of WI RVV. The table shows the identified peptide ions, their mass, charge (z), the score for the ID, ΔM (ppm), and modified residues. Carbamidomethylated cysteine and oxidized methionine residues are represented as c and m (in lower cases).

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
Enzymatic proteins								
Phospholipase A_2								
Acidic PLA_2 RV-7	400714	530.6	69.6	(C)FVHDccYGTVNDcNPK(T)	165.5	3	1985.8	1.36
				(V)HDccYGTVNDcNPK(T)	148.6	2	1721.6	5.60
				(A)AIcLGQNVNTYDK(N)	145.5	2	1495.7	4.13
				(A)IcLGQNVNTYDK(N)	140.5	2	1424.7	2.62
				(I)cLGQNVNTYDK(N)	131.1	2	1294.6	3.03
				(C)LGQNVNTYDK(N)	124.3	2	1151.6	-1.79
				(L)GQNVNTYDK(N)	114.3	2	1020.5	4.44
				(R)AAAIcLGQNV(N)	112.5	2	998.5	0.19
				(R)AAAIcLGQNVNTYDKNYEYYSISHcTEESEQc(-)	108.7	3	3817.6	4.29
				(Y)GTVNDcNPK(M)	107.6	1	986.4	3.00
				(K)EVVHSYAIYGcYcGWGGQGR(A)	82.0	2	2319.0	2.35
				(R)AAAIcLGQNVNTYDK(N)	80.3	2	1637.8	0.73
				(K)NYEYYSISHcTEESEQc-	76.7	2	2198.8	4.18
				(K)TATYSYSFENGDIVcGDNDLcLR(T)	63.5	2	2670.1	-0.11
				(R)ccFVHDccYGTVNDcNPK(T)	59.6	2	2305.9	4.82
				(K)TGKEVVHSYAIYGcYcGWGGQGR(A)	39.4	3	2605.2	1.24
				(R)TVcEcDR(A)	27.8	2	939.4	-0.87
Basic PLA_2 VRV-PL-VIIIa	24638087	688.5	75.2	(K)DATDRccFVHDccYGNLPDcNPK(S)	209.4	4	2874.1	2.41
				(K)LAIPSYSSYGcYcGWGGKGTPK(D)	196.7	3	2409.1	2.52
				(R)QNLNTYSK(K)	110.3	2	967.5	5.19
				(K)GTPKDATDR(C)	109.0	2	960.5	1.60
				(T)PKDATDR(C)	96.7	2	802.4	-3.01
				(I)LEETGK(L)	87.7	1	676.4	4.32

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
				(K)KYmLYPDFLcK(G)	35.8	2	1535.7	6.13
				(R)VNGAIVcEKGTScENRIcEcDK(A)	35.7	3	2599.1	-9.72
				(K)LAIPSYSSYGcYcGWGGK(G)	27.0	2	2025.9	6.72
				(K)GTScENRIcEcDK(A)	27.0	2	1628.6	1.38
				(R)VNGAIVcEK(G)	25.5	2	988.5	-0.15
				(R)ccFVHDccYGNLPDcNPK(S)	17.8	3	2315.9	5.15
Basic PLA_2 RV-4	400713	97.6	23.9	(R)ccFVHDcc(Y)	103.6	2	1157.4	2.85
				(K)LAIYSYSFQR(G)	57.6	2	1247.6	1.25
				(R)ccFVHDccYGGVK(G)	49.4	2	1661.6	3.63
				(R)VAANcFHQNK(N)	41.7	2	1188.6	-0.60
Basic PLA_2 RVV-VD	3914259	5514.4	57.0	(K)YHNYPPSQcTGTEQc(-)	157.9	2	1841.7	2.22
				(-)NLFQFAEMIVK(M)	141.6	2	1339.7	4.30
				(R)ccFVHDccYEK(V)	134.9	3	1577.6	3.73
				(R)DNLNTYDKK(Y)	121.1	2	1110.5	4.59
				(D)NLNTYDKK(Y)	113.6	2	995.5	2.27
				(K)GKPQDATDR(C)	110.8	2	987.5	3.93
				(R)DNLNTYDK(K)	109.9	2	982.4	5.35
				(G)KPQDATDR(C)	106.7	2	930.5	3.52
				(N)LNTYDKK(Y)	105.5	2	881.5	2.51
				(R)VAATcFR(D)	95.4	2	824.4	4.28
				(K)PQDATDR(C)	94.8	2	802.4	1.32
				(R)AVcEcDR(V)	94.6	2	909.4	2.26
				(A)VcEcDR(V)	88.4	2	838.3	5.37
				(K)KYHNYPPSQcTGTEQc(-)	26.2	2	1969.8	0.59
Basic PLA_2 3	298351762	7409.7	76.0	(K)AAAIcFR(N)	94.8	2	808.4	3.81
				(R)IcEcDK(A)	88.9	2	824.3	4.64
				(R)NLNTYSK(I)	100.5	2	839.4	2.22
				(M)MILEETGK(L)	109.8	2	920.5	4.43
				(K)LAVPFYSSYGcYcGWGGK(A)	175.7	2	2071.9	4.56

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
				(R)RNLNTYSK(I)	113.2	2	995.5	-3.57
				(I)YmLYPDFLcK(G)	135.8	2	1365.6	4.23
				(K)IYmLYPDFLcK(G)	145.1	2	1478.7	2.72
				(K)VNGAIVcEQGTScENR(I)	54.7	2	1793.8	0.88
				(K)RVNGAIVcEQGTScENR(I)	25.3	3	1949.9	-0.45
Acidic PLA_2 ammodytin I1	25453141	231.0	36.2	(K)MGTYSYSFQNGDIVcGGDDPcLR(A)	64.2	3	2654.1	7.27
				(R)ccFVHDccYGR(V)	41.7	2	1533.6	5.77
				(R)VAAIcFGENmNTYDK(K)	39.7	2	1748.8	2.08
				(R)VAAIcFGENmNTYDKK(Y)	32.9	3	1876.8	-0.02
Acidic PLA_2 DsM-a2/DsM-a2'	408407661	557.0	74.6	(K)YmLYSIFDcKEESDQc(-)	74.0	2	2103.8	1.30
				(K)KYmLYSIFDcKEESDQc(-)	51.2	2	2231.9	-1.29
				(R)VAAIcFR(E)	40.3	2	836.4	-0.16
				(R)VAAIcFRENmNTYDK(K)	39.9	2	1847.8	3.06
				(G)GKPQDATDRccFVHDccYGR(V)	39.8	3	2502.0	-0.24
				(R)AVcEcDRVAAIcFR(E)	39.7	2	1726.8	-1.14
				(K)TGNFGLLSYVYYGcYcGWGGK(G)	39.0	2	2422.1	5.84
				(K)YmLYSIFDcK(E)	33.5	2	1355.6	-0.40
				(K)TATYSYSFENGDIVcGGDDPcLR(A)	32.4	3	2597.1	0.83
Ammodytin I1(D) isoform	50874384	1203.5	43.5	(K)YmLYSLFDcK(E)	45.2	2	1355.6	3.56
				(K)MGTYSYSFENGDIVCGGDDPcLR(A)	21.4	2	2598.1	8.89
Acidic PLA_2 homolog vipoxin A chain	2851544	312.1	45.1	(R)AAAIcLGENVNTYDK(N)	53.3	2	1638.8	9.28
				(K)TATYTYSFENGDIVcGDNDLcLR(A)	33.9	2	2726.2	5.72
				(-)NLFQFGDmILQK(T)	27.6	2	1469.8	4.06
Daboiatoxin	149241831	460.3	34.4	(-)NLFQFAR(L)	27.3	2	895.5	0.14
				(K)IVcGGDDPcLR(A)	22.4	2	1261.6	0.21

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
Vaspin acidic subunit (1)	50874232	150.4	39.9	(R)AAAIcLGENVNTYDKNYEYYSISHcTEESEQc(-)	30.6	3	3818.6	-0.70
				(R)YcGWGGQGR(A)	28.5	2	1040.4	0.33
				(K)mATYTYSFENGDIVcGDNDLcLR(A)	20.3	2	2756.1	-6.35
Basic PLA_2	71912223	11115.2	66.4	(K)TATYSYSFENGGIVcGDR(D)	173.5	3	1996.9	-9.39
				(C)FVHDccYEK(V)	121.4	2	1257.5	-6.49
				(C)cFVHDccYEK(V)	128.2	3	1417.5	0.38
				(L)NTYDKK(Y)	94.5	2	768.4	1.36
				(K)NPLSSYSNYGcYcGWGGK(G)	72.5	2	2069.9	3.24
				(K)YPPSQcTGTEQc(-)	50.0	2	1427.6	0.64
Acidic PLA_2 Cvv-E6b	82209451	544.0	10.1	(K)QVCEcDRVAAIcFR(D)	42.6	3	1726.8	1.29
				(K)QVcEcDR(V)	20.7	2	966.4	-0.32
Basic PLA_2 homolog	27151648	704.1	20.5	(K)EVCEcDKAAAIcFR(D)	26.6	2	1713.7	3.71
				(R)ccFVHNccYEK(V)	25.2	3	1576.6	-0.49
Acidic PLA_2 Ts-A3	82201337	443.2	10.1	(K)AVCEcDKAAAIcFR(D)	39.0	3	1613.7	-1.52
				(K)AVcEcDK(A)	23.7	2	881.3	-0.53
Ammodytin I1(B') variant	50874310	307.8	48.6	(K)mGTYSYSFQNGAIVcGGDDPcLR(A)	32.4	2	2626.1	-9.73
				(R)AVcEcDRVAAIcFGENmNTYDKK(Y)	32.1	3	2767.2	1.58
Ammodytin I1(F) isoform	50874356	278.8	47.8	(K)LSTYSYSFENGDIVcGGDDPcLR(A)	66.9	2	2626.1	-9.98
				(K)YmLYSLLDCKEESDQc(-)	38.2	2	2012.8	-0.12
Snake venom metalloprotease								
Factor X activator light chain 2	300079896	404.7	22.2	(R)FcmEHPNNGHLVSIESmEEAEFVAK(L)	80.4	2	2937.3	2.09
				(K)FITHFWIGLR(I)	28.5	1	1289.7	-0.29
				(K)cEEPYPFVcK(V)	44.8	2	1328.6	0.34

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
				(R)mWFNHK(C)	38.3	2	878.4	0.56
Factor X activator heavy chain	300079900	329.2	13.3	(R)FDLNTLGITFLAGMcQAYR(S)	83.6	2	2191.1	2.06
				(R)SVGIVQVQGNR(N)	81.5	2	1156.6	0.22
				(K)AFIELIIIVDHSmAK(K)	75.3	1	1715.9	-1.30
				(K)IYEIVNSANEIFNPLNIHVTLIGVEFWcDR(D)	75.0	3	3575.8	-1.13
				(R)DQLQQNGQPcQNNR(G)	50.3	2	1699.7	-1.47
				(R)ARNEcDVPEHcTGQSAEcPR(D)	45.2	3	2373.0	0.59
				(K)IPcAPQDVK(C)	34.0	2	1027.5	1.38
				(R)KIPcAPQDVK(C)	32.8	2	1155.6	-0.47
				(R)GYcYNGDcPImR(N)	31.8	2	1521.6	-0.01
				(K)DScFQENLK(G)	30.4	2	1140.5	-7.26
				(R)NEcDVPEHcTGQSAEcPR(D)	28.7	3	2145.8	-1.17
				(R)NQcISLFGSR(A)	25.6	2	1181.6	-0.25
				(R)QcVDVNTAYQSTTGFSQI(-)	24.9	2	2018.9	1.67
				(K)LKPGAEcGNGLccYQcK(I)	23.6	3	2014.8	1.12
Chain A, Venom Metalloproteinase	162329887	942.0	26.2	(R)KDIVSPPVcGNEIWEEGEEcDcGSPANcQNPccDAATcK(L)	103.1	3	4513.8	-0.92
				(R)ARDEcDVPEHcTGQSAEcPR(D)	76.9	3	2374.0	2.05
				(K)SHDNALLFTDmR(F)	73.7	2	1435.7	0.93
				(R)RARDEcDVPEHcTGQSAEcPR(D)	73.1	3	2530.1	1.04
				(R)DEcDVPEHcTGQSAEcPRDQLQQNGKPcQNNR(G)	67.6	4	3827.6	-5.31
				(R)DEcDVPEHcTGQSAEcPR(D)	65.1	2	2146.8	2.70
				(T)KSHDNALLFTDmR(F)	62.9	2	1563.8	0.78
				(R)DQLQQNGKPcQNNR(G)	56.0	2	1699.8	-6.07
				(R)ARDEcDVPEHcTGQSAEcPRDQLQQNGKPcQNNR(G)	49.7	4	4054.7	-6.17
				(K)cGRLFcLNNSPR(N)	40.6	2	1493.7	-7.93
				(R)SVGIVQEQGNR(N)	39.0	2	1186.6	0.37

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
				(K)KcNSTATNTK(I)	18.2	2	1124.5	-5.38
Coagulation factor X-activating enzyme beta-chain	73621140	375.4	23.4	(K)FITHFWIGLmIK(D)	39.1	3	1521.8	0.53
Coagulation factor X activating enzyme light chain	251205	441.9	33.3	(-)VLDcPSGWLSYEQHcYK(G)	105.1	2	2141.9	3.40
				(K)SmTcNFIAPVVcKF(-)	48.7	1	1689.8	-0.28
				(K)FVVNLISENLEYPATWIGLGNmWK(D)	32.5	2	2810.4	3.50
Snake venom serine protease								
Factor V activator RVV-V alpha	134129	161.4	20.3	(R)LRRPVTYSTHIAPVSLPSR(S)	77.3	3	2150.2	-0.24
				(K)ISTTEDTYPDVPHcTNIFIVK(H)	49.9	3	2450.2	3.86
				(K)NIRNEDEQIR(V)	47.7	2	1286.6	-0.47
				(K)WcEPLYPWVPADSR(T)	44.6	2	1775.8	0.22
				(R)RPVTYSTHIAPVSLPSR(S)	39.2	2	1881.0	0.68
				(R)TLcAGILK(G)	42.6	2	875.5	-0.15
				(R)EWVLTAAHcDR(R)	39.4	2	1357.6	-0.93
				(R)NEDEQIRVPR(G)	33.4	2	1255.6	1.43
Beta-fibrinogenase-like	765684342	181.3	13.3	(K)TSTYIAPLSLPSSPPR(V)	38.5	2	1686.9	1.45
				(R)NNAEIRLPEER(F)	34.2	2	1340.7	-0.24
				(K)VYDYTDWIQSIIAGNTAATcPP(-)	52.8	2	2456.2	5.93
Venom serine proteinase-like protein 2	13959655	484.9	8.9	(R)TLcAGILQGGIDScK(V)	101.1	2	1592.8	3.59
				(R)IILGVHSK(N)	17.3	2	866.5	0.18
Serine protease, partial	297593758	222.9	12.7	(R)TLcAGILEGGIDScK(V)	89.6	2	1593.8	1.13
				(R)FHCTGTLIDNQWVLTAAR(R)	52.2	3	2088.0	1.97

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
Serine protease VLSP-3	380875417	103.1	12.0	(K)TSTHIAPLSLPSSPPSVGSVcR(I)	69.6	2	2250.2	5.34
				(K)WDKDImLIK(L)	32.9	2	1177.6	0.80
Thrombin-like enzyme	38146946	59.2	5.9	(M)vIGGDEcNINEHR(F)	45.2	2	1554.7	6.57
				(-)mVIGGDEcNINEHR(F)	32.2	3	1659.7	9.79
Phosphodiesterase								
Phosphodiesterase	586829527	964.4	17.4	(K)NEVTSFENIEVYNLMcDLLK(L)	87.0	2	2431.2	1.03
				(K)FGPVSGEIImALQmADR(T)	79.0	2	1866.9	1.85
				(R)VRDVELLTGLNFYSGLK(Q)	78.2	2	1924.1	0.68
				(R)DVELLTGLNFYSGLK(Q)	74.2	1	1668.9	0.41
				(K)VLSFILPHRPDNSEScADTSPDNLWVEER(I)	67.7	3	3384.6	3.40
				(R)VRDVELLTGLNFYSGLKQPLPETLQLK(T)	56.2	3	3071.7	1.27
				(K)DFYTFDSEGIVR(N)	41.6	1	1448.7	0.55
				(K)IPIPTHFFVVLTScENQINTPLNcPGSLK(V)	29.4	3	3296.7	1.97
				(K)GKNEVTSFENIEVYNLMcDLLK(L)	22.9	2	2616.3	-0.25
5'-Nucleotidase								
Snake venom 5'-nucleotidase	395455152	151.3	6.8	(K)cTGQDcYGGVAR(R)	62.3	2	1343.5	-0.14
				(K)QAFEHSVHR(H)	39.3	2	1093.5	-0.02
				(R)YDAmALGNHEFDNGLAGLLDPLLK(H)	23.4	3	2603.3	2.09
				(K)YLGYLNVIFDDK(G)	18.3	2	1459.7	-0.12
5'-nucleotidase, partial	586829529	121.4	11.5	(R)FHEcNLGNLIcDAVIYNNLR(H)	77.6	3	2435.2	3.48
				(R)ANNGIITLEELTSVLPFGGTFDLLQIK(G)	27.6	3	2903.6	2.54
L-amino-acid oxidase								
L-amino-acid oxidase	395406796	366.3	9.9	(K)SAGQLYQESLGK(A)	60.1	2	1280.6	0.36
				(R)ITFKPPLPPK(K)	57.6	2	1137.7	-1.44
				(K)FWEDDGIQGGK(S)	41.5	2	1251.6	-0.37
				(K)DPGLLKYPVKPSEAGK(S)	37.4	3	1698.9	0.01

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
				(K)ITFKPPLPPKK(K)	30.7	2	1265.8	0.25
				(K)KDLQTFcYPSIIQK(W)	63.2	2	1740.9	2.66
				(K)VTVLEASERPGGR(V)	26.5	2	1370.7	-0.47
				(K)AVEELKR(T)	36.9	2	844.5	-0.13
L-amino acid oxidase Lm29	704043548	55.4	3.7	(K)SAGQLYEESLGK(A)	34.6	2	1281.6	-1.27
				(R)VAEELKR(S)	26.4	2	844.5	0.02
Phospholipase B								
Phospholipase B	727360709	161.9	6.5	(R)NAGYVIAQLDGLYmGNVEWAK(R)	87.6	2	2328.1	2.04
				(R)SLEDGTLYIIEQIPK(L)	83.5	1	1718.9	0.09
Kunitz-type serine protease inhibitor								
Kunitz-type serine protease inhibitor B2	239977248	1311.9	34.5	(R)IYYNLESNKcNVFFYGGcGGNDNNFETR(D)	77.0	3	3394.4	-7.93
				(R)RIYYNLESNK(C)	52.6	2	1299.7	-1.29
				(R)IYYNLESNK(C)	38.9	2	1143.6	-0.89
Kunitz-type serine protease inhibitor C3	239977252	161.0	41.7	(K)EFIYGGcHGNANNFPTR(D)	65.3	2	1953.9	2.13
				(K)FcYLPADPGEcmAYIR(S)	49.2	2	1978.8	-5.63
				(K)cKEFIYGGcHGNANNFPTR(D)	37.8	3	2242.0	-0.61
				(R)SFYYDSESK(K)	20.6	2	1125.5	0.15
Kunitz-type protease inhibitor	379647506	2751.7	51.1	(R)QTcGAPR(K)	90.3	2	789.4	1.50
				(R)IYYNPDSNK(C)	119.8	2	1113.5	4.42
				(R)RIYYNPDSNKcEVFFYGGcGGNDNNFETR(K)	45.3	3	3493.5	-6.15
				(K)FcNLAPESGR(C)	38.8	2	1150.5	-1.25
				(R)IYYNPDSNKcEVFFYGGcGGNDNNFETRK(K)	34.3	4	3465.5	-0.89

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
				(K)cEVFFYGGcGGNDNNFETR(K)	84.2	2	2242.9	2.99
				(R)IYYNPDSNKcEVFFYGGcGGNDNNFETR(K)	72.0	3	3337.4	9.38
Kunitz protease inhibitor-II	87130864	1635.1	25.0	(K)FcFLRPDFGR(F)	131.9	3	1314.6	2.24
				(R)ENTNNFDTR(D)	117.4	2	1110.5	2.79
				(R)SRENTNNFDTR(D)	134.9	2	1353.6	3.16
				(N)NFDTR(D)	82.4	1	652.3	0.33
				(T)NNFDTR(D)	91.6	2	749.3	-3.87
Kunitz-type serine protease inhibitor 4	123913154	719.1	52.4	(R)FYYNPASNQcQGFIYGGcGGNANNFETRDQcR(H)	162.6	3	3765.5	1.96
				(R)FYYNPASNQcQGFIYGGcGGNANNFETR(D)	106.1	3	3206.4	1.51
				(K)FcHLPVDSGIcR(A)	37.1	3	1460.7	-1.15
Kunitz-type serine protease inhibitor B4	239977254	351.9	39.3	(R)IYYNLESNKcEVFFYGGcGGNDNNFSTWDEcR(H)	104.2	3	3914.6	2.39
				(K)cEVFFYGGcGGNDNNFSTWDEcR(H)	76.0	2	2791.1	1.09
				(R)RIYYNLESNKcEVFFYGGcGGNDNNFSTWDEcR(H)	26.4	4	4070.7	1.31
Kunitz-type serine protease inhibitor B1	239977245	423.7	48.8	(K)FcYLPADPGEcLAHmR(S)	64.0	2	1952.8	1.18
				(K)EFIYGGcHGNANKFPSR(D)	30.7	2	1953.9	-5.06
Kunitz-type serine protease inhibitor C6	239977259	223.0	43.8	(R)FYYNPASNQcQGFTYGGcGGNANNFETR(D)	88.7	3	3194.3	0.87
				(R)HTcGASGNVGPRPR(I)	21.1	2	1465.7	-0.64
Cysteine-rich secretory protein								
Cysteine-rich secretory protein Dr-CRPK	190195321	160.1	30.1	(R)SGcAAAYcPSSEYNYFYVcQYCPAGNIIGK(I)	55.6	3	3469.5	0.68
				(K)DFVYGQGASPANAVVGHYTQIVWYK(S)	25.5	2	2770.4	-0.20
				(R)RPEIQNEIVDLHNSLR(R)	43.0	3	1933.0	2.14

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
				(K)WTAIIHEWHK(E)	33.8	2	1320.7	2.35
				(R)cILNHSPYNSR(V)	31.9	2	1360.6	0.41
				(K)TKcPAScFcHNEII(-)	26.7	2	1736.8	2.63
				(R)RPEIQNEIVDLHNSLRR(S)	24.4	4	2089.1	1.01
				(K)qGcHSNYLK(T)	21.8	2	1089.5	-4.06
				(K)cPAScFcHNEII(-)	20.8	2	1507.6	0.32
				(K)cGENIYmSPYPmK(W)	15.9	2	1621.7	-0.13
				(K)MEWYPEAAANAER(W)	148.2	2	1537.7	3.37
				(R)SVTPTASNMLK(M)	126.7	2	1148.6	3.77
				(R)VIGGIK(C)	84.5	1	586.4	1.14
Cysteine-rich secretory protein Ch-CRPKa, partial	190195307	147.5	12.2	(R)KPEIQNEIVDLHNSLR(R)	73.0	3	1905.0	0.43
				(-)SVDFDSESPR(K)	55.7	2	1138.5	0.20
				(R)KPEIQNEIVDLHNSLRR(S)	41.2	4	2061.1	-0.14
Disintegrin								
Jerdostatin	292659514	183.4	45.7	(R)TSVSSHYcTGR(S)	71.7	2	1254.6	-0.61
				(K)LKPAGTTcWR(T)	24.6	3	1189.6	-0.47
				(R)ScEcPSYPG(N)	14.4	2	1056.4	-0.46
Nerve growth factor								
Venom nerve growth factor	400499	128.5	31.6	(R)INTAcVcVISR(K)	77.9	2	1292.6	1.18
				(K)HWNSYcTTTDTFVR(A)	60.6	2	1787.8	1.19
				(K)cKNPNPVPSGcR(G)	56.2	2	1385.6	0.23
				(K)QYFFETK(C)	109.5	2	962.5	3.55
				(K)NPNPVPSGcR(G)	114.5	2	1097.5	1.72
				(R)INTAcVcVISRK(N)	139.7	3	1420.7	7.91
				(K)NPNPVPSGcRGIDAK(H)	150.4	3	1581.8	-7.78
Vascular endothelial growth factor								
VEGF toxin VR-1	327478537	650.9	34.0	(R)ETLVSILQEHPDEISDIFRPScVAVLR(C)	55.3	3	3123.6	2.12

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
				(K)HTADIQImR(M)	50.7	2	1100.6	-0.40
				(K)QGEPEGPKEPR(R)	128.0	3	1223.6	3.68
				(K)cTPVGK(H)	81.8	2	661.3	5.22
				(K)FmEHTAcEcRPR(W)	145.0	4	1609.7	-0.23
				(R)cSGccTDESmK(C)	121.2	2	1350.4	4.33
				(A)cECRPR(W)	92.3	2	877.4	-0.18
				(H)TAcEcRPR(W)	106.5	2	1049.5	3.66
				(R)cSGccTDESmKcTPVGK(H)	15.3	3	1992.8	-0.17
Vascular endothelial growth factor A	327488518	55.7	9.4	(K)QLELNER(T)	41.2	2	901.5	-0.42
				(K)QENHcEPcSER(R)	29.5	2	1428.5	-0.83
Snaclec								
Snaclec 4	73620112	443.1	49.3	(K)FVVNLISENLEYPATWIGLGNmWK(D)	80.4	2	2810.4	5.59
				(K)ALAEESYcLImITHEK(V)	69.5	2	1923.9	5.13
				(K)KGSHLVSLHSR(E)	61.8	2	1220.7	-0.33
				(K)FVVNLISENLEYPATWIGLGNmWKDcR(M)	56.9	3	3241.6	2.44
				(R)EEEKFVVNLISENLEYPATWIGLGNmWK(D)	53.7	3	3325.7	4.26
				(K)SmTcNFIAPVVcKF(-)	53.6	2	1689.8	1.38
				(K)SmTcNFIAPVVcK(F)	49.5	2	1542.7	2.89
				(K)GSHLVSLHSR(E)	41.8	2	1092.6	-0.48
				(K)VFTEEmNWADAEK(F)	88.0	2	1585.7	1.63
				(R)mEWSDRGNVK(Y)	24.2	2	1237.6	-1.41
Snaclec 3	73620111	900.4	46.0	(K)AWNEGTNcFVFK(I)	52.2	2	1472.6	0.40
				(K)VFTEEmNWADAEKFcTEQHK(G)	26.0	3	2516.1	1.14
				(K)GSHLLSLHNIAEADFVLKK(T)	24.1	4	2092.2	1.23
Dabocetin beta subunit	300490464	756.2	26.7	(K)TWEDAEK(F)	101.3	2	878.4	3.54
				(K)VFNEK(K)	84.1	1	636.3	-1.72

Protein	Accession no. (gi|)	Protein score	% Coverage	MS/MS derived peptide(s)	Peptide score	z	Mass (Da)	ΔM (ppm)
				(K)KTWEDAEK(F)	112.9	2	1006.5	4.44
				(V)FNEK(K)	73.6	1	537.3	-1.88
				(R)WSDGVNLDYK(N)	59.3	2	1196.6	0.31
				(R)SSEEmDFVIR(M)	57.9	2	1228.6	1.34
				(R)FDFFWIGLR(D)	44.6	2	1200.6	1.88
				(R)mTFPIFR(F)	31.5	2	927.5	0.09
P68 alpha subunit	300490470	1090.2	61.4	(R)TWFNLScGDDYPFVcK(F)	75.5	2	2008.9	6.62
				(R)SGDAETFcTEQANSGHLVSIESVEEAEFVAQLISENIK(T)	66.4	3	4139.0	5.45
				(K)TPADYVWIGLR(N)	42.5	2	1290.7	5.66
				(R)KAQYcISK(W)	33.8	2	997.5	-0.51
				(K)NcFGLEK(E)	32.3	2	867.4	-1.49
				(K)AFDEPKR(S)	29.3	2	862.4	0.03
				(K)WTDGSSVIYK(N)	21.6	2	1155.6	4.70
Dabocetin alpha subunit	300490462	1659.6	36.4	(K)cFGLNK(E)	88.3	2	738.4	0.97
				(K)YHEWITLPcGDK(N)	145.6	2	1518.7	2.60
				(R)QQcSSHWTDGSAVSYETVTK(Y)	189.8	3	2271.0	4.61
				(K)cFGLNKETK(Y)	117.7	2	1096.5	1.43
				(K)NPFIcK(S)	92.2	2	778.4	-0.33
				(K)YHEWITLPcGDKNPFIcK(S)	191.1	4	2278.1	1.15
				(K)ETKYHEWITLPcGDK(N)	169.4	3	1876.9	-6.92
				(K)SWVLH-	22.1	2	641.3	5.76
				(K)YHAWIGLR(D)	20.1	2	1015.6	5.16
P31 beta subunit	300490488	113.2	16.0	(K)GSHLASIHSSEEEAFVSK(V)	64.5	2	1914.9	-0.85
				(R)IFWFNR(G)	31.6	2	882.5	4.80
P31 alpha subunit	300490478	111.8	34.5	(K)FcTEQANSGHLVSIK(S)	38.9	2	1690.8	-1.43
				(K)WDYVNcAEHYR(E)	25.3	3	1512.6	-0.18

4.1.3.2 The proteome composition of EI RVV samples

Proteomic analysis of all the GF fractions (GF1 to GF10) against the Viperidae entries of the NCBI database initially identified 1585 and 1192 redundant venom proteins in EI RVV (B) and EI RVV (N), respectively. However, following our stringent workflow for protein identification (see section 3.2.1.7), the minimum number of proteins distributed among 15 snake venom protein families of EI RVV (B) and EI RVV (N) proteomes were found to be 73 and 69, respectively (Figs. 4.10a,b; Table 4.4a). In addition to the protein families identified in WI RVV, aminopeptidase (APase), glutaminyl cyclase (GC), and hyaluronidase (Hya) were also detected in the venom proteomes of EI RVV (B) and EI RVV (N) (Table 4.4a). The relative abundances of the identified protein classes in EI RVV (B) and EI RVV (N) are shown in Figs. 4.10a,b. The alignments of MS/MS-derived peptide sequences of EI RVV (B) and EI RVV (N) with the homologous proteins from the Viperidae entries of NCBI database are shown in Figures 4.10c,d. The lists of identified peptide ions in EI RVV (B) and EI RVV (N), their m/z, charge (z), score for the ID, and ΔM (Da) are shown in Tables 4.4b,c.

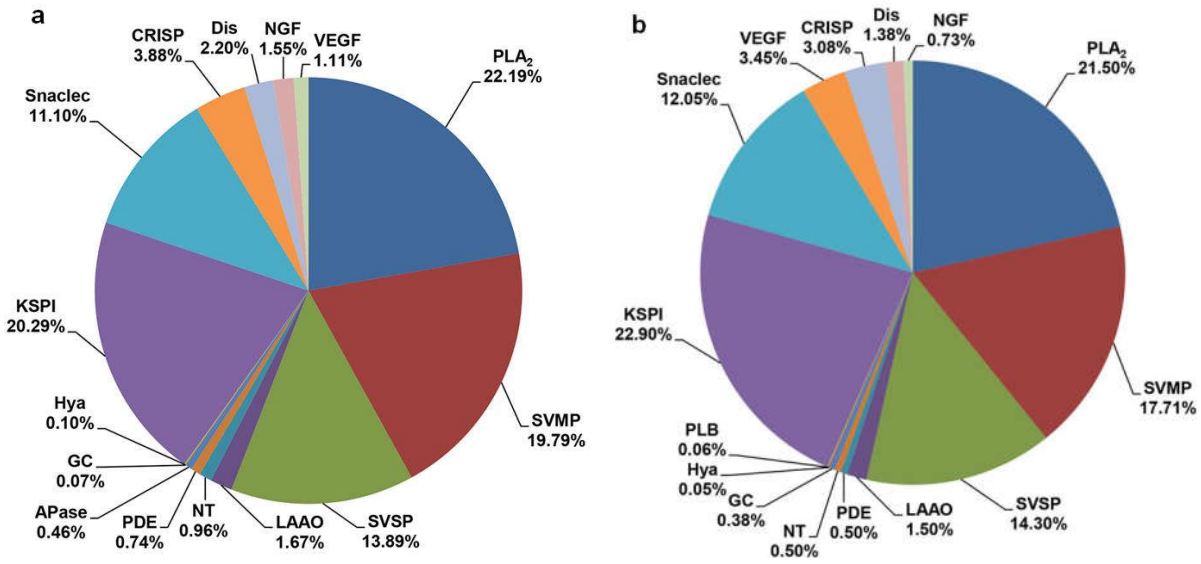

Fig. 4.10. Protein family composition of **a.** EI RVV (B) and **b.** EI RVV (N). Abbreviations: PLA_2, phospholipase A_2; SVMP, snake venom metalloprotease; SVSP, snake venom serine protease; PDE, phosphodiesterase; NT, nucleotidase; LAAO, L-amino acid oxidase; APase, aminopeptidase; GC, glutaminyl cyclase; PLB, phospholipase B; Hya, hyaluronidase; KSPI, Kunitz-type serine protease inhibitor; CRISP, cysteine-rich secretory protein; Dis, disintegrin; NGF, nerve growth factor; VEGF, vascular endothelial growth factor.

Table 4.4a. Summary of the identified proteins in EI RVV (B) and EI RVV (N) by LC-MS/MS analysis and database search against Viperidae family (taxid 8689) of proteins of the NCBI database.

Accession no.	Protein Description	Source organism	MW (Da)	EI RVV (B)				EI RVV (N)			
				-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)
Enzymatic proteins											
Phospholipase A_2											
AAZ53182.1	Basic phospholipase A_2	*D. russelii*	15864	267.7	70	1.70	1-5, 7-10	305.9	84	2.41	1-6, 8-10
AAZ53180.1	Acidic phospholipase A_2	*D. russelii*	15329	305.6	70	4.23	1-5, 9, 10	283.1	81	6.05	1-10
A8CG78.1	Acidic phospholipase A_2 DsM-a2/DsM-a2'	*D. siamensis*	15586	188.3	58	1.85	2, 4-10	198.0	41	2.27	4-6, 8-10
CAA48456.1	Phospholipase A_2	*D. russelii*	15555	162.7	25	0.91	2, 3, 5	114.1	26	0.20	2, 5
CAE47208.1	Ammodytin I2(A) variant	*V. a. aspis*	15180	94.6	23	1.08	3-6, 10	70.6	22	1.62	4-6, 10
ABY77928.1	Phospholipase A_2	*Sistrurus miliarius*	15750	69.2	8	0.81	5-7	65.3	8	0.38	6
AHJ09529.1	Phospholipase A_2	*T. albolabris*	15867	48.9	12	2.63	1-5, 7, 8	58.6	12	1.57	2-5
AAN59979.1	Vaspin A	*V. a. zinnikeri*	15411	80.5	25	0.49	3-4	46.8	11	0.05	5
ABD24037.1	Phospholipase A_2-II	*D. r. russelii*	15865	236.0	70	1.12	4	ND	ND	ND	-
P81458.1	Basic phospholipase A_2 RVV-VD	*D. russelii*	13626	178.3	54	1.97	2-9	ND	ND	ND	-

Accession no.	Protein Description	Source organism	MW (Da)	EI RVV (B)				EI RVV (N)			
				-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)
PODKR3.1	Acidic PLA_2 CbIalpha	*Pseudocerastes fieldi*	13625	102.1	39	0.31	4	ND	ND	ND	-
C0HJL8.1	PLA_2 nigroviriditoxin	*B. nigroviridis*	14126	83.5	28	0.86	4-7	ND	ND	ND	-
CAE47242.1	Ammodytin I2(C) variant	*V. a. montandoni*	15419	80.9	26	0.40	4	ND	ND	ND	-
AAM80564.1	Acidic phospholipase A_2	*C. viridis viridis*	15549	68.0	17	0.44	4-5	ND	ND	ND	-
ADG86231.1	Phospholipase A_2	*V. ursinii*	15316	66.5	26	0.36	4	ND	ND	ND	-
AHJ09559.1	Phospholipase A_2	*G. brevicaudus*	15739	58.6	14	1.01	5-6	ND	ND	ND	-
C0HK16.1	Daboxin P	*D. r. russelii*	13612	51.0	23	0.36	4	ND	ND	ND	-
AHJ09557.1	Phospholipase A_2	*G. brevicaudus*	15852	46.7	14	0.77	5-6	ND	ND	ND	-
JAV01879.1	$BATXPLA_2$	*Bothrops atrox*	15515	45.8	14	0.47	4-5	ND	ND	ND	-
P0DJJ8.1	Basic phospholipase A_2 BP-I	*P. flavoviridis*	15537	33.6	11	0.27	4	ND	ND	ND	-
F8QN51.1	Acidic PA_2 Vur-PL3	*V. renardi*	15318	31.6	18	0.18	4	ND	ND	ND	-
AAZ53183.1	Basic phospholipase A_2	*D. russelii*	15461	ND	ND	ND	-	223.6	82	2.79	1-10
ACB59359.1	Phospholipase A_2	*M. lebetina*	15459	ND	ND	ND	-	74.6	32	1.44	5
CAE47167.1	Ammodytin I1(F) isoform	*V. a. atra*	15400	ND	ND	ND	-	58.5	25	2.51	9
AAW92122.1	K49 phospholipase A_2	*T. gracilis*	15508	ND	ND	ND	-	39.3	7	1.19	6

Accession no.	Protein Description	Source organism	MW (Da)	EI RVV (B)				EI RVV (N)			
				-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)
Snake venom metalloprotease											
AAZ39880.1	Hemorrhagic metalloproteinase russelysin	*D. russelii*	69555	275.3	37	6.03	1-5, 7-10	310.9	42	3.53	1-5, 7, 9
ADJ67475.1	Factor X activator heavy chain	*D. r. russelii*	69521	252.6	25	3.97	1-4, 7, 9	256.6	31	2.01	1, 2, 4, 5
ADJ67473.1	Factor X activator light chain 2	*D. r. russelii*	18273	188.6	63	1.86	1-3	184.5	60	1.17	1-3
ADJ67474.1	Factor X activator light chain 1	*D. r. russelii*	16984	195.2	53	0.72	1-3	177.0	48	0.82	1-3
ADI47593.1	Metalloproteinase, partial	*E. c. sochureki*	28319	148.2	9	1.19	1-3	146.1	12	0.53	1-2
AAT91068.1	Factor X activator light chain 2	*M. lebetina*	18094	127.8	24	1.73	1-3	143.1	24	1.03	1-3
AFE61611.1	Factor X activator light chain 2	*D. russelii*	18324	118.0	34	1.66	1-2	123.4	34	0.88	1-2
AAX38182.1	VLAIP-B	*M. lebetina*	68843	104.0	5	1.19	1-2	108.6	5	1.56	1-2
JAC96600.1	Snake venom metalloproteinase K	*E. coloratus*	48851	79.0	3	0.81	2-4	ND	ND	ND	-
ADW54349.1	Group III snake venom metalloproteinase, partial	*E. ocellatus*	32052	84.3	12	0.61	1	ND	ND	ND	-
AAB22477.1	Coagulation factor X activating enzyme heavy chain	*D. russelii*	47975	ND	ND	ND	-	237.1	36	1.18	1-3

Accession no.	Protein Description	Source organism	MW (Da)	EI RVV (B)				EI RVV (N)			
				-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)
AAX38181.1	VLAIP-A	*M. lebetina*	68710	ND	ND	ND	-	175.8	13	1.54	1, 2, 4, 5
ADI47654.1	Metalloproteinase, partial	*E. coloratus*	55138	ND	ND	ND	-	124.3	6	0.30	1
ADI47578.1	Metalloproteinase, partial	*E. c. sochureki*	63999	ND	ND	ND	-	110.0	6	1.95	1, 2, 4, 5
Snake venom serine protease											
P18965.2	Factor V activator RVV-V gamma	*D. siamensis*	28823	296.3	72	3.92	2-8, 10	233.0	74	2.53	2-6
ADP88560.1	Serine beta-fibrinogenase-like protein precursor	*D. siamensis*	28035	169.1	39	0.79	1-2	222.5	52	1.07	1-3
AMB36342.1	Enzymatically inactive serine proteinase-like protein SPH-1	*V. a. ammodytes*	28928	173.6	30	2.25	2-10	216.2	30	2.29	2-7
E0Y418.1	Serine protease VLSP-1	*M. lebetina*	28702	175.7	29	0.95	1-3	204.1	34	0.51	2-3
P18964.1	Factor V activator RVV-V alpha	*D. siamensis*	26182	298.0	80	4.51	3-10	192.8	67	0.80	1, 5-6
E0Y420.1	Serine protease VLSP-3	*M. lebetina*	28352	157.2	16	0.08	2	187.4	20	0.44	1, 2, 5
JAS04410.1	Serine proteinase 3	*Agkistrodon piscivorus*	28246	74.5	9	0.36	2	39.4	9	0.51	3

Accession no.	Protein Description	Source organism	MW (Da)	EI RVV (B)				EI RVV (N)			
				-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)
E0Y419.1	Beta-fibrinogenase	*M.. lebetina*	28297	161.0	24	0.19	2	ND	ND	ND	-
B0FXM1.1	Thrombin-like enzyme gyroxin B1.3	*C. durissus terrificus*	29347	106.6	5	0.81	3-4	ND	ND	ND	-
E5L0E3.1	Alpha-fibrinogenase-like	*D. siamensis*	28496	ND	ND	ND	-	213.6	58	1.75	4-7
Q9PT40.1	Venom serine proteinase-like protein 2	*M. lebetina*	28894	ND	ND	ND	-	164.3	35	1.50	4-7
AMB36345.1	Serine proteinase SP-4	*V. a. ammodytes*	28587	ND	ND	ND	-	138.2	27	0.41	2-3
JAA98034.1	Kallikrein-CohLL-4	*C. oreganus helleri*	28517	ND	ND	ND	-	122.7	18	0.68	2, 5, 6
JAA98031.1	Kallikrein-CohLL-7	*C. o. helleri*	28132	ND	ND	ND	-	89.6	12	0.90	3, 5, 6
ABY65931.1	Gyroxin-like B1_7 serine protease precursor	*C. durissus terrificus*	28184	ND	ND	ND	-	86.0	12	0.32	6
E5AJX2.1	Snake venom serine protease nikobin	*V. nikolskii*	28216	ND	ND	ND	-	79.0	8	0.47	3, 5
Q5W958.1	Venom serine proteinase-like HS120	*B. jararaca*	27815	ND	ND	ND	-	50.2	7	0.08	5

Accession no.	Protein Description	Source organism	MW	EI RVV (B)	EI RVV (N)

			(Da)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)
L-amino acid oxidase											
ACF70483.1	Secreted L-amino acid oxidase precursor	*D. russelii*	56888	299.5	56	1.67	1-2	301.6	58	0.85	1, 2
Q4F867	L-amino-acid oxidase	*D. siamensis*	46372	ND	ND	ND	-	284.2	57	0.65	1
Phosphodiesterase											
BAN89426.1	Phosphodiesterase	*Ovophis okinavensis*	96239	172.1	12	0.74	1	ND	ND	ND	-
AHJ80885.1	Phosphodiesterase	*M. lebetina*	96181	ND	ND	ND	-	255.6	31	0.49	1, 2
5'-Nucleotidase											
AHJ80886.1	5'-nucleotidase, partial	*M. lebetina*	45031	213.9	46	0.96	1-2	235.6	43	0.51	1, 2, 5
Glutaminyl cyclase											
AFE84762.1	Glutaminyl-peptide cyclotransferase	*D. russelii*	42267	118.7	27	0.07	2	159.3	39	0.38	2, 3, 5
Phospholipase B											
BAN82155.1	Phospholipase B	*O. okinavensis*	64133	ND	ND	ND	-	33.5	4	0.06	2
Hyaluronidase											
ABI33950.1	Truncated hyaluronidase	*E. c. sochureki*	22537	41.9	3	0.10	1, 5	43.8	5	0.05	1, 5
Accession no.	**Protein Description**	**Source organism**	**MW**	**EI RVV (B)**				**EI RVV (N)**			

			(Da)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)
Aminopeptidase											
XP_015676063.1	Xaa-Pro aminopeptidase 2	*P. mucrosquamatus*	77032	132.4	14	0.46	1	ND	ND	ND	-
Non-enzymatic proteins											
Kunitz-type serine protease inhibitor											
ABD24041.1	Kunitz protease inhibitor-II	*D. r. russelii*	9683	260.0	64	8.33	1-10	286.5	46	8.74	1-10
ABD24040.1	Kunitz protease inhibitor-I	*D. r. russelii*	9287	228.2	56	6.51	1-10	225.2	62	6.23	1-3, 5-10
A8Y7P1.1	Kunitz-type serine protease inhibitor B1	*D. siamensis*	9318	156.9	46	0.98	5-7, 9, 10	178.9	49	2.22	3-6, 8, 10
AFD04724.1	Kunitz-type protease inhibitor	*D. russelii*	10132	142.4	50	1.25	5-8, 10	159.4	50	2.97	3-8, 10
ABD24043.1	Kunitz protease inhibitor-IV	*D. r. russelii*	9145	157.1	48	2.65	2, 4-10	128.8	48	2.74	2, 4-8
A8Y7N8.1	Kunitz-type serine protease inhibitor C5	*D. siamensis*	10006	152.3	49	0.59	7	ND	ND	ND	-
Snaclec											
ADK22822.1	Dabocetin beta subunit	*D. r. russelii*	18023	256.2	72	3.15	1-5, 7-9	260.3	75	2.55	1-5, 8
ADK22821.1	Dabocetin alpha subunit	*D. r. russelii*	17493	230.9	77	2.57	1-10	259.8	80	2.28	1-6, 8, 9
Accession no.	**Protein Description**	**Source organism**	**MW**	**EI RVV (B)**				**EI RVV (N)**			

			(Da)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)
ADK22825.1	P68 alpha subunit	*D. siamensis*	17996	200.0	61	1.09	1-4	223.3	65	1.22	1-3, 5
ABW82662.1	C-type lectin	*M. lebetina*	17759	165.3	41	0.10	2	171.7	37	0.21	2
AAY63871.1	C-type lectin-like protein subunit 2	*D. siamensis*	16923	195.2	53	0.66	1-2	177.0	48	0.82	1-3,
ADK22833.1	P31 alpha subunit	*D. r. russelii*	18106	207.6	61	0.36	2-3	154.3	56	0.53	2, 3, 5
ADK22834.1	P31 beta subunit	*D. r. russelii*	17378	164.3	32	0.90	2-3	146.2	28	0.34	2, 3
AAY63870.1	C-type lectin-like protein subunit 1	*D. siamensis*	18337	118.0	34	0.96	1-2	123.4	34	0.88	1, 2
AJO70722.1	C-type lectin-like protein 2B	*M. lebetina*	17458	109.2	16	0.22	3	46.5	6	0.05	1
AMK37409.1	C-type lectin 2	*Bitis arietans*	17891	77.5	19	0.46	1	ND	ND	ND	-
JAC96622.1	C-type lectin E, partial	*E. coloratus*	11591	69.6	16	0.22	3	ND	ND	ND	-
B4XSZ1.1	Snaclec A16	*M. lebetina*	17778	49.7	11	0.22	3	ND	ND	ND	-
Q7LZK5.1	Snaclec bitiscetin subunit alpha	*B. arietans*	14935	49.3	6	0.22	3	ND	ND	ND	-
AAY63872.1	C-type lectin-like protein subunit 3	*D. siamensis*	16910	ND	ND	ND	-	232.6	74	1.93	1, 2, 5
Q4PRC9.1	Snaclec 4	*D. siamensis*	16811	ND	ND	ND	-	198.3	69	1.11	1-3
Accession no.	**Protein Description**	**Source organism**	**MW**	**EI RVV (B)**				**EI RVV (N)**			

			(Da)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)	-10lgP	Coverage (%)	Relative abundance (%)	GF fraction (s)
ABW82659.1	C-type lectin	*M. lebetina*	17717	ND	ND	ND	-	92.3	19	0.12	2, 5
Cysteine-rich secretory protein											
ACE73567.1	CRISP Dr-CRPK	*D. russelii*	26688	255.2	41	2.24	2-7	265.4	65	1.87	2-6, 8
ALB06109.1	Cysteine-rich secretory protein	*G. intermedius*	26880	150.1	16	1.30	2-5	ND	ND	ND	-
AAP20602.1	Cysteine-rich venom protein	*P. jerdonii*	26865	78.6	6	0.33	4	ND	ND	ND	-
ACE73575.1	CRISP Da-CRPa, partial	*Deinagkistrodon acutus*	24743	ND	ND	ND	-	183.4	28	1.21	1, 4, 5
Vascular endothelial growth factor											
ACN22046.1	VR-1 precursor	*D. r. russelii*	16278	202.9	47	0.63	2-3	226.9	65	3.45	1-4,
P82475.2	VEGF toxin ICPP	*M. lebetina*	12574	90.8	25	0.49	2-3	ND	ND	ND	-
Nerve growth factor											
AAA03282.1	Nerve growth factor	*D. russelii*	13283	152.8	18	1.11	2-3	174.6	57	0.73	1-3, 5
Q2XXL6.1	Venom nerve growth factor 1	*Azemiops feae*	25024	72.6	9	0.45	3	ND	ND	ND	-
Disintegrin											
AAP20878.1	Jerdostatin	*P. jerdonii*	11849	104.1	27	2.24	6-10	91.7	19	1.38	6-8, 10

ND: not detected by LC-MS/MS analysis

Fig. 4.10c. Alignment of tryptic and semi-tryptic peptide sequences identified in EI RVV (B) with Viperidae proteins from NCBI database. The protein alignment was done using Clustal Omega programme (https://www.ebi.ac.uk/Tools/msa/clustalo/). The number of proteins in each protein classes is shown in parenthesis. The distinct peptides obtained for each of the following proteins is highlighted in green or yellow (two colours have been used in case of adjacent distinct peptides). The amino acid substitutions within the overlapping distinct peptides obtained from MS/MS are highlighted in red colour. The LC-MS/MS identified peptides other than distinct peptides are shown in blue or red colour.

Phospholipase A_2 [21]

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P0DJJ8.1        MRTLWIMAVLLLGVDGSLVQLWKMIFQETGKEAAKNYGLYGCNCGVGRRGKPKDATDSCCYVHKCCYKKVTGCDPKMDSYSYSWKNKAIVCGEKNPPCLKQVCECDKAVAICLRENLGTY
CAA48456.1      MRTLWIVAVCLIGVEGNLFQFARMINGKLGAFSVWNYISYGCYCGWGGQGTPKDATDRCCFVHDCCYGGVKGCNPKLAIYSYSFQRGNIVCGRN-NGCLRTICECDRVAANCFHQNKNTY
AAZ53182.1      MRTLWIVAMCLIGVEGNLFQFARMIDAKQEAFSFFKYISYGCYCGWGGQGTPKDASDRCCFVHDCCYARVKGCNPKLVEYSYSYRTGKIVCETY-NRCKRAVCECDRVAAICLGQNVNTY
ABD24037.1      MRTLWIVAMCLIGVEGNLFQFARMIDAKQEAFSFFKYISYGCYCGWGGQGTPKDASDRCCFVHDCCYARVKGCNPKLVEYSYSYRTGKIVCETY-NRCKRAVCECDRVAAICLGQDVNTY
AHJ09529.1      MRTLWIMAVLLVGVEGHLMQFENMIMKVAGRSGIWWYGSYGCYCGKGGQGRPQDASDRCCFVHDCCYGRANGCDPKDDFYKYSEENGDIVCEED-NPCTKEICECDKAAAICFRDNIETY
AAM80564.1      MRTLWIVAVLLLGVEGSLVQFEMLIMKVAKRSGLFSYSAYGCYCGWGGHGRPQDATDHCCFVHDCCYGKVTDCNPKTASYTYSEENGEIVCGGD-DPCKKQVCECDRVAAICFRDNIPTY
AHJ09559.1      MRTLWIMAVLLLGVEGSLIQFETLIMKVVKKSGMVWYSNYGCYCGWGGQGRPQDATDRCCFVHDCCYGKVTGCDPKMDVYSFSEENGDIVCGGD-DPCKKEICECDRAAAICFRDNLNTY
JAV01879.1      MRILWIMAVLLVGVEGNLWQFGKMINEEMGKFAFLNYVSYGCYCGWGGGGQPKDATDRCCFVHDCCYGKVTGCNAKMDIYTYSRENGDIVCGGD-DPCKKQICECDRVAVICFRDNKDTY
AAZ53180.1      MRTLWIVAVCLIGVEGNLHQFAEMIVKMTGKEAVHSYAIYGCYCGWGGQGKPQDATDRCCFVHDCCYGTVNDCNPKMATYSYSFENGDIVCGDN-NLCLKTVCECDRAAAICLGQNVNTY
P0DKR3.1        ----------------NLFQFGEMIFEKTGKEAVHSYAIYGCYCGWGGQGRAMDATDRCCFVHDCCYGRVNGCNPKMATYSTSFQNGDIVCGDN-DLCLRAVCECDRAAAICLGQNVNTY
AAN59979.1      MRTLWIVAVCLIGVEGNLFQFGDMILQKTGKEAVHSYAIYGCYCGWGGQGRAQDATDRCCFAQDCCYGRVNDCNPKMATYTYSFENGDIVCGDN-DLCLRAVCECDRAAAICLGENVNTY
P81458.1        ----------------NLFQFAEMIVKMTGKNPLSSYSDYGCYCGWGGKGKPQDATDRCCFVHDCCYEKVKSCKPKLSLYSYSFQNGGIVCGDN-HSCKRAVCECDRVAATCFRDNLNTY
A8CG78.1        MRTLWIVAVCLIGVEGNLYQFGEMINQKTGNFGLLSYVYYGCYCGWGGKGKPQDATDRCCFVHDCCYGRVKGCDPKTATYSYSFENGDIVCGGD-DPCLRAVCECDRVAAICFRENMNTY
F8QN51.1        MRTLWIVAVCLIGVEGNLFQFGKMIKYKTGKSALLSYSAYGCYCGWGGQGKPQDPTDRCCFVHDCCYGRVNGCNPKMDTYSYSFLNGDIVCGDD-DPCLRAICECDRAAAICFGENVNTY
CAE47208.1      MRTLWIVAVCLIGVEGNLYQFGNMIFKMTKKSALLSYSNYGCYCGRGGKGKPQDATDRCCFVHDCCYGGVNGCDPKLSIYSYSFENGDIVCGGD-DPCLRAVCECDRVAAICFGENLNTY
CAE47242.1      MRILWIVVVCLIGVEGNLYQFGKMIFKMTKKSALFSYSDYGCYCGWGGKGKPQDATDRCCFVHDCCYGRVNGCDPKLTIYSYSFENGDIVCGGD-DPCKRAVCECDRVAAICFGENLNTY
ADG86231.1      MRILWIVAVCLIGVEGNLYQFGKMIRYKTGKSALLSYSDYGCYCGWGGQGKPKDATDRCCFVHDCCYGRVNGCDPKLTIYSYSFENGDIVCGGD-DSCKRAVCECDRVAAICFGENLNTY
C0HK16.1        ----------------SLLEFGKMILEETGKLAIPSYSSYGCYCGWGGKGTPKDATDRCCFVHDCCYGNLPDCNNKSKRYRYKKVNGAIVCEKG-TSCENRICECDKAAAICFRQNLNTY
ABY77928.1      MRTFWIVAVLLVGVEGHLLQFNNMIKFETNKNAIPFYAFYGCYCGWGGRGRPKDATDRGCFVHDCCYEKLTDCSPKTDIYSYSWKSGVITCGEG-TPCEKQICECDRAAAVCFGENLPTY
C0HJL8.1        ----------------NLLQFNRMIKLETKKNAVPFYAFYGCYCGWGGQGQPKDATDRCCFEHDCCYGKLTKCNTKSDLYSYSSKYGFLLCGKG-TWCEEQICECDRIAATCLRRSLDTY
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AHJ09557.1      MRTLWIMAVLLLGVEGNLLQFNKMIKEETGKNAIPFYAFYGCYCGWGGQGKPKDGTDRCCFVHDCCYGRLPNCNTKSDIYSYSLKEGYITCGKG-TWCEEQICECDRVAAECFRRNLDTY
P0DJJ8.1        N-KKYTIYPKPFCKKA--DTC
CAA48456.1      N-KEYKFLSSSKCRQ-RSEQC
AAZ53182.1      N-KGYMFLSSYYCRQ-KSEQC
ABD24037.1      N-KGYMFLSSYYCRQ-KSEQC
AHJ09529.1      Q-NKYWFYPAKYCKE-ESEPC
AAM80564.1      D-NKYWRFPPENCQE-EPEPC
AHJ09559.1      NDKKYWAFGAKNCPQEESEPC
JAV01879.1      N-KKHRVLNGKNCQE-ASDPC
AAZ53180.1      D-KNYENYAISHCTE-ESEQC
P0DKR3.1        N-KNYEHYSISHCME-ESEQC
AAN59979.1      D-KNYEYYSISHCTE-ESEQC
P81458.1        D-KKYHNYPPSQCTG-TE-QC
A8CG78.1        D-KKYMLYSIFDCKE-ESDQC
F8QN51.1        D-KKYKYYSSSHCTE-TE-QC
CAE47208.1      D-KKYKNYPSSHCTE-TE-QC
CAE47242.1      D-KKYKNYPSSQCTE-TE-QC
ADG86231.1      D-KKYKNYPSSQCTE-TE-QC
C0HK16.1        S-KKYMLYPDFLCKG-ELVC-
ABY77928.1      K-KRYMFYPDFLCTD-PSEKC
C0HJL8.1        K-LKYMFYLDSYCKG-PSEKC
AHJ09557.1      N-NGYMFYRDSKCTE-TSEEC
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Snake venom metalloprotease [10]

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ADI47593.1      ------------------------------------------------------------------------------------------------------------------------
ADW54349.1      ------------------------------------------------------------------------------------------------------------------------
ADJ67475.1      MMQVLLVTISLAVFPYQGSSIILESGNVNDYEVVYPQKVTAMPKGAVKQPEQKYEDTMQYEFEVNGEPVVLHLEKNKILFSEDYSETHYYPDGREITTNPPVEDHCYYHGHIQNDGHSSA
AAZ39880.1      MMQVLLVTICLAVFPYHGSSIILESGNVNDYEVVYPQKVTAMPKEAVKQPEQKYEDAMQYKFEVNGEPVLLHLEKNKDLFSEDYSETHYSPDGREITTKPLVQDHCYYHGHIQNDAHSSA
JAC96600.1      ------------------------------------------------------------------------------------------------------------------------
AAX38182.1      MMQVLLVTICLAVFPYQGSSIILESGNVNDYEVVYPQKITALPKGAIQQPEQKYEDAIKYEFKVNGKPVVLHLEKNKGLFSEDYSETHYTPDGREITINPPVEDHCYYHGRIQNDADSTA
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ADJ67474.1      ----------------------------------------------------------------------------------------------------------------------
AAT91068.1      ----------------------------------------------------------------------------------------------------------------------
ADJ67473.1      ----------------------------------------------------------------------------------------------------------------------
AFE61611.1      ----------------------------------------------------------------------------------------------------------------------

ADI47593.1      ----------------------------------------------------------------------------------------------------------------------
ADW54349.1      ----------------------------------------------------------------------------------------------------------------------
ADJ67475.1      SISACNGLKGHFKLRGEMYFIEPLKLSNNEAHAVYKYENIEKEDETPKMCGVTQTNWESDKPIKKASQLVSTSAQ----FNKAFIELIIIVDHSMAKKCNS--TATNTKIYEIVNSANEI
AAZ39880.1      SISACNGLKGHFKLRGEMYLIEPLKLSDSEAHAVYKYENVEKEDEALKMCGVTQTNWESDEPIKKASLLVATSERNRYFNPYSYVELIITVDHSMVTKYKNDLTAIRTWVFELVNTINEI
JAC96600.1      ----------------------------------------------------QTNWESDEPFKASQLN-LTPEQRTYLKSKKYIELVIVADYIMFWKYDHDLSTIRTRIYEIVNTLNVI
AAX38182.1      SISACNGLKGHFKLQGEMYLIEPLRIPDSEAHAIYKYENIEKEDEAPKMCGVTQTNWESDEPIKASQLN-LTPEQRTYLKSKKYVELVIVADYIMFWKYDRSLSTIRTRIYEIVNTLNVI
ADJ67474.1      ----------------------------------------------------------------------------------------------------------MGRFIFVS
AAT91068.1      ----------------------------------------------------------------------------------------------------------MGRSISVS
ADJ67473.1      ----------------------------------------------------------------------------------------------------------MGRFIFVS
AFE61611.1      ----------------------------------------------------------------------------------------------------------MGRFISVS

ADI47593.1      ----------------------------------------------------------------------------------------------------MGHSLGMLHDTKSCTCGA
ADW54349.1      ------------------------------------------------RHDHAQLLTNVTLDGTTLGITFVFGMCKSDRSVELIRDYSNITFNMAYIMAHEMGHSLGMLHDTKSCTCGD
ADJ67475.1      FNPLNIHVTLIGVEF--WCDRDLINVTSSADETLDSFGEWRASDLMTRKSHDNALLFTDMRFDLNTLGITFLAGMCQAYRSVGIVQVQQGNRNFKTAVIMAHELSHNLGMYHDGKNCICND
AAZ39880.1      FKYLYIRVPLVGLEI--WKNRDLINVTSAANVTLDLFGEWRKSYLLPRKIHDNSQLLTAIDLNGLTIGMAYVSTMCQSKYSVGVVQDHSKINLRVAVTMAHEIGHNLGLTHDGVYCTCGG
JAC96600.1      YRVLNIYVALVGLEI--WCKGNLINVTSSAYDTLDSFGEWREKDLLNRKRHDNAQLLTGIDFSGAAAGRGYVGRMCQPKYSVGIVQDHNKIYLLVASAMAHEMGHNLGMDHDGIHCTCGA
AAX38182.1      YRFLNIYIALVAVEI--WSKGDLINVTSSAYDTLDSFGEWRERDLLNRKRHDNAQLLTGINFNGPSAGRGFVGRMCQPKYSVGTVQDHSKIYLLVASAMAHEMGHNLGMDHDRIDCTCGA
ADJ67474.1      FGWLVVFLSLSGTEAVLDCPSGWLSYEQHCYKGFNDLKNWTDAEKFCTEQKKGSHLVSLHS-------------REEEKFVVNLISENLE-------YPATW--IGLG--NMWKDCR---
AAT91068.1      FGLLAVFLSLSGTGAGLDCPPDSSPYRYFCYRVFKEQKNWADAERFCAERPNNGHLVSIES-------------MEEAEFVAQLLSKITGKF-----ITHFW--IGLRIEDKKQQCR---
ADJ67473.1      FGLLAVFLSLSGTGAGLDCPPDSSPYRYFCYRVFKLRKSWEAAERFCMEHPNNGHLVSIES-------------MEEAEFVAKLLSNTTGKF-----ITHFW--IGLRIKDKEQECS---
AFE61611.1      FGLLVVFLSLSGTGAGLDCPPDSSLYRYFCYRVFKEHKTWEAAERFCMEHPNNGHLVSIES-------------MEEAEFVAKLLSNTTGKF-----ITHFW--IGLMIKDKEQECS---

ADI47593.1      NPCIMFSEVSEPTPKEFSRCSYDQYRDYLPKYNPKCIFDPPLRNDIVSPAVCGNEIWE-----EGEECDCGSPADCENSCCDAATCKLKPGAECGNGECCDKCKIRTAGTECRAARDDCD
ADW54349.1      KPCIMFSKESVPPPKEFSSCSYDQYNKYLLKYNPKCILDPPLRKDIASPAVCGNGIWE-----EGEECDCGSPEDCENPCCDAATCKLKPGAECGNGECCDNCKIRKAGTECRPARDDCD
ADJ67475.1      SSCVMSPVLSDQPSKLFSNCSIHDYQRYLTRYKPKCILYPPLRKDIVSPPVCGNEIWE-----EGEECDCGSPADCQNPCCDAATCKLKPGAECGNGLCCYQCKIKTAGTVCRRARNECD
```

```
AAZ39880.1      YSCIMSAVLGDQPSKYFSNCSYNQYRRFLTEHNPECIINPPLRTDIVSPPACGNELLE-----RGEECDCGSPENCRDPCCDAASCKLHSWVECESGKCCNQCRFKRAGTECRPARDECD
JAC96600.1      KSCIMSGILRCETSYLFSDCSREAHRKYLINNMPQCILNKPLKTDIVSPPVCGNYFVE-----VGEECDCGSPRNCQDQCCDAATCKLRPGAQCGEGVCCYQCKFKRAGTVCRPANGECD
AAX38182.1      KSCIMSGILRCETSYLFSDCSREEHRKYLINKMPQCILNKPLKTDIVSPAVCGNYFVE-----VGEECDCGSPANCQDRCCDAATCKLRPGAQCGDGVCCYQCKFRRAGTVCRPANGECD
ADJ67474.1      --------------MEWSDRGNVKYKALAEESYCL-------------IMITHEKVWKSMTCNFIAPVVCKF----------------------------------------------
AAT91068.1      --------------SEWSDGSSVSYDNLLKREFRKCFGL---------EKGTGYRSWFNLNCEEPYPFVCKVPPNC----------------------------------------------
ADJ67473.1      --------------SEWSDGSSVSYDNLGKEEFRKCFVL---------QKESGYRMWFNHKCEEPYPFVCKVPPEC----------------------------------------------
AFE61611.1      --------------SEWSDGSSVSYDKLGKEEFRKCFVL---------EKESGYRMWFNRNCEERYVFVCKVPPEC----------------------------------------------

ADI47593.1      VPEHCTGQSAECPRNEFQRNGQPCLNNSGYCYNGDCPIMKNQCILLFSPNATVDVDACFQWNLRGIFDGYCTKEIGSYGRRFPCAPQDVKCGRLYCLDKSARKKKRCKTNYSPDDENKGM
ADW54349.1      VAEHCTGQSAECPRNEFQRNGQPCLNNSGYCYNGDCPIMLNQCIALFSPSATVAQDSCFQRNLQGSYYGYCRKEIGHYGKRFPCAAQDVKCGRIYCLDNSFKK----------------
ADJ67475.1      VPEHCTGQSAECPRDQLQQNGQPCQNNRGYCYNGDCPIMRNQCISLFGSRATVAKDSCFQENLKGSYYGYCRKEN---GRKIPCAPQDVKCGRLFCLNNSPRNKNPCNMHYSCMDQHKGM
AAZ39880.1      KAEQCTGRSANCPVDEFHENGRPCLHNFGYCYNGKCPIMYHQCHALFGQNVTGVQDSCFQYNRLGVYYAYCRKEN---GRKIPCAPKDEKCGRLYCSYKSPGNQIPCLPYYIPSDENKGM
JAC96600.1      VSDHCTGQSAECPTDHFQKNGQPCLLNRGYCYNGRCPIMIHQCIILWGPGTTVSPDICFQENNKGQGYFYCRREN---NKNIPCAPQDVKCGRLFCKLPI-HNTHPCNYRYSDVALDYGM
AAX38182.1      VSDLCTGQSAECPTDQFQRNGQPCQNNKGYCYNGTCPIMEKQCISLFGASATVAQDSCFQFNRRGNHYGYCRKEN---NTKIACAPEDVKCGRLYCLDNSSGHKNPCQIYYIPSDENKGM
ADJ67474.1      ----------------------------------------------------------------------------------------------------------------------
AAT91068.1      ----------------------------------------------------------------------------------------------------------------------
ADJ67473.1      ----------------------------------------------------------------------------------------------------------------------
AFE61611.1      ----------------------------------------------------------------------------------------------------------------------

ADI47593.1      VD--------------------------------
ADW54349.1      ----------------------------------
ADJ67475.1      VDPGTKCEDGKVCNNKRQCVDVNTAYQSTTGFSQI
AAZ39880.1      VDHGTKCGDGKVCSNG-QCVDLNTAY---------
JAC96600.1      VDPGTKCGDGMVCNGN-RECV--------------
AAX38182.1      VDPGTKCGDGMVCSNG-KCVDVTIAY---------
ADJ67474.1      ----------------------------------
AAT91068.1      ----------------------------------
ADJ67473.1      ----------------------------------
AFE61611.1      ----------------------------------
```

Snake venom serine protease [9]

```
P18964.1        ------------------------VVGGDECNINEHPFLVALYTSTSSTIHCCGALINREWVLTAAHCDRRNIRIKLGMHSKNIRNEDEQIRVPRGKYFCLNTKFPNGLDKDIMLIRLRR
P18965.2        MVLIKVLANLLVLQLSYAQKSSELVVGGDECNINEHPFLVALYTSASSTIHCAGALINREWVLTAAHCDRRNIRIKLGMHSKNIRNEDEQIRVPRGKYFCLNTKFPNGLDKDIMLIRLRR
B0FXM1.1        MVLIRVLANLLILQLSYAQKSSELVIGGDECNINEHNFLVALYEYWSQSFLCGGTLINGEWVLTAAHCDRKHILIYVGVHDRSVQFDKEQRRFPKEKYFFNCRNNFTKWDKDIMLIRLNK
AMB36342.1      MVLIRVLANLLVLQLSYAQKSSELVTGGDECNINEHPFLVALHTARSKRFYCAGTLINQEWVLTAARCDRKNIRIILGVHSKNVPNEDEQMRVPKEKFFCLSSKTYTRWDKDIMLIRLKR
E0Y418.1        MVLIRVLANLLVLHLSYAQKSSELVIGGDECNINEHPFLALMYNSTSMKFHCSGTLLNEEWVLTAAHCDMENMQIYLGVHDKKNPNKDQQTRVPKEMFFCLSNKSYTPWDKDIMLIRLNS
JAS04410.1      MVLIRVLANFLILQLSYAQKSSELVIGGDECNINEHRSLALMYNSS--GFICGGTLINQEWVLTAAHCNMENMKIDFGVHNGRVHYDDMQTRVPEEKFFCLSSNNDTEWDKDIMLIRLDR
ADP88560.1      MVLIKVLANLLVLQLSYAQKSSELVVGGDECNINEHRSLVFLYN-N--SFGCSGTLINQQWVLSAVHCDMENVRIYLGVHNLTLRNNA-EIRLPEERFFCLSNKNYTKWDKDIMLIKLDR
E0Y419.1        MVLIRVLANLLLLQLSHAQKSSELVVGGDECNINEHRSLVFLYN-S--SFGCGGTLINQEWVLSAAHCDMENMRIYLGWHNFSLPNMNQKRRVAKEKFFCLSSKNYTEWDKDIMLIKMNR
E0Y420.1        MVLIRVLANLLVLQLSYAQKSSELVIGGDECNINEHRSLVYLYNDS--NFQCGGTLINQEWVLSAAHCDMENMEIYLGVHNLSLPNKDQKRRDPKEKFFCLSSKNYTKWDKDIMLIKLNR

P18964.1        PVTYSTHIAPVSLPSRSRGVGSRCRIMGWGKISTTEDTYPDVPHCTNIFIVKHKWCEPLYP--WVPADSRTLCAGILKGGRDTCHGDSGGPLICNGQIQGIVAGGSEPCGQHLKPAVYTK
P18965.2        PVTYSTHIAPVSLPSRSRGVGSRCRIMGWGKISTTEDTYPDVPHCTNIFIVKHKWCEPLYP--WVPADSRTLCAGILKGGRDTCHGDSGGPLICNGEMHGIVAGGSEPCGQHLKPAVYTK
B0FXM1.1        PVSYSEHIAPLSLPSSPPIVGSVCRVMGWGTIKSPQETLPDVPHCANINLLDYEVCRTAHPQFRLPATSRILCAGVLEGGIDTCHRDSGGPLICNGEFQGIVSWGDGPCAQPDKPALYSK
AMB36342.1      PVNDSTHIAPLSLPSSPPSVGSVCRIMGWGTITTTKVTYPDVPHCADINMFDYSVCQKVYR--KLPEKSRTLCAGILQGGIDSCKVDNGGPLICNGQIQGIVSWGGYPCAQPHKPALYTN
E0Y418.1        PVTYSTHIAPFSLPSSPPTVGSVCRIMGWGAITSPNETYPDVPHCANIEIYDYSVCRKAYG--GLPEKSRTLCAGVLQGGIDTCLADSGGPLICNGQFQGIVAWGRHPCAQPQLPAFYTK
JAS04410.1      PVRNSAHIAPLSLPSNPPRLGSVCRIMGWGAITSPNETFPDVPHCANINIIRYSVCQAVYL--GMPVQSRILCAGILRGGIDSCKGDSGGPLLCNGQFQGILSAGGDPCAQPRVPGLYIK
ADP88560.1      PVKTSTYIAPLSLPSSPPRVGSVCRIMGWGAITSPNETFPGVTHCANINILPYSVCRAAYK--GLPAQSRTLCGGILEGGIGSCMGDSGGPLICNGEMHGIVAWGDDTCAQPHKPVHYTK
E0Y419.1        PVTYSTHVAPLSLPSSPPSVGSVCRIMGWGAITSPNETYPDVPHCANINILNYTVCRAAHP--WLPAQSRTLCAGILQGGIDTCKGDSGGPLICNGQIQGIVSWGDNPCAQPLKPGHYTN
E0Y420.1        PVKTSTHIAPLSLPSSPPSVGSVCRIMGWGTVTSPNETLLDVPHCANINILNYTVCRAASP--RLPTQSRTLCAGILQGGIDACKGDSGGPLICNGQIQGIVSWGNHPCAQPLKPGHYTH

P18964.1        VFDYNNWIQNIIAGNRTVTCPP
P18965.2        VFDYNNWIQSIIAGNRTVTCPP
B0FXM1.1        VFDHLDWIQNIIAGSETVNCPS
AMB36342.1      VFDYTDWIQSIIAGNITATCPP
E0Y418.1        VFDYSDWIQSIIAGNTAATCPS
JAS04410.1      VFDYTDWIQSIIAGNTAATCPP
ADP88560.1      VYDYTDWIQSIIAGNTAATCPP
E0Y419.1        VFDYTDWIQSIIAGNTTATCPP
E0Y420.1        VFDYTDWIQSIIAGNTTATCPP
```

L-amino acid oxidase [1]

ACF70483.1 MNVFFMFSLLFLATLGSCADDKNPLEECFREDDYEEFLEIAKNGLKKTSNPKHIVIVGAGMSGLSAAYVLAGAGHKVTVLEASERPGGRVRTHRNVKEGWYANLGPMRVPEKHRIIREYI
RKFGLKLNEFVQETENGWYFIKNIRKRVGEVKKDPGLLKYPVKPSEAGKSAGQLYQESLGKAVEELKRTNCSYILNKYDTYSTKEYLIKEGNLSPGAVDMIGDLLNEDSGYYVSFIESLK
HDDIFAYEKRFDEIVGGMDQLPTSMYRAIEESVHFKARVIKIQQNAEKVTVTYQTTQKNLLLETADYVIVCTTSRAARRITFKPPLPPKKAHALRSVHYRSGTKIFLTCTKKFWEDDGIQ
GGKSTTDLPSRFIYYPNHNFTTGVGVIIAYGIGDDANFFQALNLNECADIVFNDLSSIHQLPKKDLQTFCYPSIIQKWSLDKYAMGAITTFTPYQFQHFSEALTAPVGRIFFAGEYTANA
HGWIDSTIKSGLTAARDVNRASEL

Phosphodiesterase [1]

BAN89426.1 MEMFPEDKDETEMGEKSTLDLIDFQTERIIKRSTLRKYKILCVVLFISLVAVALGLGLGLGLKEPVQPQAQSWSCSKLRCGEKQIANVLCSCSEDCLEKKDCCTDYKSICKGETSWLKDK
CASPSATQCPAGFEESPLILFSMDGFRAGYLESWDSLMPNINKLKTCGTHAKYMRAVYPTKTFVNHYTIATGLYPESHGIIDNNIYDVNLNLNFSLSGSAARNPAWWGGQPIWHTATYQG
LKAATYFWPGSEVKINGSYPTIFKNYNKSIPFEARVTEMLKWLDLPKDKRPDFYTLYIEEPDTTGHKYGPVSGEIIKALEMADRTLGMLMEGLKQRNLHNCVNLILLADHGMEEISCDRL
EYMANYFNNVDFFMYEGPAPRIRSKNVPKDFYTFDSEGIVKNLTCQKPKQYFKAYLSKDLPKRLHYVNNVRIDKVNLMVDQQWMAVRDKKFTRCKGGNHGYDNEFKSMQAIFLAHGPGFN
EKNEVTSFENIEVYNLMCDLLKLKPAPNNGTHGSLNHLLKNPFYTPSPAKEQSSPLSCSFGPVPSPDVSGCKCNSITELEKVNQRLNFSNQAKTESEAHNLPYGRPEVLQNHSKYCLLHQ
AKYISAYSQDILMPLWSSYTIYRSTPTSVPPSASDCLRLDVRIPAAQSQTCSNYQPDPTITPGFLYPPNFNSSNFEQYDALITSNIVPMFKGFTRLWNYFHTTLIPKYATERNGLNVISG
PIFDYNSDGHFDSYNTSKQHVNNTKIPIPTHYFVVLTSCENEMNTPLNCLGPLKVLSFILPHRPDNSESCADTLPENLWVEERIQIHTARVRDVELLTGLNFYSGLKQPLPETLQLKTFL
PIFVNPVN

5'-Nucleotidase [1]

AHJ80886.1 AREKVGIIGYTTKETPVLSNPGPYLEFRDEVEELQIHANKLTTLGVNKIIALGHSGFFEDQRIARKVKGVDVVVGGHTNTFLYTGSPPSTEVPAGNYPFMVQSDDGRQVPVVQAYAFGKY
LGYLNVVFNDKGNVIKASGNPILLNKDIPEDQVVKAQVNKMKIQLQNYYSQEIGKTIVYLNGTTQACRFHECNLGNLICDAVIYNNLRHPDDNEWNHVSMCIVNGGGIRSPIDERANNGI
ITLEELTSVLPFGGTFDLLQIKGSALKQAFEHSVHRHGQGTGELLQVSGIKVVYDLSQKPGSRVVSLNVLCTKCRVPTYVPLEMEKTYKVLLPSFLATGGDGYHMLKGDSSNHNSGDLDI
SIVGDYIKRMEKVFPAVEGRVTFLDGTLFQAQLFLTWGLCISLLFFIL

Glutaminyl cyclase [1]

Q90YA8.1 MARERRDSKAATFFCLAWALCLALPGFPQHVSGREDRVDWTQEKYSHRPTILNATCILQVTSQTNVNRMWQNDLHPILIERYPGSPGSYAVRQHIKHRLQGLQAGWLVEEDTFQSHTPYG
YRTFSNIISTLNPLAKRHLVIACHYDSKYFPPQLDGKVFVGATDSAVPCAMMLELARSLDRQLSFLKQSSLPPKADLSLKLIFFDGEEAFVRWSPSDSLYGSRSLAQKMASTPHPPGARN
TYQIQGIDLFVLLDLIGARNPVFPVYFLNTARWFGRLEAIEQNLYDLGLLNNYSSERQYFRSNLRRHPVEDDHIPFLRRGVPILHLIPSPFPRVWHTMEDNEENLDKPTIDNLSKILQVF
VLEYLNLG

Hyaluronidase [1]

```
ABI33950.1      MYHIWIKFLAAWIFLKRFNGVHVMQAKAPMYRNEPFLVFWNAPTTQCRLRYKEDLVTTVGETAAMGAAGIVFWGSVQYASTVDSCQKVKKYMNGPLGRYIVNVTTAAKICSRVLCRKNGR
                CVRKHSDSNAFLHLFPESFRIMVYANATEKKVIVKGKLELENLIYLRENFMCQCYQGWKGLYCEEYSIKDIRKI
```

Aminopeptidase [1]

```
XP_015676063.1 MASVSSLLRAWILLSLHGCVTSYPKQADSAAEDIRNCTINPPYLPPTVIVTDERLKTLREHMKTHKLSAYIVPNTDAHLSEYVAERDKRLSWMTGFSGSEGTGVITLQKAALFTDSRYWI
                QAERQMDCNWELQKSVWINSIGQWILKEVPAGETIGLDPFLFSVDTWFNYHQVLEGTNRTLEFLEVNLVDLVWGSERLPPPTNTIYRLADDFMGSTWQEKVASARKQMEEHSKKPTAILL
                SGLEETAWLFNLRGDDIPYTPVFYAYTLLTKTDISLFANRSRLSKEALQMLTAGCPESPCVKVEDYEQIGASLRKYVHQDGVIIWIGTEYTTLGLYKEIPQENLLEDDFSPVMLSKAVKN
                HIRDAVALIRYLVWLEKNVPKNSVDEASGANYLNTLRREELHCKGPSFETISASGLNAALAHYSPSNLTSRKLSLNEMYLLDSGGQYFDGTTDITRTIHWGEPTAFQKEAYTRVLMGNID
                LSKLVFPPRSSGRLVESFARRPLWEAGLNYGHGTGHGIGNFLSVHEWPVGFQSNNVPLDKGMFTSIEPGYYHDGEFGIRLEDVALVVQAKTKYPVKEEPYLTFKVVSLVPYARNLINESL
                LSRDQIQYINKYYETIRQIIGPELQRRQLEEEYRWLEKNTEPFSHASLLAASLGTLAVSTLASGLLPAAQH
```

Kunitz-type serine protease inhibitor [6]

```
ABD24041.1      MSSGGLLLLLGLLTLWAEPTPISGQDRPKFCFLRPDFGRYGHPRPRFYYNPATNQCQGFLAQRSFENTNNFDTRDKCRQTCGRK------
A8Y7P1.1        MSSGGLLLLLGLLTLWAELTPISGHDRPKFCYLPADPGECLAHMRSFYYDSESKKCKEFTYGGCHGNANKFPSRDKCRQTCGGK------
AFD04724.1      MSSGGLLLLLGLLALWAELTPISGHDRPKFCYLPADPGECMAYIRSFYYDSESKKCKEFTYGGCHGNANNFPTRDKCRQTCRAPRKGRHT
ABD24043.1      MSSGGLLLLLGLLTLWAELTPISGQDRPKFCHLPVDSGICRAHIPRFYYNPASNQCQGFTYGGCGGNANNFETRDQCRHTCGGK------
A8Y7N8.1        MSSGGLLLLLALLTLWAELTPISGHDRPTFCNLAPESGRCRGHLRRTYYNPDSNKCEVFFYGGCGGNDNNFETRKKCRQTCGAPRKGRPT
ABD24040.1      MSSGGLLLLLGLLTLWAELTPISGHDRPTFCNLAPESGRCRGHLRRIYYNLESNKCKVFFYGGCGGNANNFETRDECRQTCGGK------
```

Snaclec [13]

```
ADK22822.1      MGRFISVGFGLLVVFLSLSGTGAKQDCLSDWSFYEGYCYKVFNEKKTWEDAEKFCNEQVNGGYLVSFRSSEEMDFVIRMTFPIFRF--DFFWIGLRDFW--RDCYWRWSDGVNLDYKAWS
AJO70722.1      MGRFISVSFGCLVVFLSLSGTGADQDCPSDWSSHEGHCYKVFNLRMNWADAEKFCTEVVSGGHLISLNSAEEVDFMIKLVFPILKF--DFIWIGLRDFW--RDCHWGWSDGVKLDYKAWS
ADK22834.1      MGRFIFVSFSLLVVFLPLSGTEAGFSCPNGWSSFGQHCYKVIEPLKNWTDAEKFCREQHKGSHLASIHSSEEEAFVSKVASKVLKF--GSVWIGLNDPW--HNCNWEWSDNARFDYKAMT
AAY63871.1      MGRFISVSFGWLVVFLSLSGTEAVLDCPSGWLSYEQHCYKGFNDLKNWTDAEKFCTEQKKGSHLVSLHSREEEKFVVNLISENLEY--PATWIGLGNMW--KDCRMEWSDRGNVKYKALA
B4XSZ1.1        MGRLISVSFGLLVVFLSLSGTGADQDCLPGWSFYEGHCYKVFNVKKTWEDAEKFCQKQSNGKHLATIEWLGKANFVADLVTLMN-SDPDLDWIGLRVEDKRQQCSSHWTDGSAVSYENVV
ADK22821.1      MGRFISVSFGLLVVFLSLSGTG--ADCPSDWSSHEGHCYKVFKLLKTWEDAEKFCTQQANGWHLASIESVEEANFVAQLASETLTKSKYHAWIGLRDQSQRQQCSSHWTDGSAVSYETVT
Q7LZK5.1        ----------------------D--PGCLPDWSSYKGHCYKVFKKVGTWEDAEKFCVEN--SGHLASIDSKEEADFVTKLASQTLTKFVYDAWIGLRDESKTQQCSPQWTDGSSVVYENVD
AAY63870.1      MGRFISVSFGLLVVFLSLSGTGAGLDCPEDSSLYRYFCYFVFKEHKTWEAAERFCMEHPNNGHLVSIESMEEAEFVAKLLSNTTGKFITHFWIGLMIKDKEQECSSEWSDGSSVSYDKLG
```

```
ADK22833.1      MGRFISVSFGLLVVFLSLSGIGADLDCPSGWSAYDQHCYQAVDEPKSWADAEKFCTEQANSGHLVSIKSVGEANFVAQLASGFMQKDGIYVWIGLRDRRKEQQCRSEWTDGSKIIYVNWK
JAC96622.1      ------------------------------------------------------------NGGHLVSIQSREEGNFVAQLVSGFIQRPGIYVWIGLRDRRKEQQCTSEWNDGSKIIYVNWK
AMK37409.1      MGRFIFLSSGLLVVFLSLSG--ADFECPTEWCPYDQHCYRAFDEPKRSVDAEKFCVEQ--AGHLASIESQEEADFVAQLVSENVKSSPDYVWIGLWNQRKEQYCNKKWTDGSSVIYQNMV
ADK22825.1      MGRFISVSFGLLVVFLSLSGTRADFDCPSGWSAHDQHCYKAFDEPKRSGDAETFCTEQANSGHLVSIESVEEAEFVAQLISENIKTPADYVWIGLRNQRKAQYCISKWTDGSSVIYKNVI
ABW82662.1      MGRFIFVRFGLLVVFLSLSGTGADFDCPPDWSAYDQHCYKAFDEPKRSGDAEKFCTQQANGGHLVSIESVEEAEFVAQLISENIKTSADYVWIGLWNQRKAPYCVSKWTDGSSVIYKNVI

ADK22822.1      R--EPNCFVSKTT--DNQWLRWNCNDPRYFVCKSRVSC--
AJO70722.1      D--EPNCYVAKTV--DYQWLFRDCNRTSRFICKSRVPR--
ADK22834.1      R--RPYCTVMVLKPDRIFWFNRGCEKTVSFVCKFLA----
AAY63871.1      E--ESYCLIMITH--EKVWKSMTCNFIAPVVCKF------
B4XSZ1.1        H--NTKCFGLDQKTGYRTWVALRCELAYHFICMSRVPRGA
ADK22821.1      K--YTKCFGLNKETKYHEWITLPCGDKNPFICKSWVLH--
Q7LZK5.1        E--PTKCFGLDVHTEYRTWTDLPCGEKNPFICKSRLPH--
AAY63870.1      KQEFRKCFVLEKESGYRMWFNRNCEERYLFVCKVPPEC--
ADK22833.1      EGESKMCQGLAKWTYFHKWDYVNCAEHYRFVCKFPPQY--
JAC96622.1      EGESKMCQGLAKWTDFHEWDNINCADRYRFVCKFPSQC--
AMK37409.1      ERFRKNCFGLEKESGYRTWLNLCCGDDYPFVCKFPPRC--
ADK22825.1      ERFIKNCFGLEKESDYRTWFNLSCGDDYPFVCKFPPRC--
ABW82662.1      ERFIKNCFGLEKETNYRTWFNLSCGDDYPFVCKSPA----
```

Cysteine-rich secretory protein [3]

```
ALB06109.1      MIVFIVLPILAAVLQQSSGSVDFDSESPRKPEIQNEIVDLHNSLRRSVNPTASNMLKMEWSFNAAQNAKRWADRCTFAYSPQNLRTVGKLKCGENLFMSSHPFPWTRVIQFWYDENKNFK
AAP20602.1      MIAFIVLPILAAVLQQSSGNVDFDSESPRKPEIQNEIIDLHNSLRRSVNPTASNMLKMEWYPEAAANAERWAYGCIESHSSRDSRVIEGIKCGENIYMSPYPMKWTDIIHAWHGEYKDFK
ACE73567.1      MIAFIVLPILAAVLQQSSGSVDFDSESPRRPEIQNEIVDLHNSLRRSVTPTASNMLKMEWYPEAAANAERWAFRCILNHSPYNSRVIGGIKCGENIYMSPYPMKWTAIIHEWHKEKKDFV

ALB06109.1      YGVGANPPNAIIGHYTQVVWYKSYLVGCAAARCPSSSYNYLYVCHYCPAGNIIGKIATPYKSGPPCGDCPSACDNGLCTNPLKYEDRFSNCNDLVKQLSCQNNNIKSSCPASCFCHNEIK
AAP20602.1      YGVGAVPSDAVVGHYTQIVWYKSYRIGCAAAYCPSAEYSYFYVCQYCPAGNMIGKTATPYTSGPPCGDCPSDCDNGLCTNPCRQENKFTNCDSLVRQSSCQDNYMKTNCPASCFCHNEII
ACE73567.1      YGQGASPANAVVGHYTQIVWYKSYRSGCAAAYCPSSEYNYFYVCQYCPAGNIIGKIATPYTSGPPCGDCPSACDNGLCTNPCSHHDEFTNCKDLVKQ-GCHSNYLKTKCPASCFCHNEII
```

Vascular endothelial growth factor [2]

```
ACN22046.1      MAAYLLAVAILFCIQGWPSGTVQGQVRPFLDVYERSACQTRETLVSILQEHPDEISDIFRPSCVAVLRCSGCCTDESMKCTPVGKHTADIQIMRMNPRTHSSKMEVMKFMEHTACECRPR
P82475.2        ------------------------QVRPFPDVYQRSACQARETLVSILQEYPDEISDIFRPSCVAVLRCSGCCTDESLKCTPVGKHTVDMQIMRVNPRTQSSKMEVMKFIEHTACECRPR

ACN22046.1      WKQGEPEGPKEPRRGGVRAKFPFD
P82475.2        RKQGEPDGPKEKPR----------
```

Nerve growth factor [2]

```
AAA03282.1      ----------------------------------------------------------------------------------------------------HPVHNQGEFSVCDS
Q2XXL6.1        GEDNVPLGSPATSDLSDTSCAKTHEALKTSRNTDQHYPAPKKAEDQEFGSAANIIVDPKLFQKRRFQSPRVLFSTQPPPLSRDEQSVEFLDNADSLNRNIRAKRGTHPVHNQGEYSVCDS

AAA03282.1      VSVWVANKTTATDMRGNVVTVMVDVNLNNNVYKQYFFETKCKNPNPVPSGCRGIDAKHWNSYCTTTDTFVRALTMERNQASWRFIRINTACVCVISRKNDNFG
Q2XXL6.1        VSVWVANKTTATDIRGNLVTVMVDINLNNNVYKQYFFETKCRNPNPVPSGCRGIDARHWNSYCTTTHTYVRALTKEGNQASWRFIRIDTACVCVISRITENFG
```

Disintegrin [1]

```
AAP20878.1      MIQVLLVTICLAVFPYQVSSKTLKSGSVNEYEVVNPGTVTGLPKGAVKQPEKKHEPMKGNTLQKLPLCTTGPCCRQCKLKPAGTTCWRTSVSSHYCTGRSCECPSYPGNG
```

Fig. 4.10d. Alignment of tryptic and semi-tryptic peptide sequences identified in EI RVV (N) with Viperidae proteins from NCBI database. The protein alignment was done using Clustal Omega programme (https://www.ebi.ac.uk/Tools/msa/clustalo/). The number of proteins in each protein classes is shown in parenthesis. The distinct peptides obtained for each of the following proteins is highlighted in green or yellow (two colours have been used in case of adjacent distinct peptides). The amino acid substitutions within the overlapping distinct peptides obtained from MS/MS are highlighted in red colour. The LC-MS/MS identified peptides other than distinct peptides are shown in blue or red colour.

Phospholipase A_2 [12]

```
AAZ53182.1      NLFQFARMIDAKQEAFSFFKYISYGCYCGWGGQGTPKDASDRCCFVHDCCYARVKGCNPKLVEYSYSYRTGKIVCETYNRCKRAVCECDRVAAICLGQNVNTYNKGYMFLPSYYCRQKSEQC
AAZ53180.1      NLFQFAEMIVKMTGKEAVHSYAIYGCYCGWGGQGKPQDATDRCCFVHDCCYGTVNDCNPKMATYSYSFENGDIVCGDNNLCLKTVCECDRAAAICLGQNVNTYDKNYENYPISHCTEESEQC
AHJ09529.1      HLMQFENMIMKVAGRSGIWWYGSYGCYCGKGGQGRPQDASDRCCFVHDCCYGRANGCDPKDDFYKYSEENGDIVCEEDNPCTKEICECDKAAAICFRDNIETYQNKYWFYPAKYCKEESEPC
CAA48456.1      NLFQFARMINGKLGAFSVWNYISYGCYCGWGGQGTPKDATDRCCFVHDCCYGGVKGCNPKLAIYSYSFQRGNIVCGRNNGCLRTICECDRVAANCFHQNKNTYNKEYKFLSSSKCRQRSEQC
ACB59359.1      DLSQFGDMINKKTGTFGLFSYIYYGCYCGWGGKGKPQDATDRCCFVHDCCYGSVNGCDPKLSTYSYSFQNGDIVCGDDDPCLRAVCECDRVAAICSGENMNTYDKKYMLYSLFDCKEESEKC
AAN59979.1      NLFQFGDMILQKTGKEAVHSYAIYGCYCGWGGQGRAQDATDRCCFAQDCCYGRVNDCNPKMATYTYSFENGDIVCGDNDLCLRAVCECDRAAAICLGENVNTYDKNYEYYSISHCTEESEQC
AAZ53183.1      NLLQFGNMIFRMTAKNPLSSYSNYGCYCGWGGKGKPQDATDRCCFVHDCCYEKVNDCNPKTATYSYSFENGGIVCGDRDPCKRAVCECDRVAATCFRQNLNTYDKKYRKYFPSQCTGTEQC-
CAE47208.1      NLYQFGNMIFKMTKKSALLSYSNYGCYCGRGGKGKPQDATDRCCFVHDCCYGGVNGCDPKLSIYSYSFENGDIVCGGDDPCLRAVCECDRVAAICFGENLNTYDKKYKNYPSSHCTETEQC-
ABY77928.1      HLLQFNNMIKFETNKNAIPFYAFYGCYCGWGGRGRPKDATDRCCFVHDCCYEKLTDCSPKTDIYSYSWKSGVITCGEGTPCEKQICECDRAAAVCFGENLPTYKKRYMFYPDFLCTDPSEKC
AAW92122.1      SLIQLWEMIFQEMGKGAAKKYGLYGCNCGMGHRGRPVDATDRCCSVHKCCYKKLTDCDPKTDRYSYSWENGAIVCGGDDPCRKEVCECDKATTICFRQNLDTYDKKYKIYLKFLCKKPEPC-
A8CG78.1        NLYQFGEMINQKTGNFGLLSYVYYGCYCGWGGKGKPQDATDRCCFVHDCCYGRVKGCDPKTATYSYSFENGDIVCGGDDPCLRAVCECDRVAAICFRENMNTYDKKYMLYSIFDCKEESDQC
CAE47167.1      HLSQFGDMINKKTGIFGIMSYIYYGCYCGWGGKGKPLDATDRCCFVHDCCYGRVNGCDPKLSTYSYSFENGDIVCGGDDPCLRAVCECDRVAAICFGENMNTYDKKYMLYSLLDCKEESDQC
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Snake venom metalloprotease [13]

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AAB22477.1      ------------------------------------------------------------------------------------------------------------------------
ADI47593.1      ------------------------------------------------------------------------------------------------------------------------
AAX38182.1      MMQVLLVTICLAVFPYQGSSIILESGNVNDYEVVYPQKITALPKGAIQQPEQKYEDAIKYEFKVNGKPVVLHLEKNKGLFSEDYSETHYTPDGREITINPPVEDHCYYHGRIQNDADSTA
ADI47578.1      ------------------------------------------------KQPEQKYEDTMQYEFKVKGEAVVLHLEKNKGLFSEDYTETHYAPDGREITTKPAVEDHCYYHGRIQNDADSSA
AAX38181.1      MMQVLLVTISLAVFPYQGSSIILESGNVNDYEVVYPQKVTAMPKGAVKQPEQKYEDAMQYEFKVKGEPVVLLLEKNKDLFSEDYSETHYSPDGREITTNPPVEDHCYYHGRIQNDADSSA
AGL45259.1      MIQVLLVIICLAVFPYQGSSIILESGNVNDYEVVYLQKVTAMNKGAVKQPEQKYEDTMQYEFKVNGEPVILHLEKNKDLFSEDYSETHYSPDGREITTNPPVEDHCYYHGRIQNDADSTA
```

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AAZ39880.1     MMQVLLVTICLAVFPYHGSSIILESGNVNDYEVVYPQKVTAMPKEAVKQPEQKYEDAMQYKFEVNGEPVLLHLEKNKDLFSEDYSETHYSPDGREITTKPLVQDHCYYHGHIQNDAHSSA
ADJ67475.1     MMQVLLVTICLAVFPYHGSSIILESGNVNDYEVVYPQKVTAMPKEAVKQPEQKYEDAMQYKFEVNGEPVLLHLEKNKDLFSEDYSETHYSPDGREITTKPLVQDHCYYHGHIQNDAHSSA
ADI47654.1     ------------------------------------------------------------------------------------------------------------------------
ADJ67474.1     ------------------------------------------------------------------------------------------------------------------------
AAT91068.1     ------------------------------------------------------------------------------------------------------------------------
AFE61611.1     ------------------------------------------------------------------------------------------------------------------------
ADJ67473.1     ------------------------------------------------------------------------------------------------------------------------

AAB22477.1     ------------------------------------------------------------------LVSTSAQ----FNKIFIELVIIVDHSMAKKCNS--TATNTKIYEIVNSANEI
ADI47593.1     ------------------------------------------------------------------------------------------------------------------------
AAX38182.1     SISACNGLKGHFKLQGEMYLIEPLRIPDSEAHAIYKYENIEKEDEAPKMCGVTQTNWESDEPIK-ASQLNLTPEQRTYLKSKKYVELVIVADYIMFWKYDRSLSTIRTRIYEIVNTLNVI
ADI47578.1     SISACNGLKGHFKLRGEMYFIEPLKIPDSEAHAVYKYENIEKEDEAPKICGVKKTNWESDKSIQEASQLNLTPEQQRYLNSEKHIKVAIIADYLIYRKYGRNLFTIRTRIYEIINILNAI
AAX38181.1     SISACNGLKGHFMLQGETYLIEPLKLPDSEAHAVYKYENVEKEDEAPKMCGVTQTNWESDEPIKKASQLNLTPEQRRYLNSPKYIKLVIVADYIMFLKYGRSLITIRTRIYEIVNILNVI
AGL45259.1     SISACNGLKGHFQLRGETYFIEPLKIPDSEAHAVYKYENVEKEDEAPKTCGVTQTNWESDELIKKASQLNLTPEQQRYLNSPKYIKLVIVADYIMFLKYGRSLITIRTRIYEIVNLLNVI
AAZ39880.1     SISACNGLKGHFKLRGEMYLIEPLKLSDSEAHAVYKYENVEKEDEALKMCGVTQTNWESDEPIKKASLLVATSERNRYFNPYSYVELIITVDHSMVTKYKNDLTAIRTWVFELVNTINEI
ADJ67475.1     SISACNGLKGHFKLRGEMYFIEPLKLSNNEAHAVYKYENIEKEDETPKMCGVTQTNWESDKPIKKASQLVSTSAQFNK----AFIELIIIVDHSMAKKCNS--TATNTKIYEIVNSANEI
ADI47654.1     SISACNGLKGHFKLRGEMYLIEPLKIPDNEAHAVYKYENIEKEDEAPKMCGVTQDNWESDEPIK-ASQLVATSEQRRFA--KRYIEFVIVVDHSMFRKYNNDSTAIRTWIYEMVNTINEI
ADJ67474.1     ------------------------------------------------------------------------------------------------------------MGRFIFVS
AAT91068.1     ------------------------------------------------------------------------------------------------------------MGRSISVS
AFE61611.1     ------------------------------------------------------------------------------------------------------------MGRFISVS
ADJ67473.1     ------------------------------------------------------------------------------------------------------------MGRFIFVS

AAB22477.1     FNPLNIHVTLIGVEFW--CDRDLINVTSSADETLNSFGEWRASDLMTRKSHDNALLFTDMRFDLNTLGITFLAGMCQAYRSVEIVQEQGNRNFKTAVIMAHELSHNLGMYHDGKNCICND
ADI47593.1     ------------------------------------------------------------------------------------------------------------MGHSLGMLHDTKSCTCGA
AAX38182.1     YRFLNIYIALVAVEIW--SKGDLINVTSSAYDTLDSFGEWRERDLLNRKRHDNAQLLTGINFNGPSAGRGFVGRMCQPKYSVGIVQDHSKIYLLVASAMAHEMGHNLGMDHDRIDCTCGA
ADI47578.1     YRAFHMHVALVFLEIW--SNGDKINVLPAANVTLDLFGKWRLSDLLNRREHDNAQLLTGINFDGPTAGLGYVGSMCEPQYSAAIVQDHNKINILVAMAMAHELGHNLGMNHDEKFCTCGA
AAX38181.1     YRVLNIYIALLGLEIW--NNGDKINVLPETKVTLDLFGKWRERDLLNRRKHDNAQLLTDINFNGPTAGLGYVGSMCDPQYSAGIVQDHNKVNFLVALAMAHEMGHNLGMEHDEIHCTCGA
AGL45259.1     YRVLNIYIALVGLEIW--NNGDKINVLPEAKVTLDLFGKWRETDLLNRRKHDNAQLLTGINFNGPTAGLGYLGSMCNPQYSAGIVQDHNKVNFLVALAMAHEMGHNLGMDHDGIQCTCGA
AAZ39880.1     FKYLYIRVPLVGLEIW--KNRDLINVTSAANVTLDLFGEWRKSYLLPRKIHDNSQLLTAIDLNGLTIGMAYVSTMCQSKYSVGVVQDHSKINLRVAVTMAHEIGHNLGLTHDGVYCTCGG
ADJ67475.1     FNPLNIHVTLIGVEFW--CDRDLINVTSSADETLDSFGEWRASDLMTRKSHDNALLFTDMRFDLNTLGITFLAGMCQAYRSVGTVQVQGNRNFKTAVIMAHELSHNLGMYHDGKNCICND
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ADI47654.1     YLTWNIRVPLVGLEIW--NKGDLINVLSSAGDTLDSFGEWRQRDLLNRKRHDNAHLLTAIDFDGQTIGLAYRGTMCQSKYSTGVVQDHSATNLLVAVAMAHELGHNLGISHDTSFCTCHA
ADJ67474.1     FGWLVVFLSLSGTEAVLDCPSGWLSYEQHCYKGFNDLKNWTDAEKFCTEQKKGSHLVSL-------------HSREEEKFVVNLISENLEY---------PATWIGLG--NMWKDCR---
AAT91068.1     FGLLAVFLSLSGTGAGLDCPPDSSPYRYFCYRVFKEQKNWADAERFCAERPNNGHLVSI-------------ESMEEAEFVAQLLSKITGK-FI------THFWIGLRIEDKKQQCR---
AFE61611.1     FGLLVVFLSLSGTGAGLDCPPDSSLYRYFCYRVFKEHKTWEAAERFCMEHPNNGHLVSI-------------ESMEEAEFVAKLLSNTTGK-FI------THFWIGLMIKDKEQECS---
ADJ67473.1     FGLLAVFLSLSGTGAGLDCPPDSSPYRYFCYRVFKLRKSWEAAERFCMEHPNNGHLVSI-------------ESMEEAEFVAKLLSNTTGK-FI------THFWIGLRIKDKEQECS---

AAB22477.1     SSCVMSPVLSDQPSKLFSNCSIHDYQRYLTR---------YKPKCIFNPPLRKDIVSPPVCGNEIWEEGEECDCGSPANCQNPCCDAATCKLKPGAECGNGLCCYQCKIKTAGTVCRTRR
ADI47593.1     NPCIMFSEVSEPTPKEFSRCSYDQYRDYLPK---------YNPKCIFDPPLRNDIVSPAVCGNEIWEEGEECDCGSPADCENSCCDAATCKLKPGAECGNGECCDKCKIRTAGTECRA--
AAX38182.1     KSCIMSGILRCETSYLFSDCSREEHRKYLIN---------KMPQCILNKPLKTDIVSPAVCGNYFVEVGEECDCGSPANCQDRCCDAATCKLRPGAQCGDGVCCYQCKFRRAGTVCRP--
ADI47578.1     KSCIMSGTLSCEGSFRFSNCSQEENRKYLIR---------KMPQCILKKPLKTDIVSPPVCGNYLVELGEDCDCGTPTFCQNPCCNAATCKLTPGSQCADGECCDQCRFRRAGTECRP--
AAX38181.1     KSCIMSGTLSCEASIRFSNCSREEHQKYLIN---------KMPQCILNKPLKTDIVSPAVCGNYLVELGEDCDCGSPRDCQNPCCNAATCKLTPGSQCADGECCDQCKFRRAGTVCRP--
AGL45259.1     KSCIMSGTLSCEASIRFSNCSQEEHRKYLIN---------KMPQCILNKPLKTDIVSPAVCGNYLVELGEDCDCGSPRDCQNPCCNAATCKLTPGSQCADGECCDQCKFGRAGTVCRP--
AAZ39880.1     YSCIMSAVLGDQPSKYFSNCSYNQYRRFLTE---------HNPECIINPPLRKDIVSPPACGNELLERGEECDCGSPENCRDPCCDAASCKLHSWVECESGKCCNQCRFKRAGTECRP--
ADJ67475.1     SSCVMSPVLSDQPSKLFSNCSIHDYQRYLTR---------YKPKCILYPPLRKDIVSPPVCGNEIWEEGEECDCGSPADCQNPCCDAATCKLKPGAECGNGLCCYQCKIKTAGTVCRR--
ADI47654.1     NSCIMAPYLSIQPSKLFSNCSEIQYEMFLTQ---------RNPQCIINKPLRREIVSPPVCGNELLEVGEECDCGSPANCRDPCCDAASCKLHSWVECESGECCDQCRFKRAGTECRP--
ADJ67474.1     ------MEWSDRGNVKYKALAEESYCLI----MITHEKVWKSMTCNFIAP--------V-------------VCKF-------------------------------------------
AAT91068.1     ------SEWSDGSSVSYDNLLKREFRKCFGLEKGTGYRSWFNLNCEEPYP--------F-------------VCKVPPNC-----------------------------------------
AFE61611.1     ------SEWSDGSSVSYDKLGKEEFRKCFVLEKESGYRMWFNRNCEERYV--------F-------------VCKVPPEC-----------------------------------------
ADJ67473.1     ------SEWSDGSSVSYDNLGKEEFRKCFVLQKESGYRMWFNHKCEEPYP--------F-------------VCKVPPEC-----------------------------------------

AAB22477.1     ARDECDVPEHCTGQSAECPRDQLQQNGKPCQNNRGYCYNGDCPIMRNQCISLFGSRANVAKDSCFQENLKGSYYGYCRKEN---GRKIPCAPQDVKCGRLFCLNNSPRNKNPCNMHYSCM
ADI47593.1     ARDDCDVPEHCTGQSAECPRNEFQRNGQPCLNNSGYCYNGDCPIMKNQCILLFSPNATVDVDACFQWNLRGIFDGYCTKEIGSYGRRFPCAPQDVKCGRLYCLDKSARKKKRCKTNYSPD
AAX38182.1     ANGECDVSDLCTGQSAECPTDQFQRNGQPCQNNKGYCYNGTCPIMEKQCISLFGASATVAQDSCFQFNRRGNHYGYCRKEN---NTKIACAPEDVKCGRLYCLDNSSGHKNPCQIYYIPS
ADI47578.1     AKDECDMADLCNGQSDECPKDQFQRNGHPCQNNNGYCYNGKCPVMGNQCISLFGSRATVAEDACFQFNRLGSDYGYCRKEN---GIKIPCAPEDVKCGRLYCFDNLPEHKNPCQIYYTLR
AAX38181.1     ANGECDVSDLCTGQSAECPTDQFQRNGQPCQNNNGYCYSGTCPIMGKQCISLFGASATVAQDACFQFNSLGNEYGYCRKEN---GRKIPCAPQDVKCGRLYCFDNLPEHKNPCQIYYTPS
AGL45259.1     ANGECDVSDVCTGQSAECPTDQFQRNGHPCQNNNGYCYNGTCPILGKQCISLFGASATVAQDACFQFNRLGNEYGYCRKEN---GRKIPCAPQDVKCGRLYCFDNLPEHKNPCQIYYTPR
AAZ39880.1     ARDECDKAEQCTGRSANCPVDEFHENGRPCLHNFGYCYNGKCPIMYHQCHALFGQNVTGVQDSCFQYNRLGVYYAYCRKEN---GRKIPCAPKDEKCGRLYCSYKSPGNQIPCLPYYIPS
ADJ67475.1     ARNECDVPEHCTGQSAECPRDQLQQNGQPCQNNRGYCYNGDCPIMRNQCISLFGSRATVAKDSCFQENLKGSYYGYCRKEN---GRKIPCAPQDVKCGRLFCLNNSPRNKNPCNMHYSCM
ADI47654.1     AKDDCDMAESCTGQSSVCPVDSFHENGQPCLHNLGYCYNGKCPITLYQCRAFLGNNAVGVDESCFQYNRLGNSYAYCRKEN---GIKIPCAPKDEKCGRLYCSYNSFGNHISCLPCYRAD
ADJ67474.1     ----------------------------------------------------------------------------------------------------------------------
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AAT91068.1      ----------------------------------------------------------------------------------------------------------------------
AFE61611.1      ----------------------------------------------------------------------------------------------------------------------
ADJ67473.1      ----------------------------------------------------------------------------------------------------------------------

AAB22477.1      DQHKGMVDPGTKCEDGKVCNNKRQCVDVNTAYQSTTG----
ADI47593.1      DENKGMVD---------------------------------
AAX38182.1      DENKGMVDPGTKCGDGMVCS-NGKCVDVTIAY---------
ADI47578.1      DENKGMVEPGTKCENGKVCI-NGKCVDVNTAY---------
AAX38181.1      DENKGMVDPGTKCGDGKACSSNRQCVDVNTAY---------
AGL45259.1      DENKGMVDPGTKCGDGMACSSNGQCVDVNTAY---------
AAZ39880.1      DENKGMVDHGTKCGDGKVCS-NGQCVDLNIAY---------
ADJ67475.1      DQHKGMVDPGTKCEDGKVCNNKRQCVDVNTAYQSTTGFSQI
ADI47654.1      EEDKGMVDEGTKCGDGKVCS-NGHCVDLNIAY---------
ADJ67474.1      ----------------------------------------
AAT91068.1      ----------------------------------------
AFE61611.1      ----------------------------------------
ADJ67473.1      ----------------------------------------
```

Snake venom serine protease [15]

```
Q5W958.1        QKSSELVIGGDECNINEHPFLAFLYTG---WIFCSGTLINKEWVLTVKQCNNRRPMRIYLGMHTRSVPNDDEEIRYPKEMFICPNKK-----KNDIMLIRLNRPVNNSEHIAPLSLPSNP
P18965.2        QKSSELVVGGDECNINEHPFLVALYTSASSTIHCAGALINREWVLTAAHCDR-RNIRIKLGMHSKNIRNEDEQIRVPRGKYFCLNTKFPNGLDKDIMLIRLRRPVTYSTHIAPVSLPSRS
P18964.1        ------VVGGDECNINEHPFLVALYTSTSSTTHCGGALINREWVLTAAHCDR-RNIRIKLGMHSKNIRNEDEQIRVPRGKYFCLNTKFPNGLDKDIMLIRLRRPVTYSTHIAPVSLPSRS
JAA98031.1      QKSSELVVGGHPCNINEHRSLVVLFNSS--GFLCAGTLINEEWVLTAAHCDS-KNFQMQLGVHSKKVLNEDEQTRDPKEKFICPNKKKDDEKDKDIMLIRLDSPVSNSEHIAPLSLPSSP
E5AJX2.1        QKSSELVIGGDECNINEHPFLAFVTSD---RRRCAGTLINQEWVLTAAHCNG-KYMKIELGVHDKMVRNEDKQTRVPKQKFFCLSSKEYTMWDKDIMLIRLNTPVNNSTHIAPVSLASRP
AMB36342.1      QKSSELVIGGDECNINEHPFLVALHTARSKRFYCAGTLINQEWVLTAARCDR-KNIRIILGVHSKNVPNEDEQMRVPKEKFFCLSSKTYTRWDKDIMLIRLKRPVNDSTHIAPLSLPSSP
Q9PT40.1        QKSSELVIGGDECNINEHPFPVALHTARSKRFYCAGTLINQEWVLTAARCDR-KNIRIILGVHSKNVPNEDQQIRVPKEKFFCLSSKTYTRWDKDIMLIRLKKPVNDSTHIVPLSLPSSP
JAA98034.1      QKSSELIIGGEECNINEHRFLVALYTFRSKREHCSGTLINQEWVLTAAHCDR-KNIRIKLGTHSTNVTNEDAQTRVPKEKFFCLSSKTYTKWDKDIMLIRLKRPVNNSPHIATLSLPSNP
E5L0E3.1        QKSSELVVGGHPCNIYEHHFLAFMYNSS--GFMCSGTLINQQWVLSAAHCDM-ENMHIYLGLHSFKLPNKDQKKRVAKEKFFCLSSKSYTKWDKDIMLIKLNKPVTYSTHIASLSLPSNP
JAS04410.1      QKSSELVIGGDECNINEHRSLALMYNSS--GFICGGTLINQEWVLTAAHCNM-ENMKIDFGVHNGRVHYDDMQTRVPEEKFFCLSSNNDTEWDKDIMLIRLDRPVRNSAHIAPLSLPSNP
ABY65931.1      QKSSELVIGGDECNINEHRLLAIVYTN---SSQCAGTLINQEWVLTAAHCDG-ENMDIYLGVHNESVQYDDEEGRVAAEKFFCLSSRNYTKWDKDIMLIRLNIPVRNSTHIAPLSLPSSP
```

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ADP88560.1      QKSSELVWGGDECNINEHRSLVFLYNN---SFGCSGTLINQQWVLSAVHCDM-ENVRIYLGVHNLTLRNNA-EIRLPEERFFCLSNKNYTKWDKDIMLIKLLRPVKTSTYIAPLSLPSSP
E0Y418.1        QKSSELVIGGDECNINEHFFLALMYNSTSMKFHCSGTLLNEEWVLTAAHCDM-ENMQIYLGVHDKKNPNKDQQTRVPKEMFFCLSNKSYTPWDKDIMLIRLNSPVTYSTHIAPFSLPSSP
AMB36345.1      QKSSELVIGGDECNINEHRSLALMYNSTSMKFHCSGTLLNQEWVLTAAHCDM-ENMQIHLGVHDVSLPNKDEKRRVAKEKFFCLSSKSYTLWNKDIMLIKLNRPVTYSTHIAPLSLPSSP
E0Y420.1        QKSSELVIGGDECNINEHRSLVYLYNDS--NFQCGGTLINQEWVLSAAHCDM-ENMEIYLGVHNLSLPNKDQKRRDPKEKFFCLSSKNYTKWDKDIMLIKLNRPVKTSTHIAPLSLPSSP

Q5W958.1        PSVGSVCRIMGWGTITPSKATYPDVPHCANINLFNYTVCRGAHA--GLPVTSRKLCAGVLEGGIDTCSADSGGPLICNGQLQGIVSWRGGSCAQPHKPGLYTKVFDYLPWIQSIIAGSTT
P18965.2        RGVGSRCRIMGWGKISTTEDTYPDVPHCTNIFIVKHKWCEPLYP--WVPADSRTLCAGILKGGRDTCHGDSGGPLICNGEMHGIVAGGSEPCGQHLKPAVYTKVFDYNNWIQSIIAGNRT
P18964.1        RGVGSRCRIMGWGKISTTEDTYPDVPHCTNIFIVKHKWCEPLYP--WVPADSRTLCAGILKGGRDTCHGDSGGPLICNGQIQGIVAGGSEPCGQHLKPAVYTKVFDYNNWIQNIIAGNRT
JAA98031.1      PSVGSVCRIMGWGTITPTKETYPDVPHCANINILDHAVCRAAYP--WNPVASTTLCAGTQQGGKDTCRADSGGPLICNGEIQGIVSWGGHPCGQAREPGVYTKVFDYTDWIQSIIAGKKT
E5AJX2.1        PVVGSVCRIMGWGTISSPKVILPDVPHCANIEIIKYSKCQGVHP--ELPAKGRVVCAGIWQGGKDSCHGDSGAPLICNGQLQGLLSWGGDPCAQPLQPGLYTDIFDYSDWIQSIIAGNTT
AMB36342.1      PSVGSVCRIMGWGTITTTKVTYPDVPHCADINMFDYSVCQKVYR--KLPEKSRTLCAGILQGGIDSCKVDNGGPLICNGQIQGIVSWGGYPCAQPHKPALYTNVFDYTDWIQSIIAGNIT
Q9PT40.1        PSVGSVCRIMGWGTITTTKVTYPDVPHCANINMFDYSVCRKVYR--KLPEKSRTLCAGILQGGIDSCKVDNGGPLICNGQIQGIVSWGGHPCAQPHKPALYTNVFDYTDWIQSIIAGNIT
JAA98034.1      PSVGSVCRIMGWGTISATKETYPDVPHCANINILDYEVCRAAH--GGLPATSRTLCAGILKGGKDSCKGDSGGPLICNGEIQGIVSWGAHPCGQSLKPGVYTNVFDYTEWIQSIIAGNTD
E5L0E3.1        PRVGSVCRIMGWGSITSPKKILPTVPHCANINIVPYTVCRVIYR--PLPEQSRTLCAGVSGRRICSCLGDSGGPLICNGQIQGIVSWGSDPCVNRGAPSIYTKVFDYTDWIHSIIAGNTA
JAS04410.1      PRLGSVCRIMGWGAITSPNETFPDVPHCANINIIRYSVCQAVYL--GMPVQSRILCAGILRGGIDSCKGDSGGPLLCNGQFQGILSAGGDPCAQPRVPGLYIKVFDYTDWIQSIIAGNTA
ABY65931.1      PSVGSVCRVMGWGTITSPNETYPDVPHCANINLFDYEVCLAAYPEFGLPATSRTLCAGIQQGGKDTCGSDSGGSLICNGQFQGIVSWGDNPCAQPHKPAIYTKVLDDTEWIQSIIAGNTA
ADP88560.1      PRVGSVCRIMGWGAITSPNETFPGVTHCANINILPYSVCRAAYK--GLPAQSRTLCGGILEGGIGSCMGDSGGPLICNGEMHGIVAWGDDTCAQPHKPVHYTKVYDYTDWIQSIIAGNTA
E0Y418.1        PTVGSVCRIMGWGAITSPNETYPDVPHCANIEIYDYSVCRKAYG--GLPTKSRTLCAGVLQGGIDTCLADSGGPLICNGQFQGIVAWGRHPCAQPQLPAIYTKVFDYSDWIQSIIAGNTA
AMB36345.1      PRVGSVCRIMGWGAITSPNETYPDVPHCANINILNYAVCRAENP--WLPAQSRTLCAGILQGGIDTCKGDSGGPLICNGQIQGIVSWGDSPCAQPLNPGHYTKVFDYTDWIQSIIAGNTN
E0Y420.1        PSVGSVCRIMGWGTVTSPNETLLDVPHCANINILNYTVCRAASP--RLPTQSRTLCAGILQGGIDACKGDSGGPLICNGQIQGIVSWGNHPCAQPLKPGHYTHVFDYTDWIQSIIAGNTT

Q5W958.1        ATCPP
P18965.2        VTCPP
P18964.1        VTCPP
JAA98031.1      VNCPP
E5AJX2.1        ATCPP
AMB36342.1      ATCPP
Q9PT40.1        ATCPP
JAA98034.1      ATCPP
E5L0E3.1        ATCPS
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JAS04410.1      ATCPP
ABY65931.1      VTCPP
ADP88560.1      ATCPP
E0Y418.1        ATCPS
AMB36345.1      ATCPP
E0Y420.1        ATCPP
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L-amino acid oxidase [2]

```
ACF70483.1      MNVFFMFSLLFLATLGSCADDKNPLEECFREDDYEEFLEIAKNGLKKTSNPKHIVIVGAGMSGLSAAYVLAGAGHKVTVLEASERPGGRVRTHRNVKEGWYANLGPMRVPEKHRIIREYI
Q4F867.2        ------------------ADDKNPLEECF----------------------------------------------------------------------------------REDDHRIVREYI

ACF70483.1      RKFGLKLNEFVQETENGWYFIKNIRKRVGEVKKDPGLLKYPVKPSEAGKSAGQLYQESLGKAVEELKRTNCSYILNKYDTYSTKEYLIKEGNLSPGAVDMIGDLLNEDSGYYVSFIESLK
Q4F867.2        RKFGLKLNEFVQETENGWYFIKNIRKRVGEVKKDPGLLKYPVKPSEAGKSAGQLYQESLGKAVEELKRTNCSYILNKYDTYSTKEYLIKEGNLSPGAVDMIGDLLNEDSGYYVSFIESLK

ACF70483.1      HDDIFAYEKRFDEIVGGMDQLPTSMYRAIEESVHFKARVIKIQQNAEKVTVTYQTTQKNLLLETADYVIVCTTSRAARRITFKPPLPPKKAHALRSVHYRSGTKIFLTCTKKFWEDDGIQ
Q4F867.2        HDDIFAYEKRFDEIVGGMDQLPTSMYRAIEESVRFKARVIKIQQNAEKVTVTYQTTQKNLLLETVDYVIVCTTSRAARRITFKPPLPPKKAHALRSVHYRSGTKIFLTCTKKFWEDDGIQ

ACF70483.1      GGKSTTDLPSRFIYYPNHNFTTGVGVIIAYGIGDDANFFQALNLNECADIVFNDLSSIHQLPKKDLQTFCYPSIIQKWSLDKYAMGAITTFTPYQFQHFSEALTAPVGRIFFAGEYTANA
Q4F867.2        GGKSTTDLPSRFIYYPNHNFTTGVGVIIAYGIGDDANFFQALNLNECADIVFNDLSSIHQLPKKDLQTFCYPSIIQKWSLDKYAMGAITTFTPYQFQHFSEALTAPVGRIFFAGEYTANA

ACF70483.1      HGWIDSTIKSGLTAARDVNRASEL
Q4F867.2        HGWIDSTIKSGLTAARDVNRASEL
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Phosphodiesterase [1]

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AHJ80885.1      MIQQKVLFISLVAVALGLGLGLGLKESVEPQVSCRYRCNETFSKMASGCSCDDKCTERQACCQDYEDTCVLPTQSWSCSKLRCSEKRMANVLCSCSEDCLEKKDCCTDYKSICKGETSWL
                KDQCASSSAAQCPSGFEQSPLILFSMDGFRAGYLETWDSLMPNINKLKTCGTHAKYMRAVYPTKTFVNHYTIVTGLYPESHGIIDNNIYDVTLNLNFSLSAPTMTNPAWWGGQPIWHTVT
                YQGLKAATYFWPGSEVKINGSYPTIYKVYNKSIPFEARVTEVLKWLDLPKAERPDFVTLYIEEPDTTGHKFGPVSGEIIMALQMADRTLGMLMEGLKQRNLHNCVNLILLADHGMEQISC
                NRLEYMTDYFDKVDFFMYEGPAPRIRSKNVPKDFYTFDSEGIVRNLTCQKPKQYFKAYLAKDLPKRLHYVNNIRIDKVNLMVDQQWMAVRNKNYNRCNGGTHGYDNEFKSMQAIFLAHGP
                GFKGKNEVTSFENIEVYNLMCDLLKLKPAPNNGTHGSLNHLLKNPFYNPSPAKEQTSPLSCPFGPVPSPDVSGCKCSSITDLGKVNERLNLNNQAKTESEAHNLPYGRPQVLQNHSKYCL
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LHQAKYISAYSQDVLMPLWSSYTINKSPPTSVPPSASDCLRLDVRIPAAQSQTCSNYQPDLTITPGFLYPPNFGSSNFEQYDALITSNLVPMFKGFTRLWNYFHGTLLPKYARERNGLNV
ISGPIFDYNYDGHFDSYDTIKEYVNDTKIPIPTHFFVVLTSCENQINTPLNCPGSLKVLSFILPHRPDNSESCADTSPDNLWVEERIQTHTARVRDVELLTGLNFYSGLKQPLPETLQLK
TFLPIFVNPVN

5'-Nucleotidase [1]

AHJ80886.1 AREKVGIIGYTTKETPVLSNPGPYLEFRDEVEELQIHANKLTTLGVNKIIALGHSGFFEDQRIARKVKGVDVVVGGHTNTFLYTGSPPSTEVPAGNYPFMVQSDDGRQVPVVQAYAFGKY
LGYLNVVFNDKGNVIKASGNPILLNKDIPEDQVVKAQVNKMKIQLQNYYSQEIGKTIVYLNGTTQACRFHECNLGNLICDAVIYNNLRHPDDNEWNHVSMCIVNGGGIRSPIDERANNGI
ITLEELTSVLPFGGTFDLLQIKGSALKQAFEHSVHRHGQGTGELLQVSGIKVVYDLSQKPGSRVVSLNVLCTKCRVPTYVPLEMEKTYKVLLPSFLATGGDGYHMLKGDSSNHNSGDLDI
SIVGDYIKRMEKVFPAVEGRVTFLDGTLFQAQLFLTWGLCISLLFFIL

Glutaminyl cyclase [1]

AFE84762.1 MARERRDSKAAAFFCLAWALGLPLLGFPQHVGGREDRADWTQEKYSHRPTILNATSILQVTSQTNVSRMWQNDLHPIMIERYPGSPGSYAVRQHIKHRLQGLQAGWLVEEDTFQSHTPYGYRT
FSNIISTLNPLAKRHLVIACHYDSKYFPPQLDGKVFVGATDSAVPCAMMLELARSLDRQLSFLKQSSLPTKADLSLKLIFFDGEEAFVRWSPSDSLYGSRSLAQKMSSTPHPPGARNTYQTQG
IDLFVLLDLIGARNPVFPVYFLNTARWFGRLEAIEQNLHDLGLLNNYSSERQYFRSNLRQHPVEDDHIPFLRRGVPILHLIPSPFPRVWHVMEDNEENLDKPTIDNLSKILQIFVLEYLNLG

Phospholipase B [1]

BAN82155.1 MIRFGNPSSSVKRRQRCRSWYWGGLLLLWAVAETRADIHYATVYWLEAEKSFQIKAVLDKNGDAYGYYNDTIQSTGWGILEIKAGYGNQPISNEILMYAAGFLEGYLTASHMSDHFANLF
PLMIKNVIIEQKVKDFIQKQDEWTRQQIKNNKDDPFWRNAGYVIVQLDGLYMGNVEWAKQQKRTPLTNFEISFLNVIGDLLDLIPALYSELRKSDFRSMPDVSRIYQWDMGHCSALIKVL
PGYENIYFAHSSWFTYAATLRIYKHLDFKITDPQTKTGRASFSSYPGFLSSLDDFYILGSMILDTKKIKLQRSLEDGTLYIIEQIPKLVKYSDQTKVLRNGYWPSYNIPFDKVIYNMSGY
REYVQRHGLEFSYEMAPRAKIFRRDQGKVTDMESMKSIMRYNNYKEDPYAKRNPCNTICCRQDLDRRTPVPAGCYDSKVADISMASKFTAYAINGPPVEKGLPVFSWVHFNKTKHQGLPE
SYNFDFVTMKPVL

Hyaluronidase [1]

ABI33950.1 MYHIWIKFLAAWIFLKRFNGVHVMQAKAPMYRNEPFLVFWNAPTTQCRLRYKEDLVTTVGETAAMGAAGIVFWGSVQYASTVDSCQKVKKYMNGPLGRYIVNVTTAAKICSRVLCRKNGRCVR
KHSDSNAFLHLFPESFRIMVYANATEKKVIVKGKLELENLIYLRENFMCQCYQGWKGLYCEEYSIKDIRKI

Kunitz-type serine protease inhibitor [5]

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ABD24040.1      MSSGGLLLLLGLLTLWAELTPISGHDRPTFCNLAPESGRCRGHLRRIYYNLESNKCKVFFYGGCGGNANNFETRDECRQTCGGK------------
A8Y7P1.1        MSSGGLLLLLGLLTLWAELTPISGHDRPKFCYLPADPGLCLAHMRSFYYDSESKKCKEFIYGGCHGNANKFPSRDKCRQTCGGK------------
AFD04724.1      MSSGGLLLLLGLLALWAELTPISGHDRPKFCYLPADPGLCMAYIRSFYYDSESKKCKEFIYGGCHGNANNFPTRDKCRQTCRAPRKGRHT------
ABD24043.1      MSSGGLLLLLGLLTLWAELTPISGQDRPKFCHLPVDSGICRAHIPRFYYNPASNQCQGFIYGGCGGNANNFETRDQCRHTCGGK------------
ABD24041.1      MSSGGLLLLLGLLTLWAEPTPISGQDRPKFCFLRPDFGRYGHPRPRFYYNPATNQCQGFLAQRSRENTNNFDTRDKCRQTCGRK------------
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Snaclec [12]

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ADK22834.1      GFSCPNGWSSFGQHCYKVIEPLKNWTDAEKFCREQHKGSHLASIHSSEEEAFVSKVASKVLKF--GSVWIGLNDPW--HNCNWEWSDNARFDYKAMTR--RPYCTVMVLKPDRIFWFNRG
ADK22822.1      KQDCLSDWSFYEGYCYKVFNEKKTWEDAEKFCNEQVNGGYLVSFRSSEEMDFVIRMTFPIFRF--DFFWIGLRDFW--RDCYWRWSDGVNLDYKAWSR--EPNCFVSKT--TDNQWLRWN
AJO70722.1      DQDCPSDWSSHEGHCYKVFNLRMNWADAEKFCTEVVSGGHLISLNSAEEVDFMIKLVFPILKF--DFIWIGLRDFW--RDCHWGWSDGVKLDYKAWSD--EPNCYVAKT--VDYQWLFRD
AAY63872.1      AFCCPSGWSAYDQNCYKVFTEEMNWADAEKFCTEQHKGSHLLSLHNIAEADFVLKKTLAMLKD--GVIWMGLNDVW--NECNWGWTDGAKLDYKAWNE--GTNCFVFKI--AKNHWSHMD
Q4PRC9.1        AFCCPSGWSAYDQNCYKVFTEEMNWADAEKFCTEQKKGSHLVSLHSREEEKFVVNLISENLEY--PATWIGLGNMW--KDCRMEWSDRGNVKYKALAE--ESYCLIMIT--HEKVWKSMT
AAY63871.1      VLDCPSGWLSYEQHCYKGFNDLKNWTDAEKFCTEQKKGSHLVSLHSREEEEFVVNLISENLEY--PATWIGLGNMW--KDCRMEWSDRGNVKYKALAE--ESYCLIMIT--HEKEWKSMT
ADK22821.1      --DCPSDWSSHEGHCYKVFKLLKTWEDAEKFCTQQANGWHLASIESVEEANFVAQLASETLTKSKYHAWIGLRDQSQRQQCSSHWTDGSAVSYETVTK--YTKCFGLNKETKWHEWITLP
ABW82659.1      DQDCLPGWSFYEGHCYKVFNVKKTWEDAEKFCQKQSNGKHLATIEWLGKANFVAELV--TLMKLETHVWIGLRVEDKRQQCSSHWTDGSAVSYENVVH--NTKCFGLDQKTGYRTWVALR
AAY63870.1      GLDCPPDSSLYRYFCYRVFKEHKTWEAAERFCMEHPNNGHLVSIESMEEAEFVAKLLSNTTGKFITHFWIGLMIKDKEQECSSEWSDGSSVSYDKLGKQEFRKCFVLEKESGYRMWFNRN
ADK22833.1      DLDCPSGWSAYDQHCYQAVDEPKSWADAEKFCTEQANSGHLVSIKSVGEANFVAQLASGFMQKDGIYVWIGLRDRRKEQQCRSEWTDGSKIIYVNWKEGESKMCQGLAKWTYFHKWDYVN
ADK22825.1      DFDCPSGWSAHDQHCYKAFDEPKRSGDAETFCTEQANSGHLVSIESVEEAEFVAQLISENIKTPADYVWIGLRNQRKAQYCISKWTDGSSVIYKNVIERFIKNCFGLEKESDYRTWFNLS
ABW82662.1      DFDCPPDWSAYDQHCYKAFDEPKRSGDAEKFCTQQANGGHLVSIESVEEAEFVAQLISENIKTSADYVWIGLWNQRKAPYCVSKWTDGSSVIYKNVIERFIKNCFGLEKETNYRTWFNLS

ADK22834.1      CEKFVSFVCKFLA----
ADK22822.1      CNDPRYFVCKSRVSC--
AJO70722.1      CNRTSRFICKSRVPR--
AAY63872.1      CSSTHNFVCKFRV----
Q4PRC9.1        CNFIAPVVCKF------
AAY63871.1      CNFIAPVVCKF------
ADK22821.1      CGDKNPFICKSWVLH--
ABW82659.1      CELAYHFICMSRVPRGA
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AAY63870.1      CEERYLFVCKVPPEC--
ADK22833.1      CAEHYRFVCKFPPQY--
ADK22825.1      CGDDYPFVCKFPPRC--
ABW82662.1      CGDDYPFVCKSPA----
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Cysteine-rich secretory protein [2]

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ACE73567.1      MIAFIVLPILAAVLQQSSGSVDFDSESPRKPEIQNEIVDLHNSLRRSVTPTASNMLKMEWYPEAAANAERWAFRCILNHSPYNSRVIGGIKCGENIYMSPYPMKWTAIIHEWHKEKKDFV
ACE73575.1      ----------SVDFDSESPRKPEIQNEIVDLHNSLRRSVNPTASNMLKMEWYPEAAANAERWAYRCIEEHSSRDSRVLEGIKCGENIYMSPNPMKWTEITHAWHGEYKDFK

ACE73567.1      YGQGASPANAVVGHYTQIVWYKSYRSGCAAAYCPSSEYNYFYVCQYCPAGNIIGKIATPYTSGPPCGDCPSACDNGLCTNPCSHHDEFTNCKDLVKQ-GCHSNYLKTKCPASCFCHNEII
ACE73575.1      YGVGADPPNAVTGHYTQIVWYKSHHLVCC-CLCPLSKYSYFYVCQYCPAGNIIGKIATPYTSGPPCGDCPSACDNGLCTNPCTQEDKYTNCKSLLQQDSCQDAGMQSKCSASCFCQNKII
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Vascular endothelial growth factor [1]

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ACN22046.1      MAAYLLAVAILFCIQGWPSGTVQGQVRPFLDVYERSACQTRETLVSILQEHPDEISDIFRPSCVAVLRCSGCCTDESMKCTPVGKHTADIQIMRMNPRTHSSKMEVMKFMEHTACECRPR
                WKQGEPEGPKEPRRGGVRAKFPFD
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Nerve growth factor [1]

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AAA03282.1      HPVHNQGEFSVCDSVSVWVANKTTATDMRGNVVTVMVDVNLNNNVYKQYFFETKCKNPNPVPSGCRGIDAKHWNSYCTTTDTFVRALTMERNQASWRFIRINTACVCVISRKNDNFG
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Disintegrin [1]

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AAP20878.1      MIQVLLVTICLAVFPYQVSSKTLKSGSVNEYEVVNPGTVTGLPKGAVKQPEKKHEPMKGNTLQKLPLCTTGPCCRQCKLKPAGTTCWRTSVSSHYCTGRSCECPSYPGNG
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Table 4.4b. List of all the proteins identified by LC-MS/MS analysis of GF fractions of EI RVV (B). The table shows the identified peptide ions, their m/z, charge (z), the score for the ID, ΔM (ppm), and modified residues. Carbamidomethylated cysteine and oxidized methionine residues are represented as c and m (in lower cases).

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
Enzymatic proteins								
Phospholipase A_2								
Acidic PLA_2	AAZ53180.1	305.6	70	(R)AAAIcLGQNVNTYDKNYENYAISHcTEESEQc(-)	70.4	3	1251.5	2.2
				(K)EAVHSYAIYGcYcGWGGQGKPQDATDR(C)	68.4	2	1523.7	2.4
				(E)GNLFQFAEMIVK(M)	61.0	2	698.9	0.7
				(C)FVHDccYGTVNDcNPK(M)	47.2	3	662.6	-0.2
				(K)TVcEcDR(A)	37.6	2	470.2	-0.2
Basic PLA_2	AAZ53182.1	267.7	70	(K)GYmFLSSYYcR(Q)	77.0	2	731.8	-1.0
				(R)AVcEcDRVAAIcLGQNVNTYNK(G)	69.0	3	852.4	-1.7
				(K)LVEYSYSYR(T)	67.0	2	590.3	-0.8
				(R)TGKIVcETYNR(C)	61.5	3	447.6	-0.5
				(K)QEAFSFFK(Y)	49.2	2	502.2	-0.3
				(C)FVHDccYAR(V)	40.8	2	614.3	-1.4
				(K)RAVcEcDR(V)	38.4	2	533.2	0.7
				(E)GNLFQFAR(M)	37.9	2	476.8	-0.7
PLA_2-II	ABD24037.1	236.0	70	(R)VAAIcLGQDVNTYNKG(Y)	49.9	2	861.9	-0.4
Basic PLA_2	CAA48456.1	162.7	25	(W)NYISYGCYcGWGGQGTPK(D)	61.6	2	1005.9	1.3

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
Acidic PLA_2	P0DKR3.1	102.1	39	(K)NYEHYSISHCmEESEQc(-)	21.5	2	1081.4	8.9
Ammodytin I2(A) variant	CAE47208.1	94.6	23	(R)ccFVHDCCYGGVN(G)	30.4	2	767.3	7.2
PLA_2 nigroviriditoxin basic subunit B	C0HJL8.1	83.5	28	(K)NAVPFYAFYGcYcGWGGQGQPKDATDR(C)	73.3	2	1543.2	-0.1
				(-)NLLQFNR(M)	20.5	2	452.8	0.0
Ammodytin I2(C) variant	CAE47242.1	80.9	26	(K)SALFSYSDYGcYcGWGGKGKPQDATDR(C)	43.5	3	1016.1	0.9
Acidic PLA_2 inhibitor vaspin A chain	AAN59979.1	80.5	25	(R)AAAIcLGENVNTYDK(N)	34.4	2	819.9	-0.2
PLA_2	ADG86231.1	66.5	26	(K)SALLSYSDYGcYCGWGGQGKPKDATDR(C)	37.1	3	985.8	1.8
Daboxin P	C0HK16.1	51.0	23	(R)ccFVHDcCYGNLPDCNNKS(K)	20.5	2	1153.4	1.4
PLA_2	AHJ09529.1	48.9	12	(Q)DASDRccFVHDcCYGRA(N)	21.5	3	697.9	-0.1
Basic PLA_2 BP-I	P0DJJ8.1	33.6	11	(K)AVAICLRENLGTYNK(K)	33.6	2	832.9	-1.8
Acidic PLA_2 Vur-PL3	F8QN51.1	31.6	18	(L)NGDIVCGDDDPcLR(A)	23.3	2	774.8	0.3
Basic PLA_2 RVV-VD	P81458.1	178.3	54	(K)YHNYPPSQcTGTEQc(-)	79.8	2	921.4	0.9
PLA_2	ABY77928.1	69.2	8	(R)GCFVHDccYEK(L)	47.1	2	709.3	0.8

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
Acidic PLA_2	AAM80564.1	68.0	17	(K)QVcEcDR(V)	32.2	2	483.7	-0.5
PLA_2	AHJ09559.1	58.6	14	(R)DNLNTYNDKK(Y)	44.0	2	612.8	-0.2
Chain A, PLA_2	AHJ09557.1	46.7	14	(R)VAAEcFR(R)	32.1	2	426.7	0.8
$BATXPLA_2$	JAV01879.1	45.8	14	(G)GGQPKDATDR(C)	31.2	2	522.8	-0.4
Acidic PLA_2	A8CG78.1	188.3	58	(K)YmLYSIFDcKEESDQc(-)	79.2	2	1052.4	0.5
				(K)TGNFGLLSYVYYGcYcGWGGKG(K)	56.2	2	1240.0	1.4
				(G)NLYQFGEmINQK(T)	52.7	2	750.9	0.6
				(K)TATYSYSFENGDIVcGGDDPcLR(A)	38.2	2	1299.1	1.5
Snake venom metalloprotease								
Hemorrhagic metalloproteinase russelysin	AAZ39880.1	275.3	37	(R)LGVYYAYcR(K)	66.8	2	582.8	-0.7
				(K)LHSWVEcESGK(C)	65.0	2	666.3	-0.2
				(K)SPGNQIPcLPYYIPSDENKGmVDHGTK(C)	59.6	2	1011.8	1.0
				(K)YKNDLTAIR(T)	57.9	2	547.3	0.4
				(K)YSVGVVQDHSK(I)	55.5	2	609.8	-0.9
				(K)VcSNGQcVDLNIAY(-)	52.6	2	806.9	-0.5
				(R)AGTEcRPARDEcDKAEQcTGR(S)	49.9	2	1234.0	1.7
				(R)SANcPVDEFHENGRPcLHNFGYcYNGK(C)	49.5	3	1081.5	1.4
				(R)GEEcDcGSPENcR(D)	42.9	3	785.3	-1.2
				(R)KSYLLPR(K)	39.7	2	438.8	0.0
				(K)IPcAPKDEK(C)	38.9	2	529.3	-0.3
				(R)LYcSYK(S)	37.4	2	417.2	0.8

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
				(R)RFLTEHNPEcIINPPLR(T)	33.0	2	702.7	-1.6
				(R)TWVFELVNTINEIFKYLYIRVPLVGLEIW K(N)	25.2	2	924.8	1.2
				(R)KIPcAPK(D)	21.5	2	407.2	1.1
Factor X activator heavy chain	ADJ67475.1	252.6	25	(R)ARNEcDVPEHcTGQSAEcPR(D)	70.8	2	1187.0	1.5
				(R)SVGIVQVQGNR(N)	67.2	3	578.8	0.4
				(K)GSYYGYcR(K)	60.9	2	513.2	-0.3
				(R)KSHDNALLFTDmR(F)	57.2	2	782.4	-1.1
				(R)KIPcAPQDVK(C)	46.0	2	578.3	0.0
				(R)DQLQQNGQPcQNNR(G)	44.8	2	567.3	1.1
				(K)RQcVDVNTAYQ(S)	44.6	2	677.3	0.4
				(K)cILYPPLRK(D)	39.3	3	580.3	-0.2
				(K)TAGTVcR(R)	33.2	2	382.7	0.0
Factor X activator light chain 1	ADJ67474.1	195.2	53	(K)FVVNLISENLEYPATWIGLGNmWK(D)	71.4	2	937.5	-0.8
				(K)SmTcNFIAPVVcKF(-)	49.3	2	845.4	1.8
				(A)VLDcPSGWLSYEQHcYKG(F)	43.0	2	1100.0	0.4
				(K)KGSHLVSLHSREEEK(F)	29.8	2	579.3	-0.1
				(K)FcTEQK(K)	29.1	2	406.7	-0.5
Factor X activator light chain 2	ADJ67473.1	188.6	63	(R)IKDKEQEcSSEWSDGSSVSYDNLGK(K)	84.2	2	950.1	0.8
				(A)GLDcPPDSSPYR(Y)	65.8	2	682.3	-0.1
				(K)FITHFWIGLR(I)	59.8	2	645.4	0.1
				(R)FcmEHPNNGHLVSIESmEEAEFVAK(L)	55.5	2	979.8	-1.7
				(K)SWEAAER(F)	42.6	2	424.7	0.2
Metalloproteinase, partial	ADI47593.1	148.2	9	(E)CRAARDDCDVPEHcTGQSAEcPR(N)	51.8	2	878.4	2.8

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
Group III snake venom metalloproteinase	ADW54349.1	84.3	12	(E)CRPARDDCDVAEHCTGQSAEcPR(N)	21.1	2	859.4	2.1
Factor X activator light chain 2	AAT91068.1	127.8	24	(L)NCEEPYPFVcK(V)	37.9	2	693.3	0.9
				(R)YFcYR(V)	31.8	2	404.7	-0.2
Factor X activator light chain 2	AFE61611.1	118.0	34	(A)GLDcPPDSSLYR(Y)	47.2	2	690.3	0.2
				(K)cFVLEK(E)	35.4	2	398.2	0.5
VLAIP-B	AAX38182.1	104.0	5	(K)YSVGIVQDHSK(I)	73.9	2	616.8	-0.1
Snake venom metalloproteinase K, partial	JAC96600.1	79.0	3	(K)NIPCAPQDVK(C)	28.4	2	542.8	-0.2
Snake venom serine protease								
Serine protease VLSP-1	E0Y418.1	175.7	29	(Q)GGIDTcLADSGGPLIcNGQFQGIVAWGR(H)	76.0	2	1460.2	1.0
				(E)IYDYSVcR(K)	47.6	2	538.2	-0.8
				(K)AYGGLPEK(S)	43.4	2	417.7	0.3
				(L)PAFYTK(V)	26.1	2	363.7	0.6
Enzymatically inactive serine proteinase-like protein SPH-1	AMB36342.1	173.6	30	(R)FYcAGTLINQEWVLTAAR(C)	103.0	2	1057.0	0.5
				(R)TLcAGILQGGIDScK(V)	63.9	2	796.9	0.4
				(K)EKFFcLSSK(T)	46.3	2	573.3	0.7
				(L)VIGGDEcNINEHPFLVALHTAR(S)	22.6	4	616.3	-0.6
Snake venom serine protease	ADP88560.1	169.1	39	(L)VVGGDEcNINEHR(S)	69.6	2	749.8	0.8
				(K)TSTYIAPLSLPSSPPR(V)	59.4	2	844.0	0.8

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
				(R)NNAEIRLPEER(F)	47.0	2	670.8	0.4
				(K)VYDYTDWIQSIIAGNTAATcPP(-)	36.5	2	1228.6	1.2
				(N)INILPYSVcR(A)	36.2	2	617.8	-0.1
				(K)LDRPVK(T)	28.7	2	364.2	0.5
				(K)WDKDImLIK(L)	28.4	2	589.3	-0.4
Beta-fibrinogenase	E0Y419.1	161.0	24	(R)TLcAGILQGGIDTcK(G)	68.2	2	803.9	0.1
				(K)FFcLSSKN(Y)	22.3	2	501.7	-0.1
Serine protease VLSP-3 precursor	E0Y420.1	157.2	16	(K)TSTHIAPLSLPSSPPSVGSVcR(I)	98.9	2	1125.6	0.5
Serine proteinase 3	JAS04410.1	74.5	9	(K)VFDYTDWIQSIIAGNTAATcPP(-)	74.5	2	1220.6	2.3
Factor V activator RVV-V alpha	P18964.1	298.0	80	(-)VVGGDEcNINEHPFLVALYTSTSSTIHcGGALINR(E)	87.7	3	1267.9	0.6
				(K)ISTTEDTYPDVPHcTNIFIVK(H)	87.4	2	1225.6	-0.7
				(K)HKWcEPLYPWVPADSR(T)	83.6	2	1021.0	-0.4
				(R)DTcHGDSGGPLIcNGQIQGIVAGGSEPcGQHLKPAVYTK(V)	74.4	3	1360.3	1.7
				(R)GKYFcLNTK(F)	67.0	2	565.8	0.7
				(K)FPNGLDKDIMLIR(L)	56.6	3	511.3	-1.3
				(R)TLcAGILKGGR(D)	55.7	2	573.3	0.2
				(R)LRRPVTYSTHIAPVSLPSR(S)	53.4	3	717.4	-0.3
				(K)NIRNEDEQIRVPR(G)	49.0	2	819.9	0.6
				(N)REWVLTAAHcDR(R)	46.4	3	505.2	-0.3
Factor V activator RVV-Vγ	P18965.2	296.3	72	(A)SSTIHcAGALINR(E)	55.0	2	700.4	2.7

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
				(M)HGIVAGGSEPcGQHLKPAVYTK(V)	35.5	4	577.3	0.9
Thrombin-like enzyme gyroxin B1.3Precursor	B0FXM1.1	106.6	5	(N)GEWVLTAAHcDR(K)	36.8	2	707.8	0.3
L-amino acid oxidase								
Secreted L-amino acid oxidase precursor	ACF70483.1	299.5	56	(R)IFFAGEYTANAHGWIDSTIK(S)	89.0	2	1121.1	1.9
				(K)SAGQLYQESLGK(A)	75.7	2	640.8	-1.0
				(K)YAmGAITTFTPYQFQHFSEALTAPVGR(I)	75.0	3	1007.5	1.0
				(K)KDLQTFcYPSIIQK(W)	69.9	2	871.0	-1.1
				(S)GLSAAYVLAGAGHK(V)	62.5	2	657.9	0.4
				(K)NLLLETADYVIVcTTSR(A)	56.3	2	984.5	4.3
				(K)HDDIFAYEKR(F)	54.2	3	431.9	-0.1
				(C)ADDKNPLEEcFREDDYEEFLEIAK(N)	52.9	3	992.4	2.4
				(K)KFWEDDGIQGGK(S)	52.7	2	690.3	2.7
				(K)VTVTYQTTQKN(L)	51.7	2	641.8	0.5
				(K)VTVLEASERPGGR(V)	45.6	2	685.9	0.2
				(L)LKYPVKPSEAGK(S)	41.6	2	658.9	0.9
				(K)YDTYSTK(E)	41.6	2	439.2	-0.5
				(K)LNEFVQETENGWYFIKN(I)	40.9	2	1066.0	0.3
				(K)SGLTAAR(D)	38.6	2	338.2	0.0
				(R)RITFKPPLPPKK(A)	37.7	3	474.6	0.3
				(R)AIEESVHFK(A)	37.5	2	530.3	-1.5
				(K)AVEELKR(T)	34.3	2	422.7	-0.5
				(K)IFLTcTK(K)	31.5	2	441.7	-0.4

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
Phosphodiesterase								
Phosphodiesterase	BAN89426.1	172.1	12	(C)VRDVELLTGLNFYSGLK(Q)	76.2	2	962.5	0.5
				(K)EQSSPLScSFGPVPSPDVSGcK©	59.4	2	1161.5	-1.9
				(K)YcLLHQAK(Y)	57.5	2	516.8	-0.4
				(K)TFLPIFVNPVN(-)	53.4	2	630.9	0.4
				(A)NVLcScSEDcLEK(K)	37.4	2	807.3	-0.2
				(K)QPLPETLQLK(T)	36.2	2	583.8	1.5
				(V)LcScSEDcLEKK(D)	33.8	3	510.2	0.5
5'-Nucleotidase								
5'-nucleotidase, partial	AHJ80886.1	213.9	46	(R)FHEcNLGNLIcDAVIYNNLR(H)	88.3	2	1218.1	1.7
				(R)HGQGTGELLQVSGIK(V)	71.1	2	762.4	-0.7
				(R)VVSLNVLcTK(C)	62.8	2	566.8	0.5
				(R)QVPVVQAYAFGK(Y)	60.7	2	653.9	0.5
				(Q)LQNYYSQEIGK(T)	58.9	2	671.8	1.0
				(K)IIALGHSGFFEDQR(I)	53.1	3	530.6	-0.4
				(K)ASGNPILLNK(D)	52.3	2	513.8	-0.6
				(K)VGIIGYTTK(E)	50.8	2	476.3	-0.1
				(R)ANNGIITLEELTSVLPFGGTFDLLQIK(G)	42.3	3	968.5	1.5
				(R)VPTYVPLEmEK(T)	41.1	2	661.3	1.0
				(K)DIPEDQVVK(A)	35.8	2	521.8	-0.4
				(K)VVYDLSQKPGSR(V)	35.0	3	450.2	0.1
				(K)ETPVLSNPGPYLEFRDEVEELQIHANK(L)	34.8	3	1042.2	-0.2
Glutaminyl cyclase								
Glutaminyl-peptide cyclotransferases	Q90YA8.1	118.7	27	(K)LIFFDGEEAFVR(W)	77.4	2	721.9	0.6
				(G)LQGLQAGWLVEEDTFQSHTPYGYR(T)	36.6	3	932.5	-0.6

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
				(R)TFSNIISTLNPLAK(R)	29.9	2	759.9	-0.2
				(R)NPVFPVYFLNTAR(W)	24.7	2	769.4	0.9
Hyaluronidase								
Hyaluronidase	ABI33950.1	41.9	3	(K)GKLELENLIYLR(E)	41.9	3	487.6	-2.0
Aminopeptidase								
Xaa-Pro aminopeptidase 2	XP_015676063.1	132.4	14	(K)EALQmLTAGcPESPcVK(V)	58.2	2	953.9	0.4
				(R)GDDIPYTPVFYAYTLLTK(T)	54.8	2	1039.0	1.1
				(R)LADDFmGSTWQEK(V)	53.2	2	772.3	-0.9
				(R)YWIQAER(Q)	44.8	2	483.2	0.0
				(R)TIHWGEPTAFQK(E)	35.4	3	472.2	0.5
				(K)VVSLVPYAR(N)	28.4	2	502.3	-0.9
				(R)YLVWLEK(N)	25.6	2	475.8	1.7
Non-enzymatic proteins								
Kunitz-type serine protease inhibitor								
KSPI B1	A8Y7P1.1	152.7	49	(K)cKEFIYGGcHGNANK(F)	24.1	4	439.4	-0.2
KSPI	AFD04724.1	142.4	50	(R)SFYYDSESKK(C)	62.6	2	627.3	-0.2
				(K)cKEFIYGGcHGNANNFPTR(D)	59.5	3	748.0	0.1
KSPI 1	ABD24040.1	228.2	56	(K)VFFYGGcGGNANNFETRDEcR(Q)	54.4	2	1235.5	1.7
KSPI C5	A8Y7N8.1	152.3	49	(R)IYYNPDSNKcEVFFYGGcGGNDNNFETR(K)	61.9	3	1113.1	3.2

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
KSPI IV	ABD24043.1	157.1	48	(A)ELTPISGQDRPK(F)	35.4	2	670.9	0.7
				(R)FYYNPASNQcQGFIYGGcGGNANNFETR(D)	63.8	2	1603.7	-0.5
				(K)FcHLPVDSGIcR(A)	55.0	2	730.8	0.6
KSPI II	ABD24041.1	260.0	64	(R)SRENTNNFDTR(D)	56.0	2	677.3	0.6
				(R)YGHPRPR(F)	40.0	2	441.7	0.0
Snaclec								
P68 alpha subunit	ADK22825.2	200.0	61	(R)TWFNLScGDDYPFVcK(F)	80.3	2	1004.9	1.2
				(K)TPADYVWIGLR(N)	71.0	2	645.8	-0.1
				(K)WTDGSSVIYK(N)	55.0	2	578.3	-0.2
				(K)AFDEPKR(R)	45.1	2	431.7	0.4
				(R)KAQYcISK(W)	43.8	2	499.3	-0.3
				(K)RSGDAETFcTEQANSGHLVSIESVEEAEFVAQLISENIK(T)	36.2	4	1074.5	0.5
				(K)NcFGLEK(E)	28.3	2	434.2	0.0
C-type lectin-like protein 2	AAY63871.1	195.2	53	(A)VLDcPSGWLSYEQHcYKG(F)	43.0	2	1100.0	0.4
C-type lectin-like protein 3A	ABW82662.1	165.3	41	(A)DFDcPPDWSAYDQHcYK(A)	66.5	2	1102.4	-2.1
						2		
C-type lectin 2	AMK37409.1	77.5	19	(R)TWLNLCcGDDYPFVcK(F)	24.9	2	995.9	1.5
Dabocetin alpha subunit	ADK22821.1	230.9	77	(K)YHEWITLPcGDKNPFIcK(S)	83.0	2	1139.5	-0.1
				(Q)RQQcSSHWTDGSAVSYETVTK(Y)	65.5	3	809.7	-0.3
				(K)SKYHAWIGLR(D)	58.1	2	615.8	0.7
				(K)TWEDAEKFcTQQANGWHLASIESVEEANFVAQLASETLTK(S)	42.8	4	1135.5	-0.3

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
				(K)SWVLH(-)	26.8	2	321.2	0.7
C-type lectin-like protein 1	AAY63870.1	118.0	34	(A)GLDcPPDSSLYR(Y)	47.2	2	690.3	0.2
				(R)FcmEHPNNGHLVSIESmEEAEFVAK(L)	46.3	4	735.1	-0.8
				(K)cFVLEK(E)	35.4	2	398.2	0.5
				(R)YFcYR(V)	31.8	2	404.7	-0.2
Dabocetin beta subunit	ADK22822.1	256.2	72	(A)KQDcLSDWSFYEGYcYK(V)	84.0	2	1125.0	0.6
				(K)KTWEDAEKFcNEQVNGGYLVSFR(S)	79.6	3	926.4	1.0
				(R)WSDGVNLDYK(A)	68.0	2	598.8	-0.3
				(R)FDFFWIGLR(D)	67.7	2	600.8	-0.2
				(K)AWSREPNcFVSK(T)	63.7	2	740.9	0.1
				(K)TTDNQWLR(W)	58.6	2	517.3	-0.1
				(R)SSEEmDFVIR(M)	56.1	2	614.8	0.0
				(R)mTFPIFR(F)	42.1	2	464.2	0.1
				(R)WNcNDPR(Y)	29.5	2	481.2	0.0
				(R)YFVcK(S)	27.3	2	358.7	0.1
P31 alpha subunit	ADK22833.1	207.6	61	(K)SVGEANFVAQLASGFmQK(D)	90.4	2	950.5	-0.9
				(A)DLDcPSGWSAYDQHcYQAVDEPK(S)	72.3	2	1371.1	0.9
				(K)SWADAEKFcTEQANSGHLVSIK(S)	69.6	2	826.7	0.5
				(K)DGIYVWIGLR(D)	54.8	3	596.3	-1.9
				(K)WDYVNcAEHYR(F)	38.8	2	756.8	-2.8
				(K)WTYFHK(W)	29.7	2	441.2	0.7
						2		
P31 beta subunit	ADK22834.1	164.3	32	(K)GSHLASIHSSEEEAFVSK(V)	108.2	2	958.0	0.1
				(A)GFScPNGWSSFGQHcYK(V)	62.6	2	1009.9	1.0

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
				(R)IFWFNR(G)	43.4	2	441.7	0.5
				(K)FVSFVcK(F)	41.7	2	443.7	-0.9
C-type lectin-like protein 2B	AJO70722.1	109.2	16	(K)FDFIWIGLR(D)	63.2	2	583.8	-0.1
C-type lectin E, partial	JAC96622.1	69.6	16	(C)TSEWNDGSKIIYVNWK(E)	50.7	2	970.5	1.9
Snaclec A16	B4XSZ1.1	49.7	11	(K)HLATIEWLGK(A)	33.7	2	584.3	0.0
Snaclec bitiscetin subunit alpha	Q7LZK5.1	49.3	6	(V)GTWEDAEK(F)	33.4	2	468.2	-0.1
Cysteine-rich secretory protein								
Cysteine-rich secretory protein Dr-CRPK	ACE73567.1	255.2	41	(K)KDFVYGQGASPANAVVGHYTQIVWYK(S)	90.3	3	966.8	-0.3
				(R)cILNHSPYNSR(V)	69.6	2	680.8	0.4
				(K)TKcPAScFcHNEII(-)	58.4	2	868.9	0.2
				(K)WTAIIHEWHK(E)	57.3	2	660.8	0.4
				(P)RRPEIQNEIVDLHNSLR(R)	49.0	3	697.0	-1.6
				(S)GSVDFDSESPR(R)	45.3	2	598.3	-0.5
				(K)QGcHSNYLK(T)	25.7	3	369.5	0.2
Cysteine-rich secretory protein	ALB06109.1	150.1	16	(R)KPEIQNEIVDLHNSLRR(S)	37.8	4	516.0	-0.9
Cysteine-rich venom protein	AAP20602.1	78.6	6	(M)KTNCPAScFcHNEII(-)	26.2	2	897.4	1.2
Vascular endothelial growth factor								
Snake venom vascular endothelial growth factor toxin VR-1	ACN22046.1	202.9	47	(R)ETLVSILQEHPDEISDIFRPScVAVLR(C)	76.7	2	1562.3	-0.3

Protein	Accession no.	-10lgP	Coverage (%)	MS/MS derived peptides	-10lgP	z	m/z	ppm
				(R)WKQGEPEGPKEPR(R)	73.5	2	769.4	0.9
				(K)HTADIQImR(M)	56.3	2	550.8	-0.5
				(K)FmEHTAcEcRPR(W)	44.6	2	805.3	0.8
				(R)SAcQTR(E)	33.6	2	361.7	-0.5
Snake venom vascular endothelial growth factor toxin	P82475.2	90.8	25	(R)PFPDVYQR(S)	38.1	2	511.3	-0.5
				(K)FTEHTAcEcRPR(R)	20.6	3	521.9	-0.1
Nerve growth factor								
Venom nerve growth factor 1	AAA03282.1	152.8	18	(K)HWNSYcTTTDTFVR(A)	85.7	2	894.4	0.4
				(R)INTAcVcVISR(K)	71.5	2	646.8	0.6
				(K)cKNPNPVPSGcR(G)	45.5	2	693.3	1.0
Venom nerve growth factor 1	Q2XXL6.1	72.6	9	(K)cRNPNPVPSGcR(G)	49.7	2	707.3	-7.2
				(K)QYFFETK(C)	45.8	2	481.7	-1.1
Disintegrin								
Jerdostatin	AAP20878.1	104.1	27	(R)TSVSSHYcTGR(S)	65.4	2	627.8	0.5
				(K)LKPAGTTcWR(T)	52.9	2	595.3	-0.6
				(R)ScEcPSYPG(N)	36.5	2	528.7	-0.5

Table 4.4c. List of all the proteins identified by LC-MS/MS analysis of GF fractions of EI RVV (N). The table shows the identified peptide ions, their m/z, charge (z), the score for the ID, ΔM (ppm), and modified residues. Carbamidomethylated cysteine and oxidized methionine residues are represented as c and m (in lower cases).

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
Enzymatic proteins								
Phospholipase A_2								
Basic PLA_2	AAZ53182.1	305.9	84	(R)VAAIcLGQNVNTYNKGYMFLSSYYcR(Q)	85.9	3	1031.5	0.8
				(R)MIDAKQEAFSFFKYISYGcYcGWGGQGTPK(D)	84.6	3	1166.2	-2.7
				(R)VKGcNPKLVEYSYSYR(T)	59.2	3	655.0	-0.9
				(K)RAVcEcDRVAAIcLGQNVNTYNK(G)	55.2	3	904.4	-0.6
				(K)DASDRCcFVHDccYAR(V)	44.6	3	678.9	0.6
				(K)GcNPKLVEYSYSYRTGK(I)	39.5	3	674.7	0.5
				(K)LVEYSYSYRTGKIVcETYNR(C)	37.0	3	834.4	2.4
Acidic PLA_2	AAZ53180.1	283.1	81	(K)MTGKEAVHSYAIYGcYcGWGGQGKPQDATDR(C)	89.7	3	1155.2	-1.2
				(-)NLFQFAEMIVKMTGK(E)	79.5	2	879.0	1.2
				(R)AAAIcLGQNVNTYDKNYENYAISHcTEESEQc(-)	73.7	3	1251.5	0.0
				(R)cCFVHDccYGTVNDCNPK(M)	60.8	2	1096.4	0.4
				(K)TVcEcDRAAAIcLGQNVNTYDK(N)	56.7	3	853.4	-0.3
				(N)GDIVcGDNNLcLK(T)	56.0	2	739.3	-0.1
PLA_2	AHJ09529.1	58.6	12	(Q)DASDRccFVHDcCYGRA(N)	22.9	3	697.9	0.4
PLA_2	CAA48456.1	114.1	26	(W)NYISYGCYcGWGGQGTPK(D)	47.6	2	1005.9	0.2
				(-)NLFQFAR(M)	21.4	2	476.8	-1.5

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
PLA_2	ACB59359.1	74.6	32	(K)YMLYSLFDcK(E)	46.7	2	670.3	-0.8
				(Q)NGDIVCGDDDPcLR(A)	25.5	2	774.8	0.3
Vaspin A	AAN59979.1	46.8	11	(R)AAAIcLGENVNTYDK(N)	46.8	2	819.9	0.3
Basic PLA_2	AAZ53183.1	223.6	82	(K)NPLSSYSNYGcYCGWGGK(G)	77.0	2	1006.9	-0.9
				(R)KYPPSQcTGTEQc(-)	66.7	2	778.3	0.8
				(R)AVcEcDRVAATcFR(D)	65.7	2	857.9	0.7
				(K)TATYSYSFENGGIVcGDRDPcK(R)	64.5	2	1249.0	-0.9
				(R)VAATcFRDNLNTYDKK(Y)	35.5	3	639.3	-0.1
				(R)ccFVHDCcYEK(V)	33.8	3	507.5	-0.7
				(-)NLLQFGR(M)	25.9	2	424.2	-1.4
				(N)GGIVcGDRDPcKR(A)	25.6	3	497.2	0.4
Ammodytin I2(A) variant	CAE47208.1	70.6	22	(R)ccFVHDCCYGGVN(G)	22.4	2	767.3	7.2
PLA_2	ABY77928.1	65.3	8	(R)GCFVHDccYEK(L)	41.9	2	709.3	0.0
K49 PLA_2-like protein	AAW92122.1	39.3	7	(R)DNLDTYDKK(Y)	39.3	2	556.3	-1.8
Acidic PLA_2 DsM-a2/DsM-a2'	A8CG78.1	198.0	41	(K)YMLYSIFDcKEESDQc(-)	96.5	2	1044.4	1.2
				(K)TGNFGLLSYVYYGcYcGWGGK(G)	77.8	2	1211.5	0.6
				(-)NLYQFGEMINQK(T)	61.1	2	742.9	0.6
				(R)AVcEcDRVAAIcFR(E)	42.1	2	863.9	-1.9
				(R)VAAIcFRENMNTYDKK(Y)	20.8	3	654.0	-0.1
Ammodytin I1(F) isoform	CAE47167.1	58.5	25	(Y)SYSFENGDIVcGGDDPcLR(A)	47.4	2	1081.0	0.6

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(K)YMLYSLLDCKEESDQc(-)	22.1	2	998.9	-3.1
Snake venom metalloprotease								
Hemorrhagic metalloproteinase russelysin	AAZ39880.1	310.9	42	(R)RFLTEHNPEcIINPPLR(T)	82.8	2	1053.6	1.7
				(R)TDIVSPPAcGNELLER(G)	73.7	2	885.9	-1.4
				(K)NDLTAIRTWVFELVNTINEIFKYLYIR(V)	71.7	3	1115.6	1.8
				(R)DPccDAAScK(L)	63.6	2	592.2	-0.4
				(K)LHSWVEcESGK(C)	63.5	2	666.3	-2.4
				(R)LGVYYAYcRK(E)	54.8	2	646.8	-0.7
				(R)SANcPVDEFHENGRPcLHNFGYcYNGK(C)	52.3	3	1081.5	-0.6
				(K)SPGNQIPcLPYYIPSDENKGmVDHGTK(C)	52.1	3	1011.8	-1.2
				(K)VcSNGQcVDLNIAY(-)	51.0	2	806.9	-1.8
				(K)YSVGVVQDHSK(I)	50.2	2	609.8	-0.8
				(R)AGTEcRPARDEcDKAEQcTGR(S)	49.0	2	1234.0	1.0
				(G)VQDScFQYNR(L)	47.8	2	658.8	-0.1
				(R)LYcSYK(S)	45.5	2	417.2	0.0
				(R)TWVFELVNTINEIFKYLYIRVPLVGLEIWK(N)	39.9	3	1232.7	5.1
				(I)KIPcAPKDEK(C)	39.3	2	593.3	0.4
				(R)KSYLLPR(K)	35.8	2	438.8	0.2
				(R)GEEcDcGSPENcR(D)	33.2	2	785.3	-3.4
				(K)YFSNcSYNQYR(R)	22.9	2	751.3	-2.2
Factor X activator heavy chain	ADJ67475.1	256.6	31	(K)IYEIVNSANEIFNPLNIHVTLIGVEFWcDR(D)	79.6	3	1192.6	0.9
				(R)GYcYNGDcPImR(N)	68.6	2	761.3	1.0

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(D)ARNEcDVPEHcTGQSAEcPR(D)	65.5	2	1187.0	1.3
				(R)SVGIVQVQGNRNFK(T)	62.3	2	773.4	-0.4
				(K)GSYYGYcR(K)	62.1	2	513.2	0.1
				(K)DScFQENLK(G)	56.6	2	570.8	-2.3
				(R)LFcLNNSPR(N)	55.6	2	560.8	-0.6
				(R)KSHDNALLFTDmR(F)	53.7	2	782.4	1.6
				(K)RQcVDVNTAYQ(S)	47.4	2	677.3	0.6
				(K)cILYPPLRK(D)	43.1	3	387.2	0.5
				(K)TAGTVcR(T)	37.3	2	382.7	-0.1
				(Q)LVSTSAQFNK(A)	34.5	2	547.8	-1.0
				(R)ASDLmTR(K)	33.3	2	405.2	-0.3
				(K)AFIELIIIVDHSmAK(K)	25.8	3	572.7	-1.9
Coagulation factor X activating enzyme heavy chain	AAB22477.1	237.1	36	(R)DEcDVPEHcTGQSAEcPR(D)	73.1	2	1073.9	3.0
Factor X activator light chain 1	ADJ67474.1	177.0	48	(K)FVVNLISENLEYPATWIGLGNmWK(D)	74.1	2	1405.7	1.4
				(A)VLDcPSGWLSYEQHcYKG(F)	49.9	2	1100.0	-1.6
				(K)SmTcNFIAPVVcKF(-)	45.9	2	845.4	-0.7
				(K)ALAEESYcLIMITHEK(V)	29.3	3	636.6	-1.7
				(K)FcTEQK(K)	26.2	2	406.7	1.1
				(K)KGSHLVSLHSREEEK(F)	22.5	4	434.7	-0.3
Metalloproteinase, partial	ADI47593.1	146.1	12	(E)CRAARDDCDVPEHcTGQSAEcPR(N)	45.2	3	878.4	2.1
Metalloproteinase, partial	ADI47654.1	124.3	6	(R)VPLVGLEIWNK(G)	38.2	2	634.4	-2.7
Factor X activator light chain 2	AFE61611.1	123.4	34	(K)cFVLEKESGYR(M)	56.7	3	463.2	0.4

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(A)GLDcPPDSSLYR(Y)	53.0	2	690.3	-0.5
				(R)YFcYR(V)	32.5	2	404.7	-2.2
Metalloproteinase, partial	ADI47578.1	110.0	6	(M)GNQcISLFGSR(A)	42.2	2	619.8	-0.7
				(D)YLIYR(K)	23.9	2	364.2	0.4
Factor X activator light chain 2	ADJ67473.1	184.5	60	(R)IKDKEQEcSSEWSDGSSVSYDNLGK(E)	87.0	3	950.1	-0.6
				(A)GLDcPPDSSPYR(Y)	60.2	2	682.3	-0.5
				(R)FcmEHPNNGHLVSIESmEEAEFVAK(L)	58.9	3	979.8	1.6
				(K)FITHFWIGLR(I)	56.1	2	645.4	-1.4
				(R)KSWEAAER(F)	41.7	2	488.7	0.0
VLAIP-A	AAX38181.1	175.8	13	(R)LYcFDNLPEHK(N)	72.2	2	718.3	0.4
				(N)VTLDLFGK(W)	53.1	2	446.8	0.2
				(K)mPQcILNKPLK(T)	50.3	2	679.4	-1.4
				(R)IYEIVNILNVIYRVLNIYIALLGLEIWNN GDK(I)	44.0	4	941.0	-0.5
				(K)AcSSNRQcVDVNTAY(-)	38.5	2	872.9	0.1
				(R)KIPcAPQDVKcGR(L)	22.6	3	510.3	-0.4
H3 metalloproteinase precursor 1	AGL45259.1	169.7	11	(R)IYEIVNLLNVIYR(V)	56.8	2	811.5	0.2
				(K)INVLPEAK(V)	38.3	2	442.3	-0.4
Factor X activator light chain 2	AAT91068.1	143.1	24	(L)NCEEPYPFVcK(V)	51.2	2	693.3	-0.9
VLAIP-B	AAX38182.1	108.6	5	(K)YSVGIVQDHSK(I)	73.4	2	616.8	-0.6
Snake venom serine protease								
Serine beta-fibrinogenase-like protein	ADP88560.1	222.5	52	(K)VYDYTDWIQSIIAGNTAATcPP(-)	73.4	2	1228.6	-0.8

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(L)VVGGDEcNINEHRS(L)	63.5	2	793.4	0.4
				(K)TSTYIAPLSLPSSPPR(V)	62.5	2	844.0	-1.0
				(R)NNAEIRLPEER(F)	60.7	2	670.8	0.3
				(M)HGIVAWGDDTcAQPHKPVHYTK(V)	38.9	4	630.1	0.0
				(R)FFcLSNK(N)	37.6	2	458.2	-0.3
				(K)LDRPVK(T)	35.3	2	364.2	0.0
				(H)cANINILPYSVcR(A)	31.6	2	790.4	-1.8
				(K)GLPAQSR(T)	21.0	2	364.7	0.2
Enzymatically inactive serine proteinase-like protein SPH-1	AMB36342.1	216.2	30	(R)FYcAGTLINQEWVLTAAR(C)	102.9	2	1057.0	0.2
				(R)TLcAGILQGGIDScK(V)	67.0	2	796.9	-0.4
				(K)EKFFcLSSK(T)	48.8	2	573.3	-0.6
				(K)TYTRWDKDIMLIR(L)	48.6	3	571.0	0.0
				(L)VIGGDEcNINEHPFLVALHTAR(S)	43.2	4	616.3	-1.3
Serine protease VLSP-1	E0Y418.1	204.1	34	(Q)GGIDTcLADSGGPLIcNGQFQGIVAWGR(H)	87.7	2	1460.2	-0.5
				(P)FSLPSSPPTVGSVcR(I)	61.3	2	795.9	1.1
				(E)IYDYSVcR(K)	49.9	2	538.2	-0.4
				(A)YGGLPEK(S)	33.5	2	382.2	-0.8
				(L)PAFYTK(V)	32.3	2	363.7	-0.2
				(L)VIGGDEcNINEHPFLAL(M)	31.4	2	949.5	-0.5
Serine protease VLSP-3	E0Y420.1	187.4	20	(K)TSTHIAPLSLPSSPPSVGSVcR(I)	94.6	2	1125.6	1.9
Serine proteinase SP-4	AMB36345.1	138.2	27	(R)TLcAGILQGGIDTcK(G)	68.2	2	803.9	0.7
				(K)FHcSGTLLNQEWVLTAA(H)	31.2	2	974.0	-1.0

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
Kallikrein-CohLL-4	JAA98034.1	122.7	18	(R)FHcSGTLINQEWVLTAA(H)	31.2	2	974.0	-1.0
Factor V activator RVV-V gamma	P18965.2	233.0	74	(K)ISTTEDTYPDVPHcTNIFIVK(H)	79.0	2	1225.6	0.9
				(K)HKWcEPLYPWVPADSR(T)	73.7	2	1021.0	-3.2
				(R)TLcAGILKGGR(D)	59.7	2	573.3	0.0
				(R)LRRPVTYSTHIAPVSLPSR(S)	55.3	3	717.4	-0.3
				(R)EWVLTAAHcDR(R)	54.6	2	679.3	-0.3
				(R)GKYFcLNTK(F)	52.8	2	565.8	0.3
				(L)VVGGDEcNINEHPFLVALYTSASSTIHcA GALINR(E)	45.8	4	947.2	1.6
				(K)YFcLNTKFPNGLDKDIMLIR(L)	43.4	4	615.3	-1.7
				(R)cRIMGWGK(I)	41.1	3	336.5	-0.1
				(R)DTcHGDSGGPLIcNGEMHGIVAGGSEPcG QHLKPAVYTK(V)	40.0	6	685.3	-0.1
				(N)IRNEDEQIRVPR(G)	35.4	3	508.9	-0.8
				(R)IKLGMHSK(N)	34.9	3	305.2	-0.1
				(K)VFDYNNWIQSIIAGNR(T)	29.4	3	637.3	-0.9
Serine proteinase 3	JAS04410.1	39.4	9	(K)VFDYTDWIQSIIAGNTAATcPP(-)	39.4	2	1220.6	0.9
Venom serine proteinase-like protein 2	Q9PT40.1	164.3	35	(K)VTYPDVPHcAN(I)	26.7	2	636.8	-1.2
				(I)IILGVHSK(N)	24.2	2	433.8	-5.0
Kallikrein-CohLL-7	JAA98031.1	89.6	12	(R)IMGWGTITPTK(E)	51.9	2	602.8	-0.2
Snake venom serine protease nikobin	E5AJX2.1	79.0	8	(R)IMGWGTISSPK(V)	42.7	2	588.8	-2.3
Venom serine proteinase-like HS120	Q5W958.1	50.2	7	(R)IMGWGTITPSKA(T)	34.7	2	631.3	-0.3

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
Alpha-fibrinogenase-like	E5L0E3.1	213.6	58	(K)KILPFVPHcANINIVPYTVcR(V)	68.7	2	1256.2	0.9
				(R)RIGScLGDSGGPLIcNGQIQGIVSWGSDPcVNR(G)	61.1	3	1177.2	-1.3
				(K)SYTKWDKDIMLIK(L)	56.5	3	547.6	-1.8
				(R)GAPSIYTKVFDYTDWIHSIIAGNTAATcPS(-)	54.8	3	1086.2	0.3
				(R)TLcAGVSGR(R)	53.0	2	460.7	-0.2
				(R)IMGWGSITSPK(K)	52.7	2	588.8	-2.1
				(R)VIYRPLPEQSR(T)	52.6	2	679.4	0.6
				(K)LNKPVTYSTHIASLSLPSNPPR(V)	43.7	3	798.1	-1.3
Factor V activator RVV-V alpha	P18964.1	192.8	67	(-)VVGGDEcNINEHPFLVALYTSTSSTIHcGGALINR(E)	69.5	3	1267.9	0.2
				(K)VFDYNNWIQNIIAGNR(T)	57.9	2	969.0	-0.5
				(K)NIRNEDEQIR(V)	22.0	2	643.8	0.6
				(R)EWVLTAAHcDRR(N)	20.6	3	505.2	-0.7
Gyroxin-like B1_7 serine protease	ABY65931.1	86.0	12	(Q)PHKPALYTK(V)	30.1	3	352.2	0.2
L-amino acid oxidase								
Secreted L-amino acid oxidase	ACF70483.1	301.6	58	(K)LNEFVQETENGWYFIK(N)	92.5	2	1009.0	-1.0
				(R)IFFAGEYTANAHGWIDSTIK(S)	87.4	2	1121.1	0.0
				(K)IQQNAEKVTVTYQTTQK(N)	87.3	2	990.5	0.4
				(K)YAmGAITTFTPYQFQHFSEALTAPVGR(I)	77.3	2	1510.7	-1.6
				(K)KDLQTFcYPSIIQK(W)	73.4	2	871.0	-1.9
				(K)SAGQLYQESLGK(A)	70.0	2	640.8	-0.7
				(K)NLLLETADYVIVcTTSR(A)	66.5	2	984.5	0.9

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(C)ADDKNPLEEcFREDDYEEFLEIAK(N)	57.8	2	1488.2	0.9
				(K)EGWYANLGPmR(V)	51.4	2	655.3	-0.6
				(R)AIEESVHFK(A)	48.6	2	530.3	-0.3
				(K)VTVLEASERPGGR(V)	45.9	2	685.9	-0.8
				(K)VTVTYQTTQKN(L)	42.7	2	641.8	0.6
				(L)LKYPVKPSEAGK(S)	40.2	2	658.9	0.5
				(K)STTDLPSR(F)	38.6	2	438.7	0.0
				(K)AVEELKR(T)	35.9	2	422.7	0.5
				(R)RITFKPPLPPKK(A)	33.8	3	474.6	0.6
				(K)SGLTAAR(D)	29.1	2	338.2	-0.1
				(K)EGNLSPGAVDmIGDLLNEDSGYYVSFIESLKHDDIFAYEK(R)	26.5	4	1117.5	5.5
				(S)IHQLPK(K)	17.2	2	368.2	-0.4
L-amino-acid oxidase	Q4F867.2	284.2	57	(K)KFWEDDGIQGGK(T)	51.4	2	690.3	2.3
				(R)AIEESVR(F)	41.7	2	402.2	0.0
				(K)IFLTcTKK(F)	19.2	3	337.5	-1.0
Phosphodiesterase								
Phosphodiesterase	AHJ80885.1	255.6	31	(K)VLSFILPHRPDNSEScADTSPDNLWVEERI(I)	79.0	3	1128.5	2.1
				(T)NPAWWGGQPIWHTVTYQGLK(A)	77.3	2	1170.1	0.7
				(K)DFYTFDSEGIVR(N)	77.2	2	724.8	-1.8
				(R)VRDVELLTGLNFYSGLK(Q)	74.1	2	962.5	0.9
				(K)FGPVSGEIImALQmADR(T)	73.2	2	934.0	-1.8
				(K)AATYFWPGSEVK(I)	71.2	2	678.3	-2.1
				(K)IPIPTHFFVVLTScENQINTPLNcPGSLK(V)	65.5	3	1099.6	1.3
				(R)LWNYFHGTLLPK(Y)	63.3	2	744.9	-2.0

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(K)YcLLHQAK(Y)	56.4	2	516.8	-0.9
				(R)cNGGTHGYDNEFK(S)	52.9	2	749.8	0.3
				(K)SPPTSVPPSASDcLR(L)	45.6	2	785.9	-0.5
				(K)TFLPIFVNPVN(-)	45.4	2	630.9	0.4
				(K)TESEAHNLPYGRPQVLQNHSK(Y)	42.8	3	802.4	0.3
				(R)LNLNNQAK(T)	38.2	2	457.8	-0.3
				(A)NVLcScSEDcLEK(D)	38.1	2	807.3	0.2
				(K)QPLPETLQLK(T)	34.7	2	583.8	-0.8
5'-Nucleotidase								
5'-nucleotidase, partial	AHJ80886.1	235.6	43	(R)FHEcNLGNLIcDAVIYNNLR(H)	95.0	2	1218.1	-0.4
				(R)HGQGTGELLQVSGIK(V)	87.4	2	762.4	-1.6
				(K)IIALGHSGFFEDQR(I)	72.4	2	795.4	-3.3
				(K)VVYDLSQKPGSR(V)	59.6	2	674.9	-1.2
				(R)VVSLNVLcTK(C)	59.2	2	566.8	-1.9
				(K)ASGNPILLNK(D)	58.6	2	513.8	-0.7
				(Q)LQNYYSQEIGK(T)	57.8	2	671.8	-0.7
				(K)VGIIGYTTK(E)	50.4	2	476.3	-0.7
				(R)ANNGIITLEELTSVLPFGGTFDLLQIK(G)	49.6	2	1452.3	0.4
				(K)DIPEDQVVK(A)	39.6	2	521.8	-0.8
				(K)QAFEHSVHR(H)	37.7	2	555.8	-0.5
				(R)VPTYVPLEmEK(T)	32.7	2	661.3	5.3
				(K)ETPVLSNPGPYLEFRDEVEELQIHANK(L)	32.5	3	1042.2	-0.5
Glutaminyl cyclase								
Glutaminyl-peptide cyclotransferase	AFE84762.1	172.0	54	(K)VFVGATDSAVPcAMMLELAR(S)	66.6	2	1069.5	0.6

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(K)LIFFDGEEAFVR(W)	61.8	2	721.9	0.3
				(R)VWHVMEDNEENLDKPTIDNLSK(I)	55.6	3	876.1	-0.6
				(R)LEAIEQNLHDLGLLNNYSSER(Q)	52.9	3	810.1	0.5
				(R)NPVFPVYFLNTAR(W)	49.0	2	769.4	-0.2
				(R)TFSNIISTLNPLAK(R)	43.4	2	759.9	1.1
				(R)LQGLQAGWLVEEDTFQSHTPYGYR(R)	40.0	3	932.5	0.3
				(Q)HPVEDDHIPFLR(G)	36.2	3	492.3	2.6
				(R)YPGSPGSYAVR(Q)	25.7	2	577.3	-1.6
				(R)RGVPILHLIPSPFPR(V)	25.1	3	567.0	-1.5
				(R)MWQNDLHPIMIER(Y)	21.1	3	561.6	-1.7
				(R)HLVIAcHYDSK(Y)	16.2	3	448.2	-6.1
Phospholipase B								
Phospholipase b	BAN82155.1	33.5	4	(R)SLEDGTLYIIEQIPK(L)	23.5	2	860.0	0.9
				(K)NNKDDPFWR(N)	20.0	2	596.3	2.1
Hyaluronidase								
Truncated hyaluronidase	ABI33950.1	43.8	5	(K)LELENLIYLR(E)	43.8	2	638.4	0.0
Non-enzymatic proteins								
Kunitz-type protease inhibitor								
KSPI I	ABD24040.1	225.2	62	(G)VFFYGGcGGNANNFETRDEcR(C)	62.7	2	878.9	0.5
				(K)RIYYNLESNKcK(Q)	50.8	3	824.0	0.1
					44.1	3	529.9	-1.1
KSPI B1	A8Y7P1.1	178.9	49	(K)FcYLPADPGEcLAHmR(S)	70.9	2	976.9	-1.0
				(K)cKEFIYGGcHGNANK(F)	69.4	2	877.9	0.3
				(R)SFYYDSESKK(C)	56.9	2	627.3	-0.5

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
KSPI	AFD04724.1	159.4	50	(K)FcYLPADPGEcMAYIR(S)	83.6	2	981.9	-0.7
				(K)cKEFIYGGcHGNANNFPTR(D)	46.9	3	748.0	-0.5
KSPI IV	ABD24043.1	128.8	48	(R)FYYNPASNQcQGFIYGGcGGNANNFETR(D)	72.7	3	1069.5	-0.8
				(K)FcHLPVDSGIcR(A)	59.0	2	730.8	-0.1
KSPI II	ABD24041.1	286.5	46	(R)FYYNPATNQcQGFLAQR(S)	87.3	2	1039.5	-1.0
				(R)SRENTNNFDTR(D)	53.9	2	677.3	-0.5
				(K)FcFLRPDFGR(Y)	52.3	2	657.8	-1.4
Snaclec								
C-type lectin-like protein subunit 3	AAY63872.1	232.6	74	(K)GSHLLSLHNIAEADFVLKK(T)	82.4	2	1046.6	-1.1
				(M)GLNDVWNEcNWGWTDGAK(L)	81.4	2	1061.5	-0.3
				(-)AFccPSGWSAYDQNcYK(V)	79.1	2	1057.4	-0.9
				(K)NHWSHmDcSSTHNFVcK(F)	70.4	2	1081.9	0.8
				(K)VFTEEmNWADAEK(F)	56.0	2	793.3	-0.6
				(K)AWNEGTNcFVFKIAKN(H)	35.4	3	633.6	-2.1
				(K)FcTEQHK(G)	24.2	3	317.1	0.3
				(K)LDYKAWNEGTNcFVFK(I)	24.1	3	664.6	-1.8
P68 alpha subunit	ADK22825.1	223.3	65	(K)TPADYVWIGLR(N)	73.5	2	645.8	0.3
				(R)SGDAETFcTEQANSGHLVSIESVEEAEFVAQLISENIK(T)	68.4	3	1380.3	0.3
				(K)AFDEPKR(S)	43.7	2	431.7	-0.3
				(R)KAQYcISK(W)	43.5	2	499.3	-1.0
				(K)NVIER(F)	28.7	2	315.7	0.7
Snaclec 4	Q4PRC9.1	198.3	69	(K)FVVNLISENLEYPATWIGLGNmWK(D)	74.1	2	1405.7	1.4

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(K)ALAEESYcLIMITHEK(V)	29.3	3	636.6	-1.7
				(K)FcTEQK(K)	26.2	2	406.7	1.1
C-type lectin-like protein subunit 1	AAY63870.1	123.4	34	(R)FcmEHPNNGHLVSIESmEEAEFVAK(L)	57.9	3	979.8	-0.5
				(K)cFVLEKESGYR(M)	56.7	3	463.2	0.4
				(-)GLDcPPDSSLYR(Y)	53.0	2	690.3	-0.5
				(R)YFcYR(V)	32.5	2	404.7	-2.2
Dabocetin beta subunit	ADK22822.1	260.3	75	(-)KQDcLSDWSFYEGYcYK(V)	76.6	2	1125.0	0.7
				(R)WSDGVNLDYK(A)	68.1	2	598.8	-0.8
				(K)KTWEDAEKFcNEQVNGGYLVSFR(S)	67.9	3	926.4	1.1
				(K)TTDNQWLR(W)	63.2	2	517.3	-0.5
				(K)AWSREPNcFVSK(T)	61.6	2	740.9	0.5
				(R)WNcNDPR(Y)	37.9	2	481.2	-0.5
				(R)MTFPIFRFDFFWIGLRDFWR(D)	35.5	3	899.8	1.1
				(R)SSEEmDFVIR(M)	29.5	2	614.8	-0.5
				(R)YFVcK(S)	21.1	2	358.7	-0.2
Dabocetin alpha subunit	ADK22821.1	259.8	80	(K)YHEWITLPcGDKNPFIcK(S)	89.0	2	1139.5	0.8
				(Q)RQQcSSHWTDGSAVSYETVTK(Y)	55.8	3	809.7	0.4
				(-)DcPSDWSSHEGHcYK(V)	49.9	2	932.9	0.6
				(K)SKYHAWIGLRDQSQR(Q)	44.0	3	615.7	-0.2
				(K)TWEDAEKFcTQQANGWHLASIESVEEANF VAQLASETLTK(K)	43.1	4	1135.5	0.5
				(K)cFGLNK(E)	36.5	2	369.7	-0.1
				(K)SWVLH(-)	28.9	2	321.2	-0.1
C-type lectin-like protein subunit 2	AAY63871.1	177.0	48	(-)VLDcPSGWLSYEQHcYK(G)	78.1	2	1071.5	0.0

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(K)SmTcNFIAPVVcK(F)	46.5	2	771.9	0.2
				(N)FIAPVVcKF(-)	28.7	2	540.8	0.2
c-type lectin	ABW82662.1	171.7	37	(R)TWFNLScGDDYPFVcK(S)	96.3	2	1004.9	-0.3
				(-)DFDcPPDWSAYDQHcYK(A)	72.7	2	1102.4	0.0
				(K)WTDGSSVIYK(N)	66.1	2	578.3	-0.6
				(K)NcFGLEK(E)	32.4	2	434.2	-0.7
P31 beta subunit	ADK22834.1	146.2	28	(K)GSHLASIHSSEEEAFVSK(V)	92.3	2	958.0	0.2
				(K)FGSVWIGLNDPWHNcNWEWSDNAR(F)	69.5	3	987.4	-0.1
C-type lectin	ABW82659.1	92.3	19	(K)HLATIEWLGK(A)	56.0	2	584.3	-1.2
P31 alpha subunit	ADK22833.1	154.3	56	(K)SVGEANFVAQLASGFMQK(D)	91.1	2	942.5	-0.3
				(K)SWADAEKFcTEQANSGHLVSIK(S)	67.6	3	826.7	0.5
				(R)FVcKFPPQY(-)	41.7	2	593.3	-2.6
				(-)DLDcPSGWSAYDQHcYQAVDEPK(S)	39.3	3	914.4	-0.3
				(K)WTYFHKWDYVNcAEHYR(F)	27.9	4	594.5	-0.9
C-type lectin-like protein 2B	AJO70722.1	46.5	6	(K)FDFIWIGLR(D)	46.5	2	583.8	1.5
Cysteine-rich secretory protein								
Cysteine-rich secretory protein Dr-CRPK	ACE73567.1	265.4	65	(K)cGENIYMSPYPmK(W)	85.6	2	803.3	0.2
				(R)SVTPTASNMLKMEWYPEAAANAER(W)	79.5	3	889.8	0.8
				(R)RPEIQNEIVDLHNSLRR(S)	71.6	3	697.0	0.2
				(K)TKcPAScFcHNEII(-)	58.9	2	868.9	-0.1
				(K)WTAIIHEWHKEK(K)	45.9	3	526.6	-0.8

Protein	Accession No.	-10lgP	Coverage (%)	MS/MS derived Peptides	-10lgP	z	m/z	ppm
				(N)PcSHHDEFTNcKDLVK(Q)	44.5	4	497.5	-0.5
				(G)SVDFDSESPRRPEIQNEIVDLHNSLR(R)	37.1	4	763.9	-0.7
				(K)EKKDFVYGQGASPANAVVGHYTQIVWYK(S)	34.5	4	789.7	-0.2
				(K)IATPYTSGPPcGD(C)	31.5	2	668.3	-0.4
Cysteine-rich secretory protein Da-CRPa, partial	ACE73575.1	183.4	28	(-)SVDFDSESPRKPEIQNEIVDLHNSLRR(S)	27.8	4	795.9	1.5
Vascular endothelial growth factor								
VR-1 precursor	ACN22046.1	226.9	65	(K)cTPVGKHTADIQIMR(M)	69.8	2	863.9	0.3
				(R)WKQGEPEGPKEPR(R)	68.0	2	769.4	0.2
				(R)SAcQTRETLVSILQEHPDEISDIFRPScVAVLR(C)	59.1	4	957.5	-1.4
				(R)cSGCcTDESMKcTPVGK(H)	48.9	3	640.6	-0.1
				(R)THSSKMEVMKFmEHTAcEcRPR(W)	28.4	4	692.8	-0.5
Nerve growth factor								
Nerve growth factor	AAA03282.1	174.6	57	(I)GIDAKHWNSYCTTTDTFVR(A)	62.3	3	739.0	-0.8
				(K)cKNPNPVPSGcR(G)	54.8	2	693.3	0.2
				(R)INTAcVcVISRK(K)	41.7	2	710.9	0.3
				(R)ALTMERNQASWR(F)	31.5	3	488.2	0.1
				(K)TTATDMRGNVVT(V)	18.8	2	633.3	-1.1
Disintegrin								
Jerdostatin	AAP20878.1	91.7	19	(R)TSVSSHYcTGR(S)	63.7	2	627.8	-0.7
				(K)LKPAGTTcWR(T)	42.3	2	595.3	-0.3

4.1.3.3 The proteome composition of SI RVV sample

In gel-trypsin digestion and subsequent MS/MS search against the Viperidae entries of the NCBI database returned 431 initial hits in SI RVV, though we eventually identified 66 distinct proteins to represent the SI RVV proteome, that were clustered into 14 enzymatic and non-enzymatic venom protein families (Table 4.5a; Fig. 4.11a). The alignment of MS/MS-derived peptide sequences of SI RVV with the homologous proteins from the Viperidae entries of NCBI database is shown in Figure 4.11b. The list of identified peptide ions in SI RVV, their m/z, charge (z), the score for the ID, and ΔM (Da) is shown in Table 4.5b.

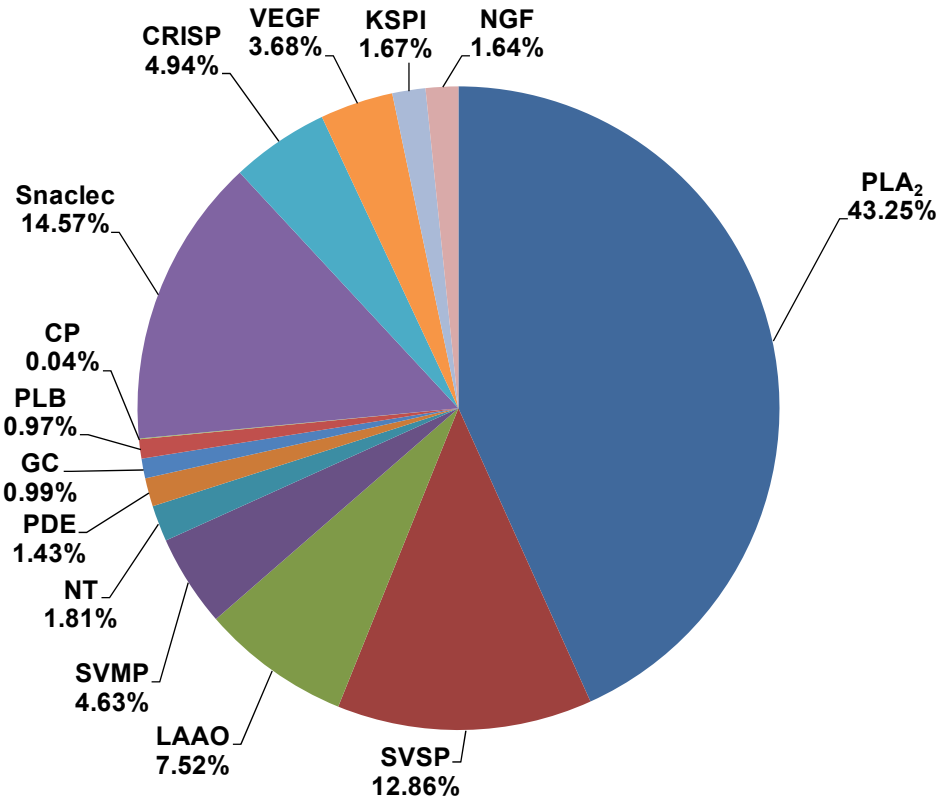

Fig. 4.11a. Protein family composition of SI RVV. The pie chart represents the relative occurrence of different enzymatic and non-enzymatic protein families of SI RVV. Abbreviations: PLA_2, phospholipase A_2; SVMP, snake venom metalloprotease; SVSP, snake venom serine protease; PDE, phosphodiesterase; NT, nucleotidase; LAAO, L-amino acid oxidase; PLB, phospholipase B; GC, glutaminyl cyclase; CP, carboxypeptidase; KSPI, Kunitz-type serine protease inhibitor; CRISP, cysteine-rich secretory protein; Dis, disintegrin; NGF, nerve growth factor; VEGF, vascular endothelial growth factor.

Table 4.5a. Summary of the identified proteins in SI RVV by LC-MS/MS analysis and database search against the Viperidae family of proteins (taxid 8689) of the NCBI database. *The gel sections are indicated in Fig. 4.8.

Accession No.	Protein description	Source organism	MW (Da)	Morpheus score	Coverage (%)	Relative abundance (%)	Gel section(s)*
Enzymatic proteins							
Phospholipase A_2							
P86368	Basic phospholipase A_2 3	*D. russelii*	13687	175.1	74.4	21.07	1-4,6-10
P59071	Basic phospholipase A_2 VRV-PL-VIIIa	*D. russelii*	13611	108.0	61.2	18.98	1,7-10
P31100	Acidic phospholipase A_2 RV-7	*D. siamensis*	15421	34.5	27.5	0.83	8
P04084	Acidic phospholipase A_2 homolog vipoxin A chain	*V. a. meridionalis*	13639	25.4	31.2	0.34	8
A7X4P4	PLA_2(IIA)-Aze2	*A. feae*	17085	17.1	11.9	0.15	9
Q6H3C5	Basic phospholipase A_2 Ts-G6D49	*T. stejnegeri*	13819	17.0	18.0	1.62	1,2,8,10
Q1RP79	Basic phospholipase A_2 chain HDP-1P	*V. nikolskii*	15566	15.0	13.0	0.12	9,10
Q7T3T5	Acidic phospholipase A_2 D toxin B chain (Fragment)	*D. siamensis*	14828	10.1	13.0	0.04	10
Q910A0	Phospholipase A_2 EC3	*E. coloratus*	15638	8.1	13.0	0.03	10
P34180	Neutral phospholipase A_2 ammodytin I2	*V. a. ammodytes*	15309	7.1	13.1	0.07	1

Accession No.	Protein description	Source organism	MW (Da)	Morpheus score	Coverage (%)	Relative abundance (%)	Gel section(s)*
Snake venom serine protease							
E5L0E3	Alpha-fibrinogenase-like	*D. siamensis*	28496	51.0	25.2	1.20	6,7
Q9PT40	Venom serine proteinase-like protein 2	*V. lebetina*	28894	33.5	12.7	1.66	4,5
E5L0E4	Beta-fibrinogenase-like	*D. siamensis*	28035	30.7	14.8	1.27	3,-5
E0Y419	Beta-fibrinogenase	*V. lebetina*	28297	17.2	5.8	0.95	2,-5
E0Y420	Serine protease VLSP-3	*V. lebetina*	28352	14.4	8.5	0.14	3,4
O13058	Snake venom serine protease 3	*P. flavoviridis*	28065	14.3	8.5	0.23	5
A7LAC6	Thrombin-like enzyme 1	*T. albolabris*	29150	14.3	8.4	0.49	5
Q6T6S7	Venom serine proteinase-like protein 1	*B. gabonica*	28982	13.4	6.9	0.84	5
B0FXM3	Thrombin-like enzyme gyroxin	*C. durissus terrificus*	28184	13.3	8.4	0.20	3,4
Q9PTU8	Snake venom serine protease BPA	*B. jararaca*	28058	13.1	10.8	0.28	5
Q8AY79	Beta-fibrinogenase stejnefibrase-2	*T. stejnegeri*	28028	12.5	8.5	0.11	3,4
A0A194ARG4	Serine proteinase 6a	*S. tergeminus*	28943	12.4	6.5	0.58	5
Q5I2B5	Thrombin-like protein 3	*D. acutus*	29071	10.1	10.8	0.60	5
Q9I8X2	Thrombin-like enzyme acutobin	*D. acutus*	28815	9.3	8.5	0.07	4

Accession No.	Protein description	Source organism	MW (Da)	Morpheus score	Coverage (%)	Relative abundance (%)	Gel section(s)*
Q7SYF1	Thrombin-like enzyme cerastocytin	*Cerastes cerastes*	27974	9.1	5.9	0.08	4
I4CHP3	Thrombin-like protein	*G. halys*	26518	8.1	6.3	0.19	4
D8MIA3	Rhinocerase 5 protein (Fragment)	*B. rhinoceros*	28620	8.1	8.5	0.13	4
P18964	Factor V activator RVV-V alpha	*D. siamensis*	26182	7.3	7.3	3.84	1,6,7
L-amino acid oxidase							
G8XQX1	L-amino-acid oxidase	*D. russelii*	56888	276.9	47.4	3.98	1-8,10
B5U6Y8	L-amino-acid oxidase	*E. ocellatus*	56523	70.8	16.1	0.44	3
A0A024BTN9	L-amino acid oxidase Bs29 (Fragment)	*B. schlegelii*	56376	59.1	10.5	1.99	2,3
T2HQ57	Amine oxidase	*O. okinavensis*	58087	50.1	10.5	0.34	3
Q90W54	L-amino-acid oxidase	*G. blomhoffii*	57092	41.0	10.7	0.15	3
P0C2D7	L-amino-acid oxidase (Fragments)	*V. berus berus*	10295	31.4	50.0	0.34	3
P81382	L-amino-acid oxidase	*Calloselasma rhodostoma*	58221	28.6	8.3	0.07	3
A0A0A1WCY6	Amine oxidase	*E. coloratus*	56738	26.7	5.8	0.15	3
Q6WP39	L-amino-acid oxidase	*T. stejnegeri*	58601	18.1	6.0	0.06	3

Accession No.	Protein description	Source organism	MW (Da)	Morpheus score	Coverage (%)	Relative abundance (%)	Gel section(s)*
Snake venom metalloprotease							
K9JAW0	Factor X activator heavy chain	*D. russelii*	69521	181.1	22.1	1.79	1-5,7
Q4VM08	Zinc metalloproteinase-disintegrin-like VLAIP-A	*V. lebetina*	68710	79.6	15.3	1.36	3,4
Q7T046	Coagulation factor X-activating enzyme heavy chain	*V. lebetina*	68775	13.3	5.9	0.48	4
K9JCB2	Factor X activator light chain 2	*D. russelii*	18273	10.1	15.8	1.00	9
5'-Nucleotidase							
F8S0Z7	Snake venom 5'-nucleotidase	*C. adamanteus*	64682	85.0	17.1	0.23	3
W8EFS0	5'-nucleotidase (Fragment)	*V. lebetina*	45031	65.6	21.8	1.58	2,4
Phosphodiesterase							
W8E7D1	Phosphodiesterase	*V. lebetina*	96181	183.5	32.8	1.03	1,2,4
J3SEZ3	Venom phosphodiesterase 1	*C. adamanteus*	96373	81.8	13.7	0.40	1,4
Phospholipase B							
F8S101	Phospholipase B	*C. adamanteus*	64049	32.6	6.1	0.97	4
Glutaminyl cyclase							
M9NCG3	Glutaminyl-peptide cyclotransferases	*D. russelii*	42116	45.8	16.0	0.99	4,5

Accession No.	Protein description	Source organism	MW (Da)	Morpheus score	Coverage (%)	Relative abundance (%)	Gel section(s)*
Carboxypeptidase							
J3RYP4	Carboxypeptidase E-like	*C. adamanteus*	53839	10.3	2.3	0.04	4
Non-enzymatic proteins							
Snaclec							
Q4PRD0	Snaclec 3	*D. siamensis*	16910	94.9	57.4	5.77	9,10
Q4PRC7	Snaclec 6	*D. siamensis*	16584	39.7	28.8	0.27	8
K9JBV0	P68 alpha subunit	*D. siamensis*	17996	35.7	17.1	1.66	7,8
Q4PRC6	Snaclec 7	*D. siamensis*	18067	33.2	19.3	0.71	7,8,10
K9JDF6	P31 beta subunit	*D. siamensis*	17338	28.4	28.0	0.35	8
A0A140DC06	C-type lectin 2	*B. arietans*	17891	22.3	19.5	0.22	8
Q38L02	Snaclec dabocetin subunit alpha	*D. siamensis*	17507	20.3	21.4	5.1	9,10
Q5FZI6	Snaclec trimecetin subunit alpha	*P. mucrosquamatus*	18255	12.3	20.5	0.23	8
K9JBU9	P31 alpha subunit	*D. siamensis*	18106	11.5	6.3	0.15	8
E2DQZ6	Snaclec jerdonuxin subunit alpha	*P. jerdonii*	18102	11.2	10.1	0.05	8
A0A0C5DQX8	C-type lectin-like protein 2B	*V. lebetina*	17458	9.7	6.0	0.06	10

Accession No.	Protein description	Source organism	MW (Da)	Morpheus score	Coverage (%)	Relative abundance (%)	Gel section(s)*
Cysteine-rich secretory protein							
F2Q6F2	Cysteine-rich secretory protein Dr-CRPK	*D. russelii*	26688	155.0	60.7	2.15	1,7,8
F2Q6F3	Cysteine-rich secretory protein Dr-CRPB (Fragment)	*D. russelii*	25044	30.3	15.4	2.79	7,8
Vascular endothelial growth factor							
P82475	Snake venom vascular endothelial growth factor toxin ICPP	*V. lebetina*	12574	16.1	24.5	3.04	9
P67861	Snake venom vascular endothelial growth factor toxin VR-1	*D. russelii*	16278	8.2	24.8	0.64	7
Nerve growth factor							
P30894	Venom nerve growth factor	*D. russelii*	13283	40.9	17.4	1.64	8,10
Kunitz-type serine protease inhibitor							
Q2ES48	Kunitz-type serine protease inhibitor 3	*D. russelii*	9417	18.9	36.7	0.92	10
A8Y7P5	Kunitz-type serine protease inhibitor B5	*D. siamensis*	9901	8.2	16.7	0.75	10

Fig. 4.11b. Alignment of tryptic and semi-tryptic peptide sequences identified in SI RVV with Viperidae proteins from NCBI database. The protein alignment was done using Clustal Omega programme (https://www.ebi.ac.uk/Tools/msa/clustalo/). The number of proteins in each protein classes is shown in parenthesis. The distinct peptides obtained for each of the following proteins is highlighted in green or yellow (two colours have been used in case of adjacent distinct peptides). The amino acid substitutions within the overlapping distinct peptides obtained from MS/MS are highlighted in red colour. The LC-MS/MS identified peptides other than distinct peptides are shown in blue or red colour.

Phospholipase A_2 [10]

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P04084.3        ----------------NLFQFGDMILQKTGKEAVHSYAIYGCYCGWGGQGRAQDATDRCCFAQDCCYGRVNDCNPKTATYTYSFENGDIVCGDNDLCLRAVCECDRAAAICLGENVNTYD
P31100.1        MRTLWIVAVCLIGVEGNLFQFGEMILEKTGKEVVHSYAIYGCYCGWGGQGRAQDATDRCCFVHDCCYGTVNDCNPKTATYSYSFENGDIVCGDNDLCLRTVCECDRAAAICLGQNVNTYD
P34180.2        MRTLWIVAVCLIGVEGNLYQFGNMIFKMTKKSALLSYSNYGCYCGWGGKGKPQDATDRCCFVHDCCYGRVNGCDPKLSIYSYSFENGDIVCGGDDPCLRAVCECDRVAAICFGENLNTYD
Q910A0.1        MRTLWIVAVWLMGVEGHLYQFENMIYQKTGKFAIIAYSNYGCYCGWGGKGKPQDATDRCCFVHDCCYGRVNGCDPKMGTYSYSFQNGDIVCGGDDPCLRAVCECDRVAANCFAENLKTYN
Q1RP79.1        MRILWIVAVCLIGVEGNLFQFAKMINGKLGAFSVWNYISYGCYCGWGGQGTPKDATDRCCFVHDCCYGRVRGCNPKLAIYAYSFKKGNIVCGKNNGCLRDICECDRVAANCFHQNQNTYN
Q7T3T5.1        --------MCLIGVEGNLFQFARLIDAKQEAFSFFKYISYGCYCGWGGQGTPKDATDRCCFVHDCCYARVKGCNPKLVEYSYSYRTGKIVCGGDDPCLRAVCECDRVAAICFRENMNTYD
A7X4P4          MRTLWIVAVLLMGVEGSLLQFGAMIIEETLRNPVTSYSAYGCYCGVGGRRQPMDATDRCCFVHDCCYGRVNDCNPKTLHYIYGRRNNVIVCRWGNECQKAVCECDKAAAICFRRNLKSYK
Q6H3C5.2        ----------------SLLEFGRMIKEETGKNPLSSYISYGCYCGWGGQGEPKDDTDRCCFVHDCCYGKLWGCSPKTDIYFYFRKNGAIVCGRGTWCEKQICECDKAAAICFRENLATYK
P86368.1        ----------------SLLEFGMMILEETGKLAVPFYSSYGCYCGWGGKATPKDATDRCCFVHDCCYGNLPDCNPKSDRYKYKRVNGAIVCEQGTSCENRICECDKAAAICFRRNLNTYS
P59071.1        ----------------SLLEFGKMILEETGKLAIPSYSSYGCYCGWGGKGTPKDATDRCCFVHDCCYGNLPDCNPKSDRYKYKRVNGAIVCEKGTSCENRICECDKAAAICFRQNLNTYS

P04084.3        KNYEYYSISHCTEESEQC----------
P31100.1        KNYEYYSISHCTEESEQC----------
P34180.2        KKYKNYPSSHCTETE-QC----------
Q910A0.1        KKYWLSSIIDCKEESEKC----------
Q1RP79.1        KNYKFLSSSRCRQTSEQC----------
Q7T3T5.1        KKYMLYSIFDCKEESDQC----------
A7X4P4          IGLQFYVDAFCRGKSPKCPEGQEKPLKITQS
Q6H3C5.2        EEYHSYGKSGCTEKSPKC----------
P86368.1        KTYMLYPDFLCKGELK-C----------
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P59071.1        KKYMLYPDFLCKGELK-C--------------
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Snake venom serine protease [18]

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Q5I2B5          MVLIRVLANLLILQLSYAQKSSELVIGGVECDINEHRFLAAFFKYQPWTFQCAGTLIHEQWVLGAAHCYKRGLNIYLGMHNQSIQFDDEQRRYAIEEHYYRCDEKLTKWEKDVVLLKLNK
Q8AY79.1        MELIRVLANLLILQLSYAQKSSELVVGGDECNINEHRSLVAIFN--STGFFCSGTLINQEWVVTAAHCDSKNFKMKFGAHSKKLLNEDEQIRNPKEKFICPNKKNNDVLDKDIMLIKLDS
P18964.1        ------------------------VVGGDECNINEHPFLVALYTSTSSTIHCGGALINREWVLTAAHCDRRNIRIKLGMHSKNIRNEDEQIRVPRGKYFCLNTKFPNGLDKDIMLIRLRR
I4CHP3          ----------------------MIIGGDECNINEHRFLVALYTSRSRTLFCGGTLINQEWVLTAAHCDRKNFRIKLGMHSKKVPNEDEQTRVPKEKFFCLSSKNYTLWDKDIMLIRLDS
A0A194ARG4      MVLIRVLANLLILQLSYAQKSSELVIGGEGCNINEHRFLVALYTFKSKRFHCSGTLINQEWVLTAAYCDRKNIRIKLGTHSTNVTNEDVQTRVPKKKFFCLSSKTYTRWDKDIMLIRLKR
Q9PT40.1        MVLIRVLANLLVLQLSYAQKSSELVIGGDECNINEHPFPVALHTARSKRFYCAGTLINQEWVLTAARCDRKNIRIILGVHSKNVPNEDQQIRVPKEKFFCLSSKTYTRWDKDIMLIRLKK
Q6T6S7.1        MVLIRVLANLLLLQLSYAQESSELVIGGDECDINEHPFLVALHTARSKRFHCAGTLLNKEWVLTAARCDRKNIRIKFGVHNKNVQNEDEEMRVPKEKHFCVSSKTYTRWDKDIMLIRLKR
D8MIA3          -VLIRVLANLLLLQLSYAQESSELVIGGDECDINEHPFLVALHTARSKRFHCAGTLLNKEWVLTAAHCDMENMQIYLGLHNISRPNQDQKRRVPKQKFFCLSNKTYTRWDKDIMLIKLNS
Q9I8X2.1        MVLIRVLANLLILQLSYAQKSSELVIGGVECDINEHRFLVALYELTSMTFLCGGTLINQEWVVTAAHCDRLQLYLYIGMHDKYVKFDDEQGREPIEKYFYNCSNNLTTRDKDIMLIRLDR
Q7SYF1.1        MVLISVLASLLVLQLSYAQKSSELVIGGAECNINEHRSLVLLYN--SSRLFGGGTLINKEWVLSAAHCDGENMKIYLGLHHFRLPNKDRQIRVAKEKYFCRDRKS--IVDKDIMLIKLNK
E5L0E3.1        MVLIRVLANLLVLQLSYAQKSSELVVGGHPCNIYEHHFLAFMYN--SSGFMCSGTLINQQWVLSAAHCDMENMHIYLGLHSFKLPNKDQKKRVAKEKFFCLSSKSYTKWDKDIMLIKLNK
A7LAC6.1        MVLITVLANLLILQLSYAQKSSELVIGGDECNINEHRFLVALYDVWSGDFLCGGTLINKEYVLTAAHCETRNMYIYLGMHNKNVQFDDEQRRYPKKKYFFRCSNNFTRWDKDIMLIRLNR
B0FXM3.1        MVLIRVLANLLILQLSYAQKSSELVIGGDECNINEHRLLAIVYT---NSSQCAGTLINQEWVLTAAHCDGENMDIYLGVHNESVQYDDEEGRVAAEKFFCLSSRNYTKWDKDIMLIRLNI
O13058.1        MVLIRVLANLLILQLSYAQKSSELVIGGDECNINEHRSLVVLFN--SSGALCGGTLINQEWVLTAAHCDMPNMQIYLGVHSASVPNDDEQARDPEEKYFCLSSNNDTEWDKDIMLIRLNR
Q9PTU8.1        MVLIRVIANLLILQLSNAQKSSELVIGGDECNITEHRFLVEIFN--SSGLFCGGTLIDQEWVLSAAHCDMRNMRIYLGVHNEGVQHADQQRRFAREKFFCLSSRNYTKWDKDIMLIRLNR
E5L0E4.1        MVLIKVLANLLVLQLSYAQKSSELVVGGDECNINEHRSLVFLYN---NSFGCSGTLINQQWVLSAVHCDMENVRIYLGVHNLTLRNNA-EIRLPEERFFCLSNKNYTKWDKDIMLIKLDR
E0Y419.1        MVLIRVLANLLLLQLSHAQKSSELVVGGDECNINEHRSLVFLYN---SSFGCGGTLINQEWVLSAAHCDMENMRIYLGWHNFSLPNMNQKRRVAKEKFFCLSSKNYTEWDKDIMLIKMNR
E0Y420.1        MVLIRVLANLLVLQLSYAQKSSELVIGGDECNINEHRSLVYLYN--DSNFQCGGTLINQEWVLSAAHCDMENMEIYLGVHNLSLPNKDQKRRDPKEKFFCLSSKNYTKWDKDIMLIKLNR

Q5I2B5          PVRNSTHIAPLSLPSSPPSIGSLCRVMGWGIMSSTKDILPDVPHCANINLLNYTECVAPYP--NIPVTTRLWCAGILEGGIDTCHQDSGGPLICDGQFQGIVSYGAHPCGQGPKPGIYTN
Q8AY79.1        SVSNSEHIAPLSLPSSPPSVGSDCRIIGWGSITPIEVTYPDVPYCANINLLDDAECKPGYP--ELLPEYRTLCAGIVEGGKDTCGGDSGGPLICNGQFHGIVSYGGHPCGQSLKPGIYTK
P18964.1        PVTYSTHIAPVSLPSRSRGVGSRCRIMGWGKISTTEDTYPDVPHCTNIFIVKHKWCEPLYP--WVPADSRTLCAGILKGGRDTCHGDSGGPLICNGQIQGIVAGGSEPCGQHLKPAVYTK
I4CHP3          PVKNSKHIAPFSLPSSPPSVGSVCRIMGWGRISPTEGTYPDVPHCVNINLLEYEMCRAPYPEFELPATSRTLCAGILEGGKDTCKGDSGGPLICNGQFQGIASWGDDPCAQPHKPAAYTK
A0A194ARG4      PFNNSEHIVPVNLPSNPPSLGSVCRIMGWGTISATKETYPDVPHCANINILDYEVCQAAYPEFGLPATSRTLCAGILKGGKDSCKGDSGGPLICNGEIQGIVSWGAHPCGQSLKPGVYTK
Q9PT40.1        PVNDSTHIVPLSLPSSPPSVGSVCRIMGWGTITTTKVTYPDVPHCANINMFDYSVCRKVYR--KLPEKSRTLCAGILQGGIDSCKVDNGGPLICNGQIQGIVSWGGHPCAQPHKPALYTN
Q6T6S7.1        PVNDGTHIAPLSLPSNPPSVGSVCRIMGWGSITTTKVTYPDVPHCANIKLFDYSVCRDAYK--GLPEKSRTLCAGILEGGIDSCKVDNGGPLICNGQFQGIGSWEGHPCAQPLKPALYTN
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D8MIA3          PVPYSTHIAPLSLPSSPPIVGSVCRIMGWGATKSPNENVPHVPHCANINILHYSVCRATYG--RLPAKSRTLCAGIPRRRIGSCLGDSGGPLICNGQVEGIVSWASKPCVHNGAPGMYTK
Q9I8X2.1        PVDNSTHIAPLSLPSRPPSVGSVCRVMGWGAISPSRDVLPDVPHCVNINLVNNAECRRAYP--RLPATSRTLCAGVMQGGIDSCNRDSGGPLICDGQFQGVVNWGGNPCAQPNMPALYTK
Q7SYF1.1        PVNNSTHIAPLSLPSSPPSVGSDCRIMGWGTITSPNDTYPKVPHCANINILEHSLCERAYN--DLSASSRTLCAGIEKGGIDTCKGDSGGPLICNGQIQGIVSWGDEVCGKPNKPGVYTK
E5L0E3.1        PVTYSTHIASLSLPSNPPRVGSVCRIMGWGSITSPKKILPFVPHCANINIVPYTVCRVIYR--PLPEQSRTLCAGVSGRRIGSCLGDSGGPLICNGQIQGIVSWGSDPCVNRGAPSIYTK
A7LAC6.1        PVRNSKHIAPLSLPSSPPSVGSVCRVMGWGTITSPNETLPDVPRCANINLLNYTVCRGVFP--RLPARSRTLCAGVLQGGIDTCKRDSGGPLICNGQLQGVVFWGPKPCAQPRKPALYTK
B0FXM3.1        PVRNSTHIAPLSLPSSPPSVGSVCRVMGWGTITSPNETYPDVPHCANINLFDYEVCLAAYPEFGLPATSRTLCAGIQQGGKDTCGSDSGGSLICNGQFQGIVSWGDNPCAQPHKPALYTK
O13058.1        SVRNSKHIAPLSLPSSPPSVGSVCRIMGWGAITSPNETYPDVPYCANIKLLRYSLCRV-YQ--RMPAQSRILCAGILQGGKGICKGDSGGPLICNGQFQGIVHGGGKTCAQPYEPGLYIK
Q9PTU8.1        PVNNSEHIAPLSLPSNPPSVGSVCRIMGWGTITSPNATFPDVPHCANINLFNYTVCRGAHA--GLPATSRTLCAGVLQGGIDTCGGDSGGPLICNGTFQGIVSWGGHPCAQPGEPALYTK
E5L0E4.1        PVKTSTVIAPLSLPSSPPFVGSVCRIMGWGAITSPNETFPGVTHCANINILPYSVCRAAYK--GLPAQSRTLCGGILEGGIGSCMGDSGGPLICNGEMHGIVAWGDDTCAQPHKPVHYTK
E0Y419.1        PVTYSTHVAPLSLPSSPPSVGSVCRIMGWGAITSPNETYPDVPHCANINILNYTVCRAAHP--WLPAQSRTLCAGILQGGIDTCKGDSGGPLICNGQIQGIVSWGDNPCAQPLKPGHYTN
E0Y420.1        PVKTSTHIAPLSLPSSPPSVGSVCRIMGWGTVTSPNETLLDVPHCANINILNYTVCRAASP--RLPTQSRTLCAGILQGGIDACKGDSGGPLICNGQIQGIVSWGNHPCAQPLKPGHYTH

Q5I2B5          VFDYTDWIQRNIAGNTDATCPP
Q8AY79.1        VFDYNDWMKSIIAGNTAATCPP
P18964.1        VFDYNNWIQNIIAGNRTVTCPP
I4CHP3          VFDHLDWIENIIAGNTDASCPP
A0A194ARG4      VFDYTEWIQSIIAGNTDATCPP
Q9PT40.1        VFDYTDWIQSIIAGNITATCPP
Q6T6S7.1        VFEYTDWIEGIIARNTTVTCPP
D8MIA3          VYDYTDWIRSIIGGNTSATCPL
Q9I8X2.1        VYDYNDWIRSITAGNTTAACPP
Q7SYF1.1        VFDYTDWIRNIIAGNTAATCPQ
E5L0E3.1        VFDYTDWIHSIIAGNTAATCPS
A7LAC6.1        VFNHLDWIQSIIAGNTTVTCPP
B0FXM3.1        VLDDTEWIQSIIAGNTAVTCPP
O13058.1        VFDYTDWIQNIIAGNTTATCPP
Q9PTU8.1        VFDYLPWIQSIIAGNTTATCPP
E5L0E4.1        VYDYTDWIQSIIAGNTAATCPP
E0Y419.1        VFDYTDWIQSIIAGNTTATCPP
E0Y420.1        VFDYTDWIQSIIAGNTTATCPP
```

L-amino acid oxidase [9]

```
G8XQX1.1        MNVFFMFSLLFLATLGSCADDKNPLEECFREDDYEEFLEIAKNGLKKTSNPKHIVIVGAGMSGLSAAYVLA---GAGHKVTVLEASERPGGRVRTHRNVKHGWYANLGPMRVPEKHRIIR
B5U6Y8.1        MNIFFMFSLLFLATLGSCADDKNPLEECFREADYEEFLEIAKNGLKKTSNPKDIVVVGAGMSGLSAAYVLA---GAGHKVTVLEASQLVGGRVRTHRNAKEGWYANLGPMRIPEKHRIVR
A0A0A1WCY6      MNVFFMFSLLFLATLGSCADDKNPLEECFREADYEEFLEIARNGLKKTSNPKDIVVVGAGMSGLSAAYVLA---GAGHKVTVLEASERVGGRVRTHRNTKEGWYANLGPMRIPEKHRIIR
P0C2D7.1        ------------------ADDKNPLEECFREDDYEEFLEIAKNGLKKTSNPKHIVYPVKPSEQLYEESLRDQLPTSMHRYPSMI---QKIFFAGEYTANAHGWIDSTIK-----------
A0A024BTN9.1    ----------------SCADDRNPLEECFQETDYEEFLEIARNGLKATSNPKHVVIVGAGMSGLSAAYVLA---GAGHQVTVLEASERAGGRVRTYRNDKEGWYANLGPMRLPEKHRIVR
P81382.2        MNVFFMFSLLFLAALGSCADDRNPLAECFQENDYEEFLEIARNGLKATSNPKHVVIVGAGMAGLSAAYVLA---GAGHQVTVLEASERPGGRVRTYRNEEAGWYANLGPMRLPEKHRIVR
Q6WP39.1        MNVFFMFSLLFLAALGSCADDRNPLEECFRETDYEEFLEIARNGLKATSNPKHVVIVGAGMSGLSAAYVLA---GAGHEVTVLEASERAGGRVRTYRNDEEGWYANLGPMRLPEKHRIVR
T2HQ57          MNVFFTFSLLFLAALGSCADDRNPLEECFRETDYEEFLEIARNGLKATSNPKHVVIVGAGMSGLSAAYVLA---GAGHQVTVLEASERAGGRVRTYRPEKEGWYANLGPMRLPEKHRIVR
Q90W54.1        MNVFFMFSLLFLAALGSCADDRNPLEECFRETDYEEFLEIARNGLKATSNPKHVVIVGAGMSGLSAAYVLS---GAGHQVTVLEASERAGGRVRTYRNDKEGWYANLGPMRLPEKHRIVR

G8XQX1.1        EYIRKFGLKLNEFVQETENGWYFIKNIRKRVGEVKKDPGLLKYPVKPSEAGKSAGQLYQESLGKAVEELKRTNCSYILNKYDTYSTKEYLIKEGNLSPGAVDMIGDLLNEDSGYYVSFIE
B5U6Y8.1        EYIRKFGLELNEFVQETDNGWYFVKNIRKRVGEVKKDPGLLKYPVKPSEAGKSAGQLYQEALGKAVEELKRTNCSYMLNKYDTYSTKEYLIKEGNLSTGAVDMIGDLMNEDSGYYVSFVE
A0A0A1WCY6      EYIRKFGLELNEFVQETDNGWYFIKNIRKRVGEVKKDPGLLKYPVKPSEAGKSAGQLYQASLKKAVKELKRTNCSYMLNKYDTYSTKEYLIKEANLSPGAVDMIGDLLNEDSGYYVSFIE
P0C2D7.1        ----------------------------------------------------------------------------------------------------------------------------
A0A024BTN9.1    EYITKFGLQLNEFSQENENAWYFIKNIRKRVGEVKKDPGLLQYPVKPSEEGKSAGQLYEESLGKVVEELKRTNCSYILDKYDTYSTKEYLIKEGNLSPGAVDMIGDLLNEDSGYYVSFIE
P81382.2        EYIRKFDLRLNEFSQENDNAWYFIKNIRKKVGEVKKDPGLLKYPVKPSEAGKSAGQLYEESLGKVVEELKRTNCSYILNKYDTYSTKEYLIKEGDLSPGAVDMIGDLLNEDSGYYVSFIE
Q6WP39.1        EYIRKFNLQLNEFSQENDNAWHFVKNIRKTVGEVKKDPGVLKYPVKPSEEGKSAEQLYEESLRKVEKELKRTNCSYILNKYDTYSTKEYLIKEGNLSPGAVDMIGDLMNEDAGYYVSFIE
T2HQ57          EYIRKFGLQLNEFSQENENAWYFIKNIRKRVGEVNKDPGLLKYPVKPSEEGKSAGQLYEESLGKVVEELKRTNCSYILNKYDTYSTKEYLLKEGNLSPGAVDMIGDVLNEDSGYYVSFIE
Q90W54.1        EYIRKFGLQLNEFSQENDNAWYFIKNIRKRVGEVKKDPGVLKYPVKPSEEGKSAGQLYEESLGKVVEELKRTNCSYILNKYDTYSTKEYLLKEGNLSPGAVDMIGDLMNEDSGYYVSFPE

G8XQX1.1        SLKHDDIFAYEKRFDEIVGGMDQLPTSMYRAIEESVHFKARVIKIQQNAEKVTVTYQTTQKNLLLETADYVIVCTTSRAARRITFKPPLPPKKAHALRSVHYRSGTKIFLTCTKKFWEDD
B5U6Y8.1        SMKHDDIFAYEKRFDEIVGGMDQLPTSMYRAIEKSVLFKARVTKIQQNAEKVRVTYQTAAKTLSDVTADYVIVCTTSRAARRINFKPPLPPKKAHALRSVHYRSATKIFLTCTKKFWEDD
A0A0A1WCY6      SLKHDDIFAYEKRFDEIVGGMDRLPTSMYRAIEKSVLFKARVTKIQQNAEKVRVTYQTAAKTLSYVTADYVIVCTTSRAARRINFKPPLPPKKAHALRSVHYRSGTKIFLTCTKKFWEDD
P0C2D7.1        ----------------------------------------------------------------------------------------------------------------------------
A0A024BTN9.1    SLKHDNIFGYEKRFNEIVDGMDKLPTSMYQAIEEKVRFNARVIKIQQNDNEVTVTYQTSENEMSPVTADYVIVCTTSRAARRITFEPPLPPKKAHALRSVHYRSGTKIFLTCTKKFWEDD
P81382.2        SLKHDDIFAYEKRFDEIVDGMDKLPTAMYRDIQDKVHFNAQVIKIQQNDQKVTVVYETLSKETPSVTADYVIVCTTSRAVRLIKFNPPLLPKKAHALRSVHYRSGTKIFLTCTTKFWEDD
Q6WP39.1        SMKHDDIFAYEKRFDEIVDGMDKLPTSMYRAIEEKVHFNAQVIKIQKNAEEVTVTYHTPEKDTSFVTADYVIVCTTSRAARRIKFEPPLPLKKAHALRSVHYRSGTKIFLTCTKKFREDE
T2HQ57          SLKHDDIFAYEKRFDEIVGGMDQLPTCMCRAIEEKVHFNARVIKIQQDAKKVTVTYQTPAKDTSLVTADYVIVCTTSRATRRIKFEPPLPPKKAHALRSVHYRSGTKIFLTCTKKFWEDE
Q90W54.1        SLRHDDIFAYEKRFDEIVCGMDKLPTSMYRAIEEKVHLNAQVIKIQKNAEKVTVVYQTPAKEMASVTADYVIVCTTSRATRRIKFEPPLPPKKAHALRSVHYRSGTKIFLTCTKKFWEDE
```

```
G8XQX1.1        GIQGGKSTTDLPSRFIYYPNHNFTTGVGVIIAYGIGDDANFFQALNLNECADIVFNDLSSIHQLPKKDLQTFCYPSIIQKWSLDKYAMGAITTFTPYQFQHFSEALTAPVGRIFFAGEYT
B5U6Y8.1        GIQGGKSTTDLPSRFIYYPNHNFTSGVGVIIAYGIGDDSNFFLSLTLNECADIVFSDLSSIHQLPKNDIQKFCNPSVIQKWSLDRYAMGAITTFTPYQFQDYSKALTAPAGRVYFAGEYT
A0A0A1WCY6      GIHGGKSTTDLPSRFIYYPNHNFTSGVGVIIAYGIGDDANFFQALSLNECADIVFNDLSSIHQLPKSDIQKFCCPSMIQKWSLDKYAMGAITTFTPYQFQHFSEALTAPAGRIYFAGEYT
P0C2D7.1        ----------------------------------------------------------------------------------------------------------------------------
A0A024BTN9.1    GIHGGKSTTDLPSRFVYYPNHDFSSGSAVIMAYGIGDDANFFQALDHKDCGDTVINDLSLIHQLTKEEIQSFCYLSKIQRWSLDKYAMGGITTFTPYQFQHFSEALTAPFKRIYFAGEYT
P81382.2        GIHGGKSTTDLPSRFIYYPNHNFTNGVGVIIAYGIGDDANFFQALDFKDCADIVFNDLSLIHQLPKKDIQSFCYPSVIQKWSLDKYAMGGITTFTPYQFQHFSDPLTASQGRIYFAGEYT
Q6WP39.1        GIHGGKSTTDLPSRFIYYPNHNFTSGVGVIIAYGIGDDANFFQALDLKDCGDIVINDLSLIHQLPREEIQTFCYPSMIQKWSLDKYAMGGITTFTPYQFQHFSEALTSHVDRIYFAGEYT
T2HQ57          GIHGGKSTTDLPSRFIYYPNHNFTSGVGVIIAYGIGDDANFFQALDFKDCADIVINDLSLIHQLSREEIQAFCYPSVIQKWSLDEYAMGGITTFTPYQFQHFSEPLTAPVGKVFFAGEYT
Q90W54.1        GIHGGKSTTDLPSRFIYYPNHNFTSGVGVIIAYGIGDDANFFQALDFKDCADIVINDLSLIHQLPREEIQTFCYPSMIQKWSLDKYAMGGITTFTPYQFQHFSEPLTASVDRIYFAGEHT

G8XQX1.1        ANAHGWIDSTIKSGLTAARDVNRASEL------------
B5U6Y8.1        ANAHGWIDSTIKSGLTAARDVNQASEL------------
A0A0A1WCY6      ANAHGWIDSTIKSGLTAARDVNRASEL------------
P0C2D7.1        ---------------------------------------
A0A024BTN9.1    AQFHGWIDSTIKSGLTAARDVNRASENPSGIHLSNDN--
P81382.2        AQAHGWIDSTIKSGLRAARDVNLASENPSGIHLSNDNEL
Q6WP39.1        AHAHGWIDSSIKSGLTAARDVNRASENPSGIHLSNDDEL
T2HQ57          AQAHGWIDSTIKSGLTAARDVNRASENPSGIHLSNDNEL
Q90W54.1        AEAHGWIDSTIKSGLRAARDVNRASEQ------------
```

Snake venom metalloprotease [4]

RVV-X heavy chain and zinc metalloprotease (3)

```
K9JAW0          MMQVLLVTISLAVFPYQGSSIILESGNVNDYEVVYPQKVTAMPKGAVKQPEQKYEDTMQYEFEVNGEPVVLHLEKNKILFSEDYSETHYYPDGREITTNPPVEDHCYYHGHIQNDGHSSA
Q7T046.1        MMQVLLVTISLAVFPYQGSSIILESGNVNDYEVVYPQKITALPEEAVQQPEQKYEDTMQYEFEVNGEPVVLHLEKNKDLFSEDYSETRYSPDGRETTTKPPVQDHCYYHGRIQNDAYSSA
Q4VM08.1        MMQVLLVTISLAVFPYQGSSIILESGNVNDYEVVYPQKVTAMPKGAVKQPEQKYEDAMQYEFKVKGEPVVLLLEKNKDLFSEDYSETHYSPDGREITTNPPVEDHCYYHGRIQNDADSSA

K9JAW0          SISACNGLKGHFKLRGEMYFIEPLKLSNNEAHAVYKYENIEKEDETPKMCGVTQTNWESDKPIKKASQLVSTSA--QFN--KAFIELIIIVDHSMAKKCNST--ATNTKIYEIVNSANEI
Q7T046.1        SISACNGLKGHFKLQGETYLIEPLKIPDSEAHAVYKYENIEKEDEAPKMCGVTQTNWESDEPIKKASQLVATSAKRKFH--KTFIELVIVVDHRVVKKYDSA--ATNTKIYEIVNTVNEI
Q4VM08.1        SISACNGLKGHFMLQGETYLIEPLKLPDSEAHAVYKYENVEKEDEAPKMCGVTQTNWESDEPIKKASQLNLTPEQRRYLNSPKYIKLVIVADYIMFLKYGRSLITIRTRIYEIVNILNVI
```

```
K9JAW0          FNPLNIHVTLIGV--EFWCDRDLINVTSSADETLDSFGEWRASDLMTRKSHDNALLFTDMRFDLNTLGITFLAGMCQAYRSVGIVQVQGNRNFKTAVIMAHELSHNLGMYHDGKNCICND
Q7T046.1        FIPLNIRLTLIGV--EFWCNRDLINVTSSADDTLDSFGEWRGSDLLNRKRHDNAQLFTDMKFDLSTLGITFLDGMCQAYRSVGIVQEHGNKNFKTAVIMAHELGHNLGMYHDRKNCICND
Q4VM08.1        YRVLNIYIALLGL--EIWNNGDKINVLPETKVTLDLFGKWRERDLLNRRKHDNAQLLTDINFNGPTAGLGYVGSMCDPQYSAGIVQDHNKVNFLVALAMAHEMGHNLGMEHDEIHCTCGA

K9JAW0          SSCVMSPVLSDQPSKLFSNCSIHDYQRYLTRYKPKCILYEPLRKDIVSPPVCGNEIWEEGEECDCGSPADCQNPCCDAATCKLKPGAECGNGLCCYQCKIKTAGTVCRRARNECDVPEHC
Q7T046.1        SSCIMSAVLSSQPSKLFSNCSNHDYRRYLTTYKPKCILNPPLRKDIASPPICGNEIWEEGEECDCGSPKDCQNPCCDAATCKLTPGAECGNGLCCEKCKIKTAGTVCRRARDECDVPEHC
Q4VM08.1        KSCIMSGTLSCEASIRFSNCSREEHQKYLINKMPQCILNKPLKTDIVSPAVCGNYLVELGEDCDCGSPRDCQNPCCNAATCKLTPGSQCADGECCDQCKFRRAGTVCRPANGECDVSDLC

K9JAW0          TGQSAECPRDQLQQNGQPCQNNRGYCYNGDCPIMRNQCISLFGSRATVAKDSCFQENLKGSYYGYCRKENGRKIPCAPQDVKCGRLFCLNNSPRNKNPCNMHYSCMDQHKGMVDPGTKCE
Q7T046.1        TGQSAECPADGFHANGQPCQNNNGYCYNGDCPIMTKQCISLFGSRATVAEDSCFQENQKGSYYGYCRKENGRKIPCAPQDIKCGRLYCLDNSPGNKNPCKMHYRCRDQHKGMVEPGTKCE
Q4VM08.1        TGQSAECPTDQFQRNGQPCQNNNGYCYSGTCPIMGKQCISLFGASATVAQDACFQFNSLGNEYGYCRKENGRKIPCAPQDVKCGRLYCFDNLPEHKNPCQIYYTPSDENKGMVLPGTKCG

K9JAW0          DGKVCNNKRQCVDVNTAYQSTTGFSQI
Q7T046.1        DGKVCNNKRQCVDVNTAY---------
Q4VM08.1        DGKACSSNRQCVDVNTAY---------
```

RVV-X light chain (1)

```
K9JCB2          MGRFIFVSFGLLAVFLSLSGTGAGLDCPPDSSPYRYFCYRVFKLRKSWEAAERFCMEHPNNGHLVSIESMEEAEFVAKLLSNTTGKFITHFWIGLRIKDKEQECSSEWSDGSSVSYDNLGK
                EEFRKCFVLQKESGYRMWFNHKCEEPYPFVCKVPPEC
```

Glutaminyl cyclase [1]

```
M9NCG3          MARERRDSKAAAFFCLAWALGLPLLGFPQHVGGREDRADWTQEKYSHRPTILNATSILQVTSQTNVSRMWQNDLHPIMIERYPGSPGSYAVRQHIKHRLQGLQAGWLVEEDTFQSHTPYG
                YRTFSNIISTLNPLAKRHLVIACHYDSKYFPPQLDGKVFVGATDSAVPCAMMLELARSLDRQLSFLKQSSLPTKADLSLKLIFFDGEEAFVRWSPSDSLYGSRSLAQKMSSTPHPPGARN
                TYQTQGIDLFVLLDLIGARNPVFPVYFLNTARWFGRLEAIEQNLHDLGLLNNYSSERQYFRSNLRQHPVEDDHIPFLRRGVPILHLIPSPFPRVWHVMEDNEENLDKPTIDNLSKILQIF
                VLEYLNLG
```

Phosphodiesterase [2]

```
W8E7D1          MIQQKVLFISLVAVALGLGLGLGLKESVEPQVSCRYRCNETFSKMASGCSCDDKCTERQACCQDYEDTCVLPTQSWSCSKLRCSEKRMANVLCSCSEDCLEKKDCCTDYKSICKGETSWL
J3SEZ3.2        MIQQKVLFISLVAVTLGLGLGLGLKESVQPQVSCRYRCNETFSKMASGCSCDDKCTERQACCSDYEDTCVLPTQSWSCSKLRCGEKRIANVLCSCSDDCLEKKDCCTDYKSICKGETSWL
```

```
W8E7D1          KDQCASSSAAQCPSGFEQSPLILFSMDGFRAGYLETWDSLMPNINKLKTCGTHAKYMRAVYPTKTFVNHYTIVTGLYPESHGIIDNNIYDVTLNLNFSLSAPTMTNPAWWGGQPIWHTVT
J3SEZ3.2        KDKCASSGATQCPAGFEQSPLILFSMDGFRAGYLENWDSLMPNINKLKTCGTHAKYMRAVYPTKTFVNHYTIATGLYPESHGIIDNNIYDVNLNLNFSLSSSTARNPAWWGGQPIWHTAT

W8E7D1          YQGLKAATYFWPGSEVKINGSYPTIYKVYNKSIPFEARVTEVLKWLDLPKAERPDFVTLYIEEPDTTGHKFGPVSGEIIMALQMADRTLGMLMEGLKQRNLHNCVNLILLADHGMEQISC
J3SEZ3.2        YQGLKAATYFWPGSEVKINGSYPTIFKNYNKSIPFEARVTEVLKWLDLPKAKRPDFLTLYIEEPDTTGHKYGPVSGEIIKALQMADRTLGMLMEGLKQRNLHNCVNLILLADHGMEEISC

W8E7D1          NRLEYMTDYFDKVDFFMYEGPAPRIRSKNVPKDFYTFDSEGIVRNLTCQKPKQYFKAYLAKDLPKRLHYVNNIRIDKVNLMVDQQWMAVRNKNYNRCNGGTHGYDNEFKSMQAIFLAHGP
J3SEZ3.2        DRLEYMANYFNNVDFFMYEGPAPRIRSKNVPKDFYTFDSEGIVKNLTCRKPKQYFKAYLSKDLPKRLHYANNIRIDKVNLMVDQQWMAVRDKKFTRCKGGTHGYDNEFKSMQAIFLAHGP

W8E7D1          GFKGKNEVTSFENIEVYNLMCDLLKLKPAPNNGTHGSLNHLLKNPFYNPSPAKEQTSPLSCPFGPVPSPDVSGCKCSSITDLGKVNERLNLNNQAKTESEAHNLPYGRPQVLQNHSKYCL
J3SEZ3.2        GFNEKNEVTSFENIEVYNLMCDLLKLKPAPNNGTHGSLNHLLKNPFYTPSPAKEQSSPLSCPFGPVPSPDVSGCKCSSITELEKVNQRLNLNNQAKTESEAHNLPYGRPQVLQNHSKYCL

W8E7D1          LHQAKYISAYSQDVLMPLWSSYTINKSPPTSVPPSASDCLRLDVRIPAAQSQTCSNYQPDLTITPGFLYPPNFGSSNFEQYDALITSNLVPMFKGFTRLWNYFHGTLLPKYARERNGLNV
J3SEZ3.2        LHQAKYISAYSQDILMPLWSSYTIYRSTSTSVPPSASDCLRLDVRIPAAQSQTCSNYQPDLTITPGFLYPPNFNSSNFEQYDALITSNIVPMFKGFTRLWNYFHTTLIPKYARERNGLNV

W8E7D1          ISGPIFDYNYDGHFDSYDTIKEYVNDTKIPIPTHFFVVLTSCENQINTPLNCPGSLKVLSFILPHRPDNSESCADTSPDNLWVEERIQTHTARVRDVELLTGLNFYSGLKQPLPETLQLK
J3SEZ3.2        ISGPIFDYNYDGHFDSYDTIKQHVNNTKIPIPTHYFVVLTSCENQINTPLNCLGPLKVLSFILPHRPDNSESCADTSPENLWVEERIQIHTARVRDVELLTGLNFYSGLKQPLPETLQLK

W8E7D1          TFLPIFVNPVN
J3SEZ3.2        TFLPIFVNPVN
```

Phospholipase B [1]

```
F8S101.1        MIRFGNPSSSDKRRQRCRSWYWGGLLLLWAVAETRADIHYATVYWLEAEKSFQIKDVLDKNGDAYGYYNDAIQSTGWGILEIKAGYGNQPISNEILMYAAGFLEGYLTASHMSDHFANLFPL
                MIKNVIIEQKVKDFIQKQDEWTRQQIKNNKDDPFWRNAGYVIAQLDGLYMGNVEWAKRQKRTPLTDFEISFLNAIGDLLDLIPALHSELRKSDFRSMPDVSRIYQWDMGHCSALIKVLPGYE
                NIYFAHSSWFTYAATLRIYKHLDFRITDPQTKTGRASFSSYPGLFGSLDDFYILGSGLIMLQTTNSVFNLSLLKKVVPESLFAWERVRIANMMADSGKTWAETFEKQNSGTYNNQYMILDTK
                KIKLQRSLEDGTLYIIEQVPKLVKYSDQTKVLRNGYWPSYNIPFDKEIYNMSGYGEYVQRHGLEFSYEMAPRAKIFRRDQGKVTDMESMKFIMRYNNYKEDPYAKHNPCNTICCRQDLDRRT
                PVPAGCYDSKVADISMAAKFTAYAINGPPVEKGLPVFSWVHFNKTKHQGLPESYNFDFVTMKPVL
```

5'-Nucleotidase [2]

```
F8S0Z7.2        MQTPKRRRGAQGCPRSSPSPPLLLLVRAVWFCAALSVAAGSFELTILHTNDVHARVEQTSRDSGKCTGQDCYGGVARRATKIRELRAKHRHVLLLDAGDQYQGTVWFNFFKGREVVKFMN
W8EFS0          ------------------------------------------------------------------------------------------------------------------------

F8S0Z7.2        SLRYDAMALGNHEFDNGLAGLLDPLLKHANFPILSANIRPKGSIASNISGYILPYKIINVGSEKVGIIGYTTKETPVLSNPGPYLEFRDEVEELQNHANKLTTLGVNKIIALGHSGFSED
W8EFS0          ------------------------------------------------------------AREKVGIIGYTTKETPVLSNPGPYLEFRDEVEELQTHANKLTTLGVNKIIALGHSGFFED

F8S0Z7.2        QRIARKVKGVDVVVGGHTNTFLYTGSPPSTEVAAGNYPFMVQSDDGRQVPVVQAYAFGKYLGYLNVIFDDKGNVIKSSGNPILLNKDISEDQDIKAEVNKMKIQLHNYSSQEIGKTIVYL
W8EFS0          QRIARKVKGVDVVVGGHTNTFLYTGSPPSTEVPAGNYPFMVQSDDGRQVPVVQAYAFGKYLGYLNVVFNDKGNVIKASGNPILLNKDIPEDQVVKAQVNKMKIQLQNYYSQEIGKTIVYL

F8S0Z7.2        NGTTQACRFHECNLGNLICDAVIYNNVRHPDDNEWNHVSMCIVNGGGIRSPIDERINNGTITLEELTAVLPFGGTFDLLQIKGSALKQAFEHSVHRHGEGMGELLQVSGIKVVYDLSRKP
W8EFS0          NGTTQACRFHECNLGNLICDAVIYNNLRHPDDNEWNHVSMCIVNGGGIRSPIDERANNGTITLEELTSVLPFGGTFDLLQIKGSALKQAFEHSVHRHGQGTGELLQVSGIKVVYDLSQKP

F8S0Z7.2        GSRVLSLNVLCTECRVPTYVPLEKEKTYKLLLPSFLAAGGDGYHMLKGDSSNHSSGNLDISIVGDYIKRMGKVFPAVEGRMIFSAGTLFQAQLFLTWGLCVSLLYFIL
W8EFS0          GSRVVSLNVLCTKCRVPTYVPLEMEKTYKVLLPSFLATGGDGYHMLKGDSSNHNSGDLDISIVGDYIKRMEKVFPAVEGRVTFLDGTLFQAQLFLTWGLCISLLFFIL
```

Carboxypeptidase [1]

```
J3RYP4          MAGRGQVWALALALCALPGSLCLQETEATEPETPAALGGGANRRRRLSQEDGISFEYHRYPELREALVSVWLQCPSISRIYTVGRSFEGRELLVIEVSDNPGEHEPGEPEFKYVGNMHGN
                EAVGRELLIFLAQYLCNEYQKGNETIINLIHSTRIHIMPSLNPDGFEKAASQPGELKDWFVGRSNAQGIDLNRNFPDLDRIVYVNEREGGPNNHLLKNMKKAVDQNLKLAPETKGVIHWI
                MDIPFVLSANLHGGDLVANYPYDETRTGSAHEYSSCPDDAIFQSLARSYSSFHPAMSNPNRPPCRKNDDDSSFIDGTTNGGAWYSVPGGMQDFNYLSSNCFEITVELSCEKFPPEETLKS
                YWEDNKNSLISYIEQIHRGIKGFIRDLQGNPIANATISVEGINHDITSAKDGDYWRLLVPGNYKVTASASGYLAITKKVAVPFSPAIRVDFDLESLSERKEEEKEELMEWWKMMSETLNF
```

Snaclec [11]

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K9JDF6          MGRFIFVSFGLLVVFLSLSGTEAGFSCPNGWSSFGQHCYKVIEPLKNWTDAEKFCREQHKGSHLASIHSSEEEAFVSKVASKVLKHGS--VWIGLNDPW--HNCNWEWSDNARFDYKAMT
Q4PRD0.1        MGRFISVSFGLLVVFLSLSGTEAAFCCPSGWSAYDQNCYKVFTEEMNWADAEKFCTEQHKGSHLLSLHNIAEADFVLKKTLAMLKDGV--IWMGLNDVW--NECNWGWTDGAKLDYKAWN
Q4PRC6.1        MGRFISISFGLLVVFLSLSGTGAKQDCLSDWSFYEGYCYKVFNEKKTWEDAEKFCNEQVNGGYLVSFRSSEEVDFVIRMTFPIFRFDF--FWIGLRDFW--RDCYWRWSDGVNLDYKAWS
A0A0C5DQX8      MGRFISVSFGCLVVFLSLSGTGADQDCPSDWSSHEGHCYKVFNLRMNWADAEKFCTEVVSGGHLISLNSAEEVDFMIKLVFPILKFDF--IWIGLRDFW--RDCHWGWSDGVKLDYKAWS
Q4PRC7.1        MGRFISVSFGLLVVFLSLSGTGA--DCPSEWSSHEGHCYKVFKLLKTWEDAEKFCTEQKKGSHLVSLHSFEEEKFVVNLISENLEYPA--TWIGLGNMW--KDCRMEWSDRGNVKYKALA
K9JBU9          MGRFISVSFGLLVVFLSLSGIGADLDCPSGWSAYDQHCYQAVDEPKSWADAEKFCTEQANSGHLVSIKSVGEANFVAQLASGFMQKDGIYVWIGLRDRRKEQQCRSEWTDGSKIIYVNWK
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K9JBV0          MGRFISVSFGLLVVFLSLSGTRADFDCPSGWSAHDQHCYKAFDEPKRSGDAETFCTEQANSGHLVSIESVEEAEFVAQLISENIKTPADYVWIGLRNQRKAQYCISKWTDGSSVIYKNVI
A0A140DC06      MGRFIFLSSGLLVVFLSLSG--ADFECPTEWCPYDQHCYRAFDEPKRSVDAEKFCVEQ--AGHLASIESQEEADFVAQLVSENVKSSPDYVWIGLWNQRKEQYCNKKWTDGSSVIYQNMV
Q38L02.1        MGRFISVSFGLLVVFLSLSGTGA--DCPSEWSSHEGHCYKVFKLLKTWEDAEKFCTQQANGWHLASIESVEEANFVAQLASETLTKSKYHAWIGLRDQSKRQQCSSHWTDGSAVSYETVT
Q5FZI6.1        MGRFIFVSFGLLVVFLSLSGTGA--DCPSDWSSFRRYCYKPFKQLKTWEDAERFCWEQVKGAHLVSIESSGEGDFVAQLLSENIKTTKYHVWIGLSIQNKRQQCRSIWSDGSSVSYENLV
E2DQZ6.1        MGRFTFVSFGLLVVFLSLSGTGADFDCIPGWSAYDRYCYQAFSEPKNWEDAESFCEEGVKTSHLVSIESSGEGDFVAQLVSEKIKTSFQYVWIGLRIQNKEQQCRSEWTDASSVNYENLI

K9JDF6          R--RPYCTVMVLKPDRIFWFNRGCEKFVSFVCKFLA--
Q4PRD0.1        E--GTNCFVF--KIAKNHWSHMDCSSTHNFVCKFRV--
Q4PRC6.1        R--EPNCFVS--KTTDNQWLRWNCNDPRYFVCKSRVSC
A0A0C5DQX8      D--EPNCYVA--KTVDYQWLFRDCNRTSRFICKSRVPR
Q4PRC7.1        EES----YCLIMITHEKVWKSMTCNFIAPVVCKF----
K9JBU9          EGESKMCQGLAKWTYFHKWDYVNCAEHYRFVCKFPPQY
K9JBV0          ERFIKNCFGLEKESDYRTWFNLSCGDDYPFVCKFPPRC
A0A140DC06      ERFRKNCFGLEKESGYRTWLNLCCGDDYPFVCKFPPRC
Q38L02.1        K--YTKCFGLNKETKYHEWITLPCGDKNPFICKSWVLH
Q5FZI6.1        KPFSKKCFVLKKESEFHKWFNIYCGERNLFMCKFLQPR
E2DQZ6.1        KQFSKKCYALKKGTELRTWFNVYCGTENPFVCKYTPEC
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Vascular endothelial growth factor [2]

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P67861          MAAYLLAVAILFCIQGWPSGTVQGQVRPFLDVYERSACQTRETLVSILQEHPDEISDIFRPSCVAVLRCSGCCTDESMKCTPVGKHTADIQIMRMNPRTHSSKMEVMKFMEHTACECRPR
P82475          ------------------------QVRPFTDVYQRSACQARETLVSILQEYPDEISDIFRPSCVAVLRCSGCCTDESLKCTPVGKHTVDMQIMRVNPRTQSSKMEVMKFTEHTACECRPR

P67861          WKQGEPEGPKEPRRGGVRAKFPFD
P82475          RKQGEPDGPKEKPR----------
```

Nerve growth factor [1]

```
P30894.1        HPVHNQGEFSVCDSVSVWVANKTTATDMRGNVVTVMVDVNLNNNVYKQYFFETKCKNPNPVPSGCRGIDAKHWNSYCTTTDTFVRALTMERNQASWRFIRINTACVCVISRKNDNFG
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Cysteine rich secretory protein [2]

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F2Q6F2          ------------------MIAFIVLPILAAVLQQSSGSVDFDSESPRRPEIQNEIVDLHNSLRRSVTPTASNMLKMEWYPEAAANAERWAFRCILNHSPYNSRVIGGIKCGENIYMSPYP
F2Q6F3          ------------------------------------SVDFDSESPRKPEIQNEIVEFHNSLRRSVNPTASNMLKMEWYPEAAANAERWAFRCILDHSPYNSRVIGGIKCGENIYMSSNP

F2Q6F2          MKWTAIIHEWHKEKKDFWYGQGASPANAVVGHYTQIVWYKSYRSGCAAAYCPSSEYNYFYVCQYCPAGNIIGKIATPYTSGPPCGDCPSACDNGLCTNPCSHHDEFTNCKDLVK-QGCHS
F2Q6F3          IKWIEIIRKWHDEKKNFIYGKGANPSNAVVGHYTQVVWYKSYRIGCAAAYCPSSAYKYFYVCQYCPAGNIVGRTATPYKSGQPCGDCPSACDNGLCTNPCRREDVFTNCIDMAKGRSCQD

F2Q6F2          NYLKTKCPASCFCHNEII
F2Q6F3          NYMKLNCPAACFCRNEIK
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Kunitz-type serine protease inhibitor [2]

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Q2ES48          MSSGGLLLLLGLLTLWAELTPISGHDRPKFCYLPADPGECMAYIRSFHYDSESKKCKEFIYGGCHGNANNFPTRDKCRQTCRGK------
A8Y7P5          MSSGGLLLLLGLLTLWAELTPISGHDRPKFCYLPADPGECLAHMRSFYYDSESKKCKEFIYGGCHGNANKFPSRDKCRQTCGASAKGRPT
```

Table 4.5b. List of all the proteins identified by LC-MS/MS analysis of SDS-PAGE bands of SI RVV. The table shows the identified peptide ions, their m/z, charge (z), the score for the ID, ΔM (Da), and modified residues. Carbamidomethylated cysteine and oxidized methionine residues are represented as c and m (in lower cases).

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
Phospholipase A_2							
P86368	Basic PLA_2 3	175.1	(K)IYMLYPDFLcKGELK(C)	16.4	630.0	3	-2.022
			(K)RVNGAIVcEQGTScENR(I)	14.2	650.6	3	-0.009
			(-)SLLEFGmmILEETGKLAVPFYSSYGcYcGWGGK(A)	13.1	946.4	4	-0.049
			(R)RNLNTYSKIYMLYPDFLcK(G)	10.1	1220.1	2	-0.100
			(K)LAVPFYSSYGcYcGWGGKATPK(D)	4.1	823.7	3	-0.006
P59071	Basic PLA_2	108.0	(K)KYMLYPDFLcKGELK(C)	16.2	635.3	3	-1.007
			(-)SLLEFGKmILEETGK(L)	12.3	855.4	2	-1.050
			(K)mILEETGKLAIPSYSSYGcYcGWGGK(G)	9.1	981.8	3	-0.013
			(R)ccFVHDccYGNLPDcNPK(S)	6.3	772.6	3	-0.011
			(K)GTScENRIcEcDKAAAIcFR(Q)	5.1	605.3	4	-0.032
			(K)RVNGAIVcEKGTScENR(I)	2.1	651.0	3	0.967
			(K)SDRYK(Y)	1.5	334.7	2	0.008
			(K)AAAIcFRQNLNTYSK(K)	1.1	585.6	3	-2.026
			(R)QNLNTYSKKYmLYPDFLcK(G)	1.1	814.0	3	-2.069
P31100	Acidic PLA_2	34.5	(K)TATYSYSFENGDIVcGDNDLcLR(T)	18.2	1336.1	2	0.986
			(-)NLFQFGEmILEK(T)	15.6	742.9	2	-0.002
			(R)AAAIcLGQNVNTYDK(N)	14.1	819.4	2	-0.007

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
			(R)ccFVHDccYGTVNDcNPK(M)	11.0	769.0	3	-1.014
P04084	Acidic PLA_2 homolog vipoxin A chain	25.4	(K)TATYTYSFENGDIVcGDNDLcLR(A)	13.2	1342.6	2	-0.022
			(K)TGKEAVHSYAIYGcYcGWGGQGR(A)	6.1	645.0	4	-0.034
A7X4P4	PLA_2(IIA)-Aze2	17.1	(R)ccFVHDccYGRVNDcNPK(T)	17.1	787.0	3	-1.992
Q6H3C5	Basic PLA_2	17.0	(-)SLLEFGRMIKEETGK(N)	8.3	868.4	2	-2.097
Q1RP79	Basic PLA_2 chain HDP-1P	15.0	(R)ccFVHDccYGRVRGcNPK(L)	15.0	782.0	3	-1.086
Q7T3T5	Acidic PLA_2 daboiatoxin B	10.1	(R)ccFVHDccYARVKGcNPK(L)	10.1	777.3	3	-1.098
Q910A0	PLA_2 EC3	8.1	(K)FAIIAYSNYGcYcGWGGK(G)	8.1	696.0	3	-1.026
P34180	Neutral PLA_2 ammodytin I2	7.1	(K)SALLSYSNYGcYcGWGGK(G)	7.1	1021.0	2	-1.969
Snake venom serine protease							
E5L0E3	Alpha-fibrinogenase-like	51.0	(K)VFDYTDWIHSIIAGNTAATcPS(-)	20.3	1220.1	2	-0.014
			(K)LNKPVTYSTHIASLSLPSNPPR(V)	12.2	798.1	3	-0.006
			(K)KILPFVPHcANINIVPYTVcR(V)	8.2	837.8	3	0.024
Q9PT40	Venom serine proteinase-like protein 2	33.5	(R)TLcAGILQGGIDScK(V)	18.2	796.9	2	0.001
			(R)FYcAGTLINQEWVLTAAR(C)	15.3	1057.0	2	-0.014
			(K)NIRIILGVHSK(N)	3.1	625.4	2	-0.059

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
			(K)NVPNEDQQIRVPK(E)	3.1	513.3	3	0.982
E5L0E4	Beta-fibrinogenase-like	30.7	(K)VYDYTDWIQSIIAGNTAATcPP(-)	16.1	819.4	3	0.011
			(K)LDRPVKTSTYIAPLSLPSSPPR(V)	6.1	599.6	4	-0.017
			(R)NNAEIRLPEER(F)	5.2	447.9	3	0.984
			(K)GLPAQSR(T)	3.7	365.7	2	1.999
E0Y419	Beta-fibrinogenase	17.2	(R)TLcAGILQGGIDTcK(G)	17.2	803.9	2	-0.002
E0Y420	MACLB Serine protease VLSP-3	14.4	(K)TSTHIAPLSLPSSPPSVGSVcR(I)	14.4	750.7	3	-0.009
O13058	Snake venom serine protease 3	14.3	(R)NSKHIAPLSLPSSPPSVGSVcR(I)	14.3	764.7	3	2.007
			(K)VFDYTDWIQNIIAGNTTATcPP(-)	3.2	833.1	3	-0.015
A7LAC6	Thrombin-like enzyme 1	14.3	(R)LNRPVRNSEHIAPLSLPSSPPSVGSVcR(V)	9.0	1010.2	3	1.928
Q6T6S7	Venom serine proteinase-like protein 1	13.4	(R)FHcAGTLLNKEWVLTAAR(C)	13.4	696.4	3	-0.048
B0FXM3	Thrombin-like enzyme gyroxin B1.7	13.3	(R)NSTHIAPLSLPSSPPSVGSVcR(V)	13.3	755.4	3	1.021
Q9PTU8	Snake venom serine protease BPA	13.1	(R)FAREKFFcLSSR(N)	4.0	774.4	2	-0.051
Q8AY79	Beta-fibrinogenase stejnefibrase-2	12.5	(K)VFDYNDWMKSIIAGNTAATcPP(-)	12.5	1235.6	2	-0.968
A0A194ARG4	Serine proteinase 6a	12.4	(K)KKFFcLSSK(T)	5.2	573.3	2	0.948

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
Q5I2B5	Thrombin-like protein 3	10.1	(K)LNKPVRNSTHIAPLSLPSSPPSIGSLcR(V)	10.1	1000.2	3	-0.133
Q9I8X2	Thrombin-like enzyme acutobin	9.3	(K)VYDYNDWIRSITAGNTTAAcPP(-)	9.3	829.7	3	1.997
Q7SYF1	Thrombin-like enzyme cerastocytin	9.1	(R)TLcAGIEKGGIDTcK(G)	9.1	810.9	2	-1.974
			(R)QIRVAKEK(Y)	2.1	486.3	2	-0.048
I4CHP3	Thrombin-like protein	8.1	(R)TLcAGILEGGKDTcK(G)	8.1	810.9	2	-1.987
D8MIA3	Rhinocerase 5 protein	8.1	K(VYDYTDWIRSIIGGNTSATcPL(-)	8.1	834.4	3	-1.103
P18964	Factor V activator RVV-V alpha	7.3	(-)VVGGDEcNINEHPFLVALYTSTSSTIHcGGALINR(E)	14.1	951.2	4	-0.025
			(R)DTcHGDSGGPLIcNGQIQGIVAGGSEPcGQHLKPAVYTK(V)	13.2	816.6	5	-0.016
			(K)VFDYNNWIQNIIAGNR(T)	8.1	969.5	2	0.975
			(R)LRRPVTYSTHIAPVSLPSR(S)	7.3	538.3	4	-0.008
			(R)TLcAGILK(G)	4.4	438.3	2	-0.004
L-amino acid oxidase							
G8XQX1	L-amino-acid oxidase	276.9	(K)NLLLETADYVIVcTTSR(A)	24.7	984.5	2	0.002
			(K)EGNLSPGAVDmIGDLLNEDSGYYVSFIESLKHDDIFAYEK(R)	15.2	1118.0	4	1.969
			(K)RFDEIVGGmDQLPTSmYR(A)	13.5	716.3	3	-0.002
			(K)SAGQLYQESLGK(A)	13.4	640.8	2	-0.001
			(K)KDLQTFcYPSIIQK(W)	12.3	581.0	3	0.001
			(K)WSLDKYAmGAITTFTPYQFQHFSEALTAPVGR(I)	12.2	913.2	4	0.006

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
			(K)HIVIVGAGmSGLSAAYVLAGAGHKVTVLEASE RPGGR(V)	12.1	730.6	5	1.963
			(K)VTVTYQTTQK(N)	11.5	584.8	2	0.001
			(R)IFFAGEYTANAHGWIDSTIK(S)	11.2	747.7	3	-0.020
			(R)ITFKPPLPPKK(A)	9.4	422.6	3	-0.002
			(K)TSNPKHIVIVGAGmSGLSAAYVLAGAGHK(V)	9.1	706.4	4	-0.005
			(R)RITFKPPLPPK(K)	8.3	431.9	3	0.001
			(K)EGWYANLGPmRVPEK(H)	8.2	588.3	3	0.013
			(K)AVEELKR(T)	7.1	422.1	2	-1.359
			(K)IFLTcTKKFWEDDGIQGGK(S)	6.1	747.7	3	-2.033
			(K)SGLTAAR(D)	4.6	338.2	2	-0.001
			(K)YDTYSTK(E)	4.4	439.2	2	0.002
			(R)SGTKIFLTcTK(K)	4.2	419.2	3	0.001
			(K)LNEFVQETENGWYFIKNIR(K)	4.1	801.1	3	0.982
			(K)FGLKLNEFVQETENGWYFIK(N)	4.1	821.4	3	0.002
			(K)KFWEDDGIQGGKSTTDLPSR(F)	4.1	1118.1	2	-1.983
			(K)YPVKPSEAGK(S)	3.4	359.5	3	0.994
			(R)AIEESVHFKAR(V)	3.3	429.6	3	0.000
			(R)VGEVKKDPGLLK(Y)	2.5	428.3	3	0.008
B5U6Y8	L-amino-acid oxidase	70.8	(K)EGNLSTGAVDmIGDLmNEDSGYYVSFVESMKH DDIFAYEK(R)	15.1	1127.5	4	-1.951
			(K)SAGQLYQEALGK(A)	8.2	632.8	2	-0.001
A0A024BTN9	L-amino acid oxidase Bs29 (Fragment)	59.1	(K)EGNLSPGAVDmIGDLLNEDSGYYVSFIESLKH DNIFGYEK(R)	3.1	1484.4	3	-1.038
T2HQ57	Amine oxidase	50.1	(K)RFDEIVGGMDQLPTcmcR(A)	5.1	551.0	4	-0.056

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
			(K)EGNLSPGAVDMIGDVLNEDSGYYVSFIESLKH DDIFAYEKR(F)	3.1	1149.0	4	-0.192
Q90W54	L-amino-acid oxidase	41.0	(K)SAGQLYEESLGK(V)	14.5	641.3	2	0.000
			(R)FDEIVGGmDKLPTSMYR(A)	7.3	659.0	3	-0.038
			(K)EGNLSPGAVDMIGDLMNEDSGYYVSFPESLRH DDIFAYEK(R)	7.1	1121.3	4	1.073
P0C2D7	L-amino-acid oxidase (Fragment)	31.4	(-)ADDKNPLEEcFREDDYEEFLEIAK(N)	20.2	744.6	4	-0.018
P81382	L-amino-acid oxidase	28.6	(R)FDEIVDGmDKLPTAMYR(D)	5.1	672.6	3	-1.015
			(R)SVHYRSGTKIFLTcTTK(F)	4.1	1001.0	2	1.921
			(K)EGDLSPGAVDMIGDLLNEDSGYYVSFIESLKH DDIFAYEK(R)	3.1	1113.5	4	-0.938
A0A0A1WCY6	Amine oxidase	26.7	(K)RFDEIVGGmDRLPTSmYR(A)	12.3	725.3	3	-1.020
			(K)EANLSPGAVDmIGDLLNEDSGYYVSFIESLK(H	9.1	1122.2	3	2.044
			(K)TLSYVTADYVIVcTTSR(A)	7.3	650.7	3	1.023
Q6WP39	L-amino-acid oxidase	18.1	(K)RFDEIVDGMDKLPTSmYR(A)	9.2	547.8	4	-1.023
			(K)EGNLSPGAVDMIGDLMNEDAGYYVSFIESMKH DDIFAYEK(R)	7.1	1118.8	4	1.031
Snake venom metalloprotease							
K9JAW0	Factor X activator heavy chain	181.1	(K)AFIELIIIVDHSmAK(K)	10.2	573.0	3	1.002
			(K)cILYPPLRK(D)	7.4	580.3	2	0.001
			(R)DQLQQNGQPcQNNR(G)	6.2	851.4	2	1.967
			(R)SVGIVQVQGNRNFK(T)	5.1	516.0	3	0.001

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
			(K)PKcILYPPLR(K)	4.1	628.4	2	-0.967
Q4VM08	Zinc metalloproteinase-disintegrin-like VLAIP-A	79.6	(R)KIPcAPQDVK(C)	10.4	577.3	2	-2.026
			(R)VLNIYIALLGLEIWNNGDK(I)	9.4	1079.6	2	0.010
			(R)LYcFDNLPEHK(N)	9.3	479.2	3	0.001
			(K)NPcQIYYTPSDENKGmVDPGTK(C)	9.1	844.1	3	0.032
			(K)VTLDLFGK(W)	8.6	446.8	2	0.000
			(K)YLINKmPQcILNKPLK(T)	5.1	664.4	3	1.968
			(R)TRIYEIVNILNVIYR(V)	4.4	627.0	3	0.007
			(K)ScImSGTLScEASIR(F)	4.1	844.8	2	0.947
			(R)KHDNAQLLTDINFNGPTAGLGYVGSMcDPQYS AGIVQDHNK(V)	4.0	890.4	5	1.924
			(K)ASQLNLTPEQR(R)	3.1	628.4	2	-0.907
Q7T046	Coagulation factor X-activating enzyme heavy chain	13.3	(K)QcISLFGSR(A)	13.3	533.3	2	-2.009
			(K)TAVImAHELGHNLGmYHDR(K)	5.2	550.0	4	-0.017
			(K)GmVEPGTK(C)	3.2	418.7	2	2.016
K9JCB2	Factor X activator light chain 2	10.1	(R)MWFNHKcEEPYPFVcK(V)	3.0	724.7	3	0.007
Glutaminyl cyclase							
M9NCG3	Glutaminyl-peptide cyclotransferases	45.8	(R)NTYQTQGIDLFVLLDLIGAR(N)	10.5	750.7	3	-0.032
			(R)VWHVmEDNEENLDKPTIDNLSK(I)	7.2	661.3	4	0.015
			(R)LEAIEQNLHDLGLLNNYSSER(Q)	7.2	810.1	3	-0.004
			(K)ILQIFVLEYLNLG(-)	3.2	768.0	2	0.022

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
			(K)QSSLPTK(A)	1.5	380.7	2	-0.004
Phosphodiesterase							
W8E7D1	Phosphodiesterase	183.5	(K)FGPVSGEIImALQmADR(T)	16.3	934.0	2	-0.004
			(K)GKNEVTSFENIEVYNLmcDLLK(L)	12.2	878.1	3	-0.017
			(R)IPAAQSQTcSNYQPDLTITPGFLYPPNFGSSNFEQYDALITSNLVPmFK(G)	11.3	1375.4	4	-0.131
			(K)VLSFILPHRPDNSEScADTSPDNLWVEER(I)	10.3	846.6	4	-0.056
			(K)NVPKDFYTFDSEGIVR(N)	9.3	629.6	3	-0.009
			(K)cSSITDLGK(V)	9.2	490.7	2	0.000
			(K)NPFYNPSPAK(E)	8.2	567.8	2	-0.004
			(K)IPIPTHFFVVLTScENQINTPLNcPGSLK(V)	8.2	1099.6	3	0.000
			(K)SmQAIFLAHGPGFK(G)	7.1	760.4	2	-0.002
			(R)LWNYFHGTLLPK(Y)	6.2	744.9	2	-0.004
			(K)SPPTSVPPSASDcLR(L)	4.3	785.9	2	0.001
			(R)LEYmTDYFDKVDFFmYEGPAPR(I)	4.1	922.7	3	-0.012
			(K)RLHYVNNIR(I)	3.2	395.6	3	-0.002
J3SEZ3	Venom phosphodiesterase 1	81.8	(R)VRDVELLTGLNFYSGLKQPLPETLQLK(T)	11.3	768.7	4	-0.009
			(K)VLSFILPHRPDNSEScADTSPENLWVEER(I)	11.2	850.4	4	0.999
			(K)TFLPIFVNPVN(-)	10.5	630.9	2	-0.004
			(K)AATYFWPGSEVK(I)	9.4	678.3	2	-0.012
			(K)AKRPDFLTLYIEEPDTTGHK(Y)	7.1	778.0	3	0.933
			(R)LNLNNQAK(T)	6.4	457.8	2	0.000
			(K)TESEAHNLPYGRPQVLQNHSK(Y)	6.2	602.1	4	-0.015

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
			(K)YcLLHQAK(Y)	6.1	517.8	2	1.994
			(R)IDKVNLmVDQQWmAVR(D)	5.1	660.0	3	-0.001
			(K)SIPFEAR(V)	3.9	410.2	2	0.000
			(K)ALQmADRTLGMLMEGLK(Q)	3.1	947.9	2	0.918
			(K)DKcASSGATQcPAGFEQSPLILFSmDGFR(A)	3.1	1065.1	3	-0.063
Phospholipase B							
F8S101	Phospholipase B	32.6	(K)HQGLPESYNFDFVTmKPVL(-)	13.1	746.7	3	0.001
			(K)QDEWTRQQIKNNK(D)	2.1	563.6	3	0.860
5'-Nucleotidase							
F8S0Z7	Snake venom 5'-nucleotidase	85.0	(R)YDAmALGNHEFDNGLAGLLDPLLK(H)	18.3	868.4	3	-0.005
			(K)LLLPSFLAAGGDGYHmLK(G)	14.2	641.0	3	1.973
			(K)YLGYLNVIFDDKGNVIK(S)	13.4	657.7	3	-0.003
			(R)TNNGTITLEELTAVLPFGGTFDLLQIK(G)	11.3	1452.8	2	-0.997
			(-)SFELTILHTNDVHAR(V)	11.2	585.3	3	1.009
			(K)HANFPILSANIRPK(G)	10.3	526.6	3	0.001
			(K)GDSSNHSSGNLDISIVGDYIK(R)	9.2	727.0	3	0.981
			(R)QVPVVQAYAFGK(Y)	8.4	653.9	2	-0.002
			(K)VFPAVEGR(M)	6.7	437.7	2	-0.001
			(R)HPDDNEWNHVSmcIVNGGGIR(S)	6.1	606.8	4	0.982
			(K)cTGQDcYGGVAR(R)	5.3	672.8	2	0.976
			(K)TIVYLNGTTQAcR(F)	5.1	749.4	2	0.990
			(K)ETPVLSNPGPYLEFRDEVEELQNHANK(L)	5.0	782.1	4	0.002
			(R)SPIDER(T)	4.3	358.7	2	0.002

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
W8EFS0	5'-nucleotidase (Fragment)	65.6	(R)FHEcNLGNLIcDAVIYNNLR(H)	16.2	812.4	3	-0.007
			(R)ANNGIITLEELTSVLPFGGTFDLLQIK(G)	13.3	1452.8	2	0.973
			(R)HGQGTGELLQVSGIK(V)	11.5	508.6	3	0.005
			(R)VVSLNVLcTK(C)	10.4	566.8	2	-0.001
			(-)AREKVGIIGYTTK(E)	9.4	479.2	3	-0.159
			(R)cRVPTYVPLEmEK(T)	7.4	546.6	3	-0.001
			(K)ASGNPILLNKDIPEDQVVK(A)	7.2	684.4	3	0.980
			(K)IQLQNYYSQEIGK(T)	7.2	528.6	3	0.041
			(K)VVYDLSQKPGSR(V)	6.6	450.2	3	0.002
Carboxypeptidase							
J3RYP4	Carboxypeptidase E-like	10.3	(R)VDFDLESLSER(K)	10.3	655.3	2	-0.007
			(K)VAVPFSPAIR(V)	7.1	529.8	2	1.873
			(R)ELLVIEVSDNPGEHEPGEPEFK(Y)	5.2	822.1	3	-0.021
			(R)LLVPGNYK(V)	4.4	452.3	2	-0.004
			(K)AASQPGELKDWFVGR(S)	3.3	554.3	3	-0.002
Snaclec							
Q4PRD0	Snaclec 3	94.9	(K)VFTEEMNWADAEK(F)	20.5	785.3	2	-0.010
			(K)AWNEGTNcFVFK(I)	14.5	736.8	2	-0.006
			(K)GSHLLSLHNIAEADFVLKK(T)	12.2	523.8	4	-0.020
			(K)NHWSHmDcSSTHNFVcK(F)	10.1	541.0	4	-1.991
			(K)KTLAmLK(D)	3.4	410.8	2	0.007
			(K)TLAmLKDGVIWmGLNDVWNEcNWGWTDGAK(L)	2.1	1171.5	3	-0.032
Q4PRC7	Snaclec 6	39.7	(K)SmTcNFIAPVVcKF(-)	14.3	845.4	2	-0.006

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
			(R)EEEKFVVNLISENLEYPATWIGLGNMWK(D)	13.1	1103.9	3	-0.064
			(K)GSHLVSLHSR(E)	8.3	546.8	2	-0.002
			(R)MEWSDRGNVK(Y)	3.1	611.3	2	0.003
K9JBV0	P68 alpha subunit	35.7	(K)TPADYVWIGLR(N)	14.3	645.8	2	0.000
			(R)KAQYcISK(W)	8.2	499.3	2	-0.004
Q4PRC6	Snaclec 7	33.2	(R)SSEEmDFVIR(M)	13.4	614.8	2	-0.004
			(R)FDFFWIGLR(D)	10.5	600.8	2	-0.002
			(R)WSDGVNLDYK(A)	9.3	598.8	2	-0.006
			(K)FcNEQVNGGYLVSFR(S)	7.1	598.0	3	2.018
			(R)MTFPIFR(F)	5.3	456.2	2	-0.005
K9JDF6	P31 beta subunit	28.4	(K)FGSVWIGLNDPWHNcNWEWSDNAR(F)	17.3	987.4	3	-0.008
			(K)FVSFVcK(F)	9.4	442.7	2	-2.012
			(K)RPYcTVmVLKPDR(I)	6.2	550.3	3	-1.989
			(R)EQHKGSHLASIHSSEEEAFVSK(V)	3.2	488.2	5	-0.003
A0A140DC06	C-type lectin 2	22.3	(R)TWLNLccGDDYPFVcK(F)	10.1	1023.9	2	-1.038
Q38L02	Snaclec dabocetin subunit alpha	20.3	(K)TWEDAEKFcTQQANGWHLASIESVEEANFVAQ LASETLTK(S)	13.2	1135.8	4	0.958
			(K)YHEWITLPcGDKNPFIcK(S)	12.3	570.3	4	-0.008
			(K)SKYHAWIGLR(D)	8.0	410.9	3	-0.001
			(K)SWVLH(-)	4.5	321.2	2	0.000
			(K)cFGLNK(E)	3.2	369.7	2	0.003

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
Q5FZI6	Snaclec trimecetin subunit alpha	12.3	(R)FcWEQVKGAHLVSIESSGEGDFVAQLLSENIK(T)	12.3	1193.9	3	1.972
K9JBU9	P31 alpha subunit	11.5	(K)DGIYVWIGLR(D)	11.5	596.3	2	-0.010
			(K)WDYVNcAEHYR(F)	6.1	504.9	3	-0.007
			(K)FcTEQANSGHLVSIK(S)	5.2	564.6	3	0.997
			(K)WTYFHK(W)	3.1	441.2	2	-0.002
E2DQZ6	Snaclec jerdonuxin subunit alpha	11.2	(R)TWFNVYcGTENPFVcK(Y)	11.2	1011.9	2	0.970
A0A0C5DQX8	C-type lectin-like protein 2B	9.7	(K)FDFIWIGLR(D)	9.7	583.8	2	-0.004
Vascular endothelial growth factor							
P82475	VEGF toxin ICPP	16.1	(R)ETLVSILQEYPDEISDIFRPScVAVLR(C	16.1	1051.2	3	2.012
			(R)PFPDVYQR(S)	5.3	511.3	2	-0.001
P67861	VEGF toxin	8.2	(R)ETLVSILQEHPDEISDIFRPScVAVLR(C)	8.2	781.7	4	-0.015
			(R)PFLDVYERSAcQTR(E)	2.1	872.4	2	2.024
			(K)cTPVGKHTADIQImR(M)	2.0	872.4	2	0.991
			(K)QGEPEGPKEPRR(G)	2.0	689.4	2	-1.998
			(R)MNPRTHSSKmEVmK(F)	1.0	853.4	2	-1.929
Nerve growth factor							
P30894	Venom nerve growth factor	40.9	(R)INTAcVcVISR(K)	14.4	646.8	2	-0.002
			(K)HWNSYcTTTDTFVR(A)	10.2	596.6	3	-0.002
			(R)ALTMER(N)	4.5	360.7	2	-0.004

Accession No.	Protein Description	Protein Morpheus Score	Peptide Sequence(s)	Peptide Morpheus Score	m/z	z	ΔM (Da)
Cysteine-rich secretory protein							
F2Q6F2	CRISP Dr-CRPK	155.0	(R)SGcAAAYcPSSEYNYFYVcQYcPAGNIIGK(I)	19.4	1157.5	3	-0.017
			(R)RPEIQNEIVDLHNSLRR(S)	13.5	523.0	4	-0.007
			(R)SVTPTASNmLKmEWYPEAAANAER(W)	12.3	900.4	3	-0.008
			(K)WTAIIHEWHK(E)	8.1	660.8	2	-0.006
			(K)TKcPAScFcHNEII(-)	7.1	868.9	2	-0.010
			(K)DFVYGQGASPANAVVGHYTQIVWYKSYR(S)	3.1	794.9	4	-0.050
			(R)cILNHSPYNSRVIGGIKcGENIYMSPYPMK(W)	3.0	1166.8	3	-0.213
			(K)QGcHSNYLK(T)	2.1	554.3	2	1.011
			(K)EKKDFVYGQGASPANAVVGHYTQIVWYK(S)	1.0	1051.9	3	-1.954
F2Q6F3	CRISP Dr-CRPB (Fragment)	30.3	(R)KPEIQNEIVEFHNSLR(R)	6.1	651.0	3	-2.048
			(R)cILDHSPYNSR(V)	3.1	454.5	3	0.006
			(K)KNFIYGK(G)	2.1	434.8	2	-0.994
			(K)WIEIIRKWHDEK(K)	2.0	552.2	3	1.844
			(R)REDVFTNcIDMAKGR(S)	1.0	906.5	2	0.053
			(K)GANPSNAVVGHYTQVVWYK(S)	1.0	697.4	3	0.060
			(K)PEIQNEIVEFHNSLRRSVNPTASNMLK(M)	1.0	1041.9	3	0.008
Kunitz-type serine protease inhibitor							
Q2ES48	KSPI 3	18.9	(K)FcYLPADPGEcmAYIR(S)	9.5	989.9	2	-0.005
			(K)EFIYGGcHGNANNFPTR(D)	9.3	652.0	3	-0.008
A8Y7P5	KSPI B5	8.2	(K)EFIYGGcHGNANK(F)	5.5	489.6	3	-0.004

4.1.3.4 A comparative analysis of the RVV proteomes from EI, WI, and SI

A comparative analysis of the RVV proteomes from EI, WI, and SI suggested that only 11 proteins (2 SVMPs, 3 SVSPs, and single isoforms each of NT, LAAO, NGF, VEGF, snaclec, and CRISP) were shared (based on presence of homologous distinct peptides) by all the RVV samples, whereas 25, 15, 21, and 39 proteins were uniquely represented in EI RVV (B), EI RVV (N), WI RVV, and SI RVV, proteomes, respectively (Fig. 4.12a). Further, there was significant variation in number of identified toxin isoforms and relative abundances of enzymatic as well as non-enzymatic classes of proteins in RVV samples from EI, WI, and SI and these differences are shown in Table 4.6 and Figs. 4.12b,c.

Table 4.6. Distribution of toxin isoforms identified in RVV samples from different geographical locations of India by proteomic analysis.

Protein family	WI RVV	EI RVV (B)	EI RVV (N)	SI RVV
PLA_2	17	21	12	10
SVMP	5	10	13	4
SVSP	6	9	15	18
LAAO	2	1	2	9
PDE	1	1	1	2
NT	2	1	1	2
Hya	ND	1	1	1
PLB	1	ND	1	1
GC	ND	1	1	1
AMT	ND	ND	ND	ND
APase	ND	1	ND	ND
KSPI	8	6	5	2
Snaclec	7	13	12	11
CRISP	2	3	2	2
VEGF	2	2	1	2
NGF	1	2	1	1
Dis	1	1	1	ND
Total	**55**	**73**	**69**	**66**

ND: not detected by LC-MS/MS analysis

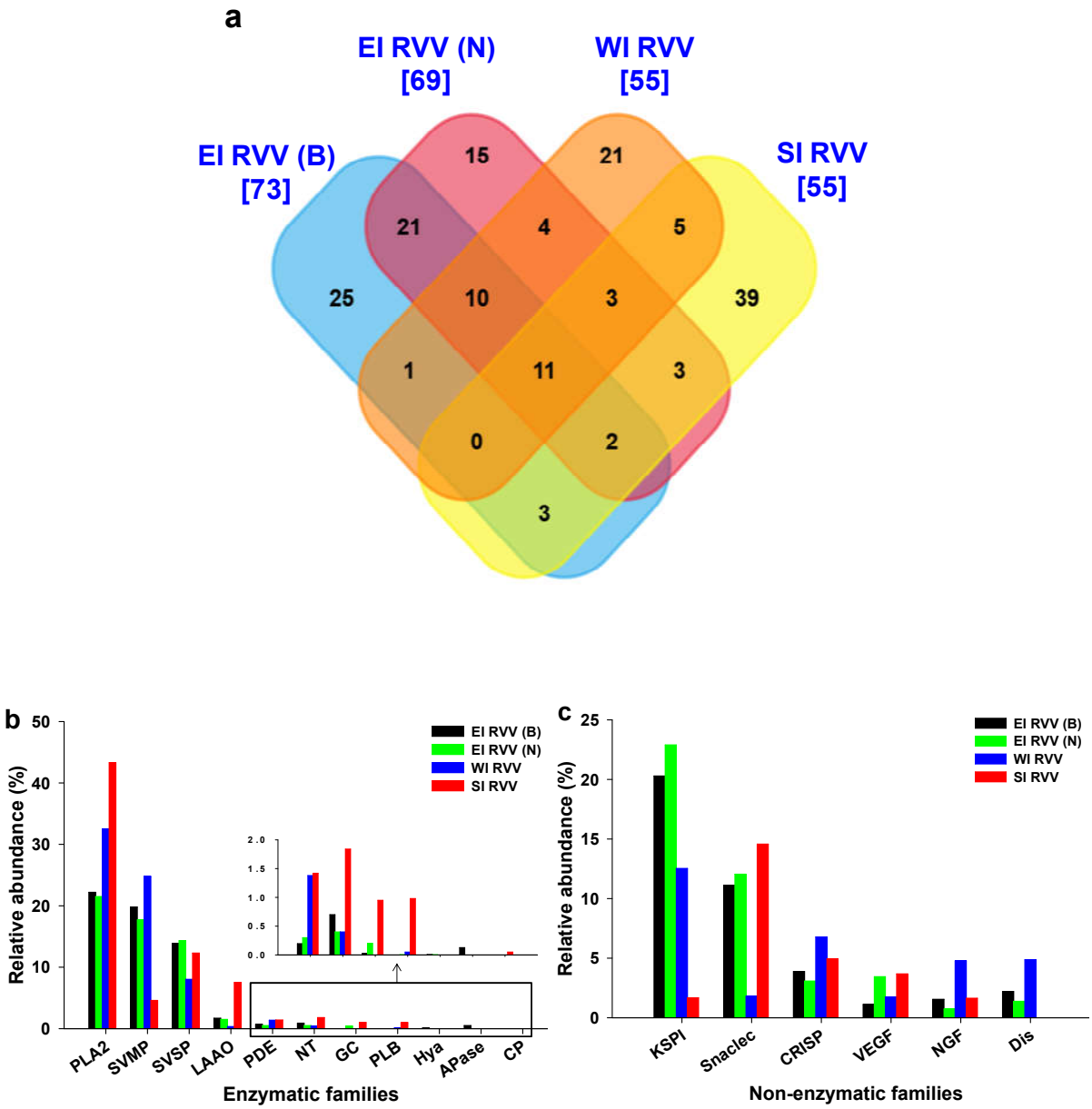


Fig. 4.12a. A Venn diagram representing the distribution of shared and unique proteins/toxins among RVV samples from different regions of India. The Venn diagram was generated using FunRich_V3 Tool. The numbers in parentheses indicate the total number of proteins identified in the respective RVV proteomes. Variation in relative abundance of **b.** enzymatic proteins and **c.** non-enzymatic proteins in RVV samples from WI, SI, and Burdwan and Nadia districts representing EI RVV samples.

4.1.4 Enzymatic activities of crude and/or GF fractions of WI, EI, and SI RVV samples

A comparative analysis of the enzymatic activities (specific activity) displayed by RVV samples from WI, EI, and SI is summarized in Table 4.7. While SI RVV exhibited significantly higher ($p<0.05$) PLA_2, LAAO, ATPase, ADPase and AMPase activities compared to the same activities of RVV samples from two other regions of India, it exhibited poor SVMP, fibrinogenolytic, and TAME and BAEE esterase activities. On the contrary, WI RVV was characterized with significantly higher ($p<0.05$) SVMP, fibrinogenolytic, PDE, TAME and BAEE-esterase activities, albeit it exhibited relatively poor hyaluronidase, LAAO, and PLA_2 activities compared to other RVV samples (Table 4.7). Further, SVMP, fibrinogenolytic, TAME and BAEE-esterase activities of EI RVV were superior to SI RVV; however, was significantly lower compared to WI RVV. In addition, EI RVV was characterized with highest hyaluronidase activity and relatively poor ATPase, ADPase and AMPase activities compared to RVV samples from other parts of India (Table 4.7).

Table 4.7. A comparison of enzymatic and esterolytic activities exhibited by RVV from different regions of India. Values are mean ± SD of triplicate determinations. Significance of difference compared to other RVV samples, *$p<0.05$ (ANOVA).

Enzymatic activity (U/mg)	Origin of RVV sample			
	WI	EI (Burdwan)	EI (Nadia)	SI
PLA_2 [a] ($\times 10^3$)	0.6 ± 0.03	0.8 ± 0.02	0.9 ± 0.02	1.1 ± 0.03*
SVMP [b]	0.15 ± 0.03*	0.10 ± 0.021	0.07 ± 0.011	0.012 ± 0.01
LAAO [c]	19.8 ± 0.92	26.7 ± 0.71	24.7 ± 0.6	105.9 ± 2.2*
Fibrinogenolytic [d]	9.8 ± 0.21*	7.6 ± 0.13	5.4 ± 0.11	0.8 ± 0.02
Fibrinolytic [d]	0.7 ± 0.04	0.5 ± 0.01	0.3 ± 0.01	0.9 ± 0.01*
ATPase [e] ($\times 10^3$)	4.5 ± 0.15	1.5 ± 0.05	1.9 ± 0.06	90.0 ± 20.0*
ADPase [e] ($\times 10^3$)	6.4 ± 0.25	2.4 ± 0.09	2.4 ± 0.05	180.0 ± 41.2*
AMPase [e] ($\times 10^4$)	1.7 ± 0.05	0.5 ± 0.02	0.4 ± 0.02	31.2 ± 8.80*

Enzymatic activity (U/mg)	**Origin of RVV sample**			
	WI	**EI (Burdwan)**	**EI (Nadia)**	**SI**
Hyaluronidase [f]	63.4 ± 2.11	1918.2 ± 64.1*	1946.4 ± 56.3*	126.0 ± 2.3
PDE [g]	11.8 ± 0.08*	4.5 ± 0.10	4.3 ± 0.12	4.7 ± 0.11
TAME [h] ($\times 10^2$)	19.1 ± 0.8*	3.4 ± 0.11	3.2 ± 0.09	1.6 ± 0.05
BAEE [i] ($\times 10^2$)	2.8 ± 0.08	2.0 ± 0.07	2.0 ± 0.06	0.007 ± 0.04

[a] One unit is defined as a decrease by 0.01 in absorbance at 740 nm after 10 min of incubation. [b] One unit is defined as change in absorbance at 450 nm per min at 37 °C. [c] One unit is defined as 1 nmol of kynurenic acid produced per min. [d] One unit is defined as 1.0 µg of tyrosine equivalent liberated per min per ml of enzyme. [e] One unit is defined as micromoles of Pi released per min. [f] One unit is defined as a 1% decrease in turbidity at 405 nm in comparison to control (100% turbidity). [g] One unit is defined as micromoles of *p*-nitrophenol released per min. [h] One unit is defined as an increase by 0.01 in absorbance at 254 nm during the first 5 min of the reaction at 37 °C. [i] One unit is defined as an increase by 0.01 in absorbance at 244 nm during the first 10 min of the reaction at 37 °C.

Further, the peak GF1 of WI and EI RVV samples were characterized with highest ATPase, ADPase, AMPase, LAAO, PDE, hyaluronidase, SVMP, and fibrinogenolytic activities, while esterolytic activities were prominent through fractions GF3 and GF4 of WI RVV, and fractions GF2 and GF3 of EI RVV (Tables 4.8a-c). PLA_2 activity was predominant in fractions GF5 and/or GF6, while fibrinolytic enzymes eluted through fractions GF2 to GF4 of WI and EI RVV (Tables 4.8a-c). However, due to very low amount of SI RVV sample available to us, the gel-filtration chromatography of this RVV sample could not be done.

Table 4.8a. Assay of enzymatic and esterolytic activities of WI RVV and its GF fractions. Values are mean ± SD of triplicate determinations.

Properties	WI RVV GF fractions									
	GF1	**GF2**	**GF3**	**GF4**	**GF5**	**GF6**	**GF7**	**GF8**	**GF9**	**GF10**
Protein content (% yield)	6.6 ± 0.8	4.3 ± 0.2	8.4 ± 0.9	16.0 ± 0.10	9.6 ± 0.9	14.5 ± 0.11	11.1 ± 0.9	1.8 ± 0.3	4.4 ± 0.3	4.0 ± 0.2
Enzymatic activity (Unit/mg)										
PLA_2 [a] ($\times 10^3$)	0.2 ± 0.01	0.1 ± 0.01	1.9 ± 0.06	2.7 ± 0.11	4.7 ± 0.20	1.7 ± 0.05	1.2 ± 0.04	0.7 ± 0.02	0.6 ± 0.01	1.2 ± 0.08
SVMP [b]	2.33 ± 0.05	0.70 ± 0.01	-	-	-	-	-	-	-	-
LAAO [c]	23.7 ± 0.96	19.7 ± 0.86	-	-	-	-	-	-	-	-
Fibrinogenolytic [d]	10.7 ± 0.30	7.8 ± 0.25	2.6 ± 0.10	4.5 ± 0.17	5.7 ± 0.25	-	1.4± 0.12	-	1.2 ± 0.24	-
Fibrinolytic [d]	-	-	2.4 ± 0.12	6.0 ± 0.25	0.5 ± 0.02	2.5 ± 0.11	-	-	0.7 ± 0.14	-
ATPase [e] ($\times 10^3$)	9.5 ± 0.26	0.3 ± 0.13	-	-	-	-	-	-	-	-
ADPase [e] ($\times 10^3$)	8.5 ± 0.28	0.2 ± 0.19	-	-	-	-	-	-	-	-
AMPase [e] ($\times 10^4$)	4.1 ± 0.11	-	-	-	-	-	-	-	-	-
Hyaluronidase [f]	71.4 ± 2.54	-	-	-	-	-	-	-	-	-
PDE [g]	22.6 ± 0.11	1.0 ± 0.02	-	-	-	-	-	-	-	-
TAME [h] ($\times 10^2$)	1.9 ± 0.08	0.9 ± 0.04	-	5.7 ± 0.12	0.8 ± 0.04	2.4 ± 0.10	-	-	-	-
BAEE [i] ($\times 10^2$)	-	3.3 ± 0.09	2.8 ± 0.05	4.0 ± 0.10	0.5 ± 0.04	0.2 ± 0.01	-	-	-	-

[a] One unit is defined as a decrease by 0.01 in absorbance at 740 nm after 10 min of incubation. [b] One unit is defined as change in absorbance at 450 nm per min at 37 °C. [c] One unit is defined as 1 nmol of kynurenic acid produced per min. [d] One unit is defined as 1.0 µg of tyrosine equivalent liberated per min per ml of enzyme. [e] One unit is defined as micromoles of Pi released per min. [f] One unit is defined as a 1% decrease in turbidity at 405 nm in comparison to control (100% turbidity). [g] One unit is defined as micromoles of *p*-nitrophenol released per min. [h] One unit is defined as an increase by 0.01 in absorbance at 254 nm during the first 5 min of the reaction at 37 °C. [i] One unit is defined as an increase by 0.01 in absorbance at 244 nm during the first 10 min of the reaction at 37 °C.

Table 4.8b. Assay of enzymatic and esterolytic activities of EI RVV (B) and its GF fractions. Values are mean ± SD of triplicate determinations.

Properties	EI RVV (B) GF fractions									
	GF1	**GF2**	**GF3**	**GF4**	**GF5**	**GF6**	**GF7**	**GF8**	**GF9**	**GF10**
Protein content (% yield)	17.2 ± 0.5	3.9 ± 0.1	10.4 ± 0.1	17.3 ± 0.5	4.7 ± 0.2	12.5 ± 0.4	5.4 ± 0.1	3.9 ± 0.1	4.3 ± 0.1	1.2 ± 0.02
Enzymatic activity (Unit/mg)										
PLA_2 [a] (x 10^3)	0.8 ± 0.02	1.0 ± 0.03	1.8 ± 0.06	3.2 ± 0.09	8.5 ± 0.21	8.4 ± 0.26	3.3 ± 0.10	1.8 ± 0.05	2.3 ± 0.1	0.4 ± 0.01
SVMP [b]	0.19 ± 0.02	0.03 ± 0.003	-	-	-	-	-	0.01 ± 0.001	-	-
LAAO [c]	38.0 ± 1.10	15.0 ± 0.50	-	-	-	-	-	-	-	-
Fibrinogenolytic [d]	10.1 ± 0.21	7.0 ± 0.18	1.4 ± 0.08	1.6 ± 0.09	1.7 ± 0.11	-	-	2.1 ± 0.13	-	-
Fibrinolytic [d]	-	4.0 ± 0.13	2.6 ± 0.10	1.7 ± 0.09	2.4 ± 0.07	0.7 ± 0.02	-	-	-	-
ATPase [e] (x 10^3)	3.3 ± 0.11	0.1 ± 0.01	-	-	-	-	-	-	-	-
ADPase [e] (x 10^3)	3.3 ± 0.07	2.9 ± 0.04	0.5 ± 0.01	-	-	-	-	-	-	-
AMPase [e] (x 10^4)	2.8 ± 0.08	-	-	-	-	-	-	-	-	-
Hya [f] (x 10^3)	3.0 ± 0.15	-	-	-	-	-	-	-	-	-
PDE [g]	41.7 ± 1.4	9.1 ± 0.3	-	-	-	-	-	-	-	-
TAME [h] (x 10^2)	0.8 ± 0.01	6.2 ± 0.18	-	-	-	0.8 ± 0.02	-	-	-	-
BAEE [i] (x 10^2)	0.8 ± 0.02	2.2 ± 0.08	4.2 ± 0.11	0.4 ± 0.01	0.2 ± 0.01	0.5 ± 0.01	-	-	-	-

[a] One unit is defined as a decrease by 0.01 in absorbance at 740 nm after 10 min of incubation. [b] One unit is defined as change in absorbance at 450 nm per min at 37 °C. [c] One unit is defined as 1 nmol of kynurenic acid produced per min. [d] One unit is defined as 1.0 µg of tyrosine equivalent liberated per min per ml of enzyme. [e] One unit is defined as micromoles of Pi released per min. [f] One unit is defined as a 1% decrease in turbidity at 405 nm in comparison to control (100% turbidity). [g] One unit is defined as micromoles of *p*-nitrophenol released per min. [h] One unit is defined as an increase by 0.01 in absorbance at 254 nm during the first 5 min of the reaction at 37 °C. [i] One unit is defined as an increase by 0.01 in absorbance at 244 nm during the first 10 min of the reaction at 37 °C.

Table 4.8c. Assay of enzymatic and esterolytic activities of EI RVV (N) and its GF fractions. Values are mean ± SD of triplicate determinations.

Properties	EI RVV (N) GF fractions									
	GF1	**GF2**	**GF3**	**GF4**	**GF5**	**GF6**	**GF7**	**GF8**	**GF9**	**GF10**
Protein content (% yield)	18.3 ± 0.4	5.3 ± 0.2	10.1 ± 0.1	15.6 ± 0.5	4.9 ± 0.1	13.1 ± 0.4	11.5 ± 0.2	2.4 ± 0.1	3.9 ± 0.1	1.1 ± 0.1
Enzymatic activity (Unit/mg)										
PLA_2 [a] (x 10^3)	1.2 ± 0.03	1.9 ± 0.07	2.2 ± 0.08	3.2 ± 0.09	9.4 ± 0.26	8.8 ± 0.29	4.1 ± 0.1	3.1 ± 0.1	2.5 ± 0.08	2.7 ± 0.09
SVMP [b]	0.16 ± 0.02	0.01 ± 0.001	-	-	-	-	-	-	-	-
LAAO [c]	43.8 ± 1.1	14.2 ± 0.5	-	-	-	-	-	-	-	-
Fibrinogenolytic [d]	9.2 ± 0.17	6.2 ± 0.19	1.2 ± 0.09	1.3 ± 0.10	0.7 ± 0.05	-	-	-	1.4 ± 0.09	-
Fibrinolytic [d]	-	4.9 ± 0.15	2.5 ± 0.11	2.7 ± 0.07	1.4 ± 0.12	0.5 ± 0.02	-	-	-	-
ATPase [e] (x 10^3)	4.0 ± 0.12	0.4 ± 0.02	-	-	-	-	-	-	-	-
ADPase [e] (x 10^3)	9.7 ± 0.07	2.6 ± 0.03	0.3 ± 0.01	-	-	-	-	-	-	-
AMPase [e] (x 10^4)	2.0 ± 0.06	-	-	-	-	-	-	-	-	-
Hya [f] (x 10^3)	2.8 ± 0.11	-	-	-	-	-	-	-	-	-
PDE [g]	40.9 ± 1.2	4.0 ± 0.2	-	-	-	-	-	-	-	-
TAME [h] (x 10^2)	3.9 ± 0.10	7.1 ± 0.15	1.3 ± 0.05	-	-	0.3 ± 0.02	-	-	-	-
BAEE [i] (x 10^2)	0.1 ± 0.01	3.5 ± 0.12	1.7 ± 0.09	0.2 ± 0.01	-	0.2 ± 0.09	-	-	-	

[a] One unit is defined as a decrease by 0.01 in absorbance at 740 nm after 10 min of incubation. [b] One unit is defined as change in absorbance at 450 nm per min at 37 °C. [c] One unit is defined as 1 nmol of kynurenic acid produced per min. [d] One unit is defined as 1.0 µg of tyrosine equivalent liberated per min per ml of enzyme. [e] One unit is defined as micromoles of Pi released per min. [f] One unit is defined as a 1% decrease in turbidity at 405 nm in comparison to control (100% turbidity). [g] One unit is defined as micromoles of *p*-nitrophenol released per min. [h] One unit is defined as an increase by 0.01 in absorbance at 254 nm during the first 5 min of the reaction at 37 °C. [i] One unit is defined as an increase by 0.01 in absorbance at 244 nm during the first 10 min of the reaction at 37 °C.

4.1.5 Some pharmacological properties of WI, EI, and SI RVV samples and their GF fractions

All the RVV samples demonstrated pro-coagulant activity under *in vitro* conditions and could reduce both prothrombin time and activated partial thromboplastin time; however, to a different extent (Table 4.9). In addition, prothrombin activation property of WI RVV was comparable to EI RVV (B) and superior to EI RVV (N) and SI RVV (Figs. 4.13a,b). The RVV samples were devoid of direct haemolytic activity; however, they exhibited profound haemolysis of goat erythrocytes in presence of egg-yolk phospholipids (Table 4.9). Further, the SI RVV sample demonstrated superior platelet aggregation property against goat PRP compared to WI and EI RVV samples, while EI RVV samples reduced the platelet count (thrombocytopenia) to a significantly higher extent ($p<0.05$) than WI and SI RVV (Table 4.9).

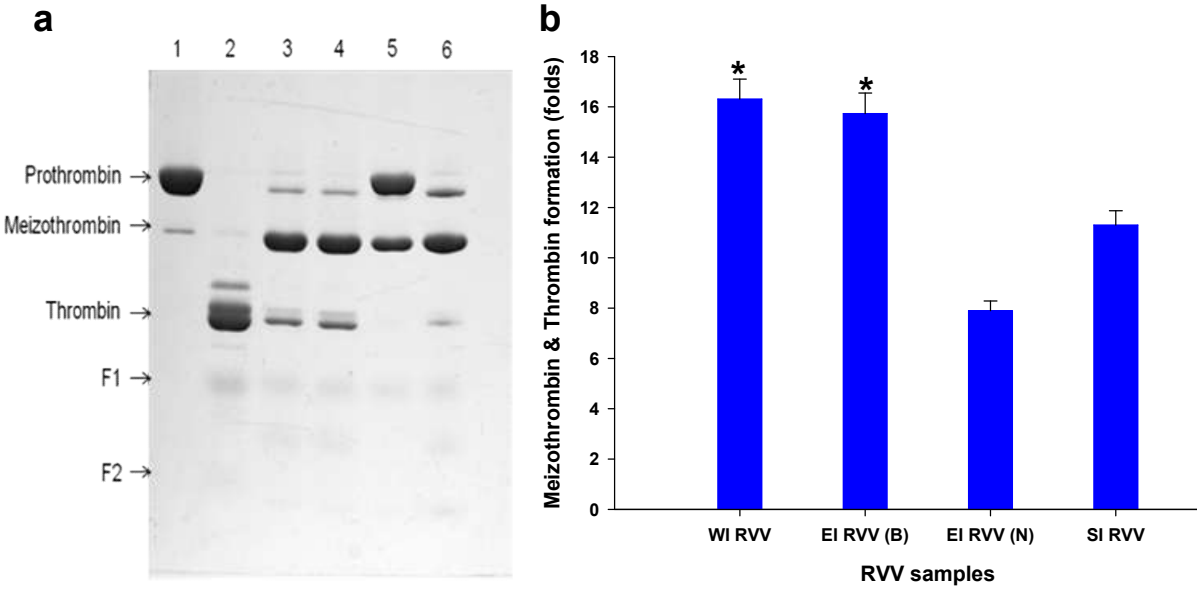


Fig. 4.13a. Prothrombin (PTH) activation by crude RVVs (40 µg/ml) from different regions of India. Lanes 1 and 2 contain control PTH and PTH treated with FXa, respectively. Lanes 3 to 6 contain PTH treated with WI RVV, EI RVV (B), EI RVV (N), and SI RVV, respectively. **b.** The cumulative band intensity (calculated from densitometry of the gel) of meizothrombin and thrombin formed in the negative control (lane 1) was considered as 1 and fold increase in band intensity of the same in the samples was calculated. Significance of difference with respect to EI RVV (N) and SI RVV, *$p<0.05$.

Notably, high molecular weight pro-coagulant enzymes (>30 kDa) were separated in fractions GF1 to GF4 of WI and EI RVV samples. Nevertheless, WI and EI RVV proteins eluted through fractions GF5 to GF8 exhibited anticoagulant activity; however, GF8 of EI RVV (B) was found to be pro-coagulant in nature (Tables 4.10a-c). Further, indirect haemolytic activity was significantly higher in fractions GF5 and GF6 of WI and EI RVV samples, while fractions GF1 to GF4 of WI and EI RVV demonstrated a significant reduction in platelet counts (Tables 4.10a-c). In addition, platelet aggregation property was more pronounced in fractions GF1 to GF4 of EI RVV, while the latter fractions, GF5 to GF7, caused deaggregation of platelets (Tables 4.10a-c).

Table 4.9. A comparison of pharmacological properties exhibited by RVV from different regions of India. Values are mean ± SD of triplicate determinations. Significance of difference compared to other RVV samples, *p<0.05 (ANOVA).

Pharmacological property (40 µg/ml)	**Origin of RVV sample**			
	WI	**EI (Burdwan)**	**EI (Nadia)**	**SI**
Pro-coagulant activity (U/mg) [a]	1700.0 ± 71.0*	956.2 ± 31.4	832.1 ± 32.4	685.3 ± 25.1
PT (U/mg) [a] ($\times 10^3$)	5.2 ± 0.1*	2.7 ± 0.06	2.6 ± 0.06	1.1 ± 0.05
APTT (U/mg) [a] ($\times 10^3$)	18.2 ± 0.7*	10.1 ± 0.1	9.3 ± 0.1	3.8 ± 0.11
Direct haemolysis (%) [b]	0.2 ± 0.01	0.4 ± 0.01	0.3 ± 0.01	0.7 ± 0.1*
Indirect haemolysis (%) [b]	18.0 ± 0.5	31.0 ± 1.10	34.8 ± 1.21	41.0 ± 1.60*
Reduction in platelet count (%) [c]	36.5 ± 1.1	53.0 ± 1.2*	52.6 ± 1.4*	22.7 ± 0.8
Platelet aggregation (%) [d]	13.8 ± 0.31	27.6 ± 1.0	25.7 ± 1.1	35.3 ± 0.9*

[a] One unit of pro-coagulant activity was defined as a decrease in 1 s of clotting time of PPP incubated with RVV samples, compared to control PPP (1X PBS, pH 7.4). [b] Haemolytic activity was assayed against 5% (v/v) mammalian (goat) erythrocytes. [c] Platelet count of control was $5.2 \pm 0.21 \times 10^6$ cells/ml. [d] Platelet modulation was assessed using goat PRP.

Table 4.10a. Some pharmacological properties of WI RVV (40 µg/ml) and its GF fractions (10 µg). Values are mean ± SD of triplicate determinations. Significance of difference with respect to negative control (1X PBS, pH 7.4), *p<0.05.

Pharmacological property	**GF-1**	**GF-2**	**GF-3**	**GF-4**	**GF-5**	**GF-6**	**GF-7**	**GF-8**	**GF-9**	**GF-10**
Plasma clotting activity (U/mg) ($\times 10^4$) [a]	7.4 ± 0.10	11.5 ± 0.21	10.0 ± 0.15	8.7 ± 0.11	1.5 ± 0.04	11.9 ± 0.14	1.0 ± 0.03	2.6 ± 0.09	ND	ND
Coagulant / Anticoagulant	C	C	C	C	AC	AC	AC	AC	-	-
PT (U/mg) ($\times 10^2$) [a]	7.2 ± 0.21*	4.9 ± 0.32*	3.6 ± 0.11*	2.3 ± 0.10*	1.5 ± 0.07*	3.0 ± 0.12*	0.7 ± 0.02	1.2 ± 0.01*	0.5 ± 0.02	0.3 ± 0.01
APTT (U/mg) ($\times 10^3$) [a]	1.6 ± 0.06*	1.9 ± 0.04*	1.3 ± 0.03*	1.1 ± 0.01*	1.1 ± 0.04*	1.4 ± 0.06*	0.3 ± 0.01*	0.1 ± 0.02	0.2 ± 0.01	0.2 ± 0.01
Direct haemolysis (%) [b]	1.0 ± 0.03	-	-	1.3 ± 0.04	0.9 ± 0.02	-	-	-	0.8 ± 0.02	-
Indirect haemolysis (%) [b]	26.1 ± 1.1*	6.7 ± 0.4*	2.5 ± 0.1	4.8 ± 0.3*	16.4 ± 0.5*	27.3 ± 1.1*	0.3 ± 0.1	1.1 ± 0.1	8.1 ± 0.2*	5.6 ± 0.1
Reduction in platelet count (%) [c]	53.8 ± 0.9*	46.2 ± 1.1*	50.0 ± 1.4*	46.2 ± 1.3*	13.5 ± 0.4*	3.8 ± 0.1	3.5 ± 0.1	1.7 ± 0.1	1.5 ± 0.1	0.2 ± 0.1

[a] One unit of pro-coagulant activity was defined as a decrease in 1 s of clotting time of PPP incubated with RVV samples, compared to control PPP (1X PBS, pH 7.4). [b] Haemolytic activity was assayed against 5% (v/v) mammalian (goat) erythrocytes. [c] Platelet count of control was $5.2 \pm 0.21 \times 10^6$ cells/ml.

Table 4.10b. Some pharmacological properties of EI RVV (B) (40 µg/ml) and its GF fractions (10 µg). Values are mean ± SD of triplicate determinations. Significance of difference with respect to negative control (1X PBS, pH 7.4), *p<0.05.

Pharmacological property	**GF1**	**GF2**	**GF3**	**GF4**	**GF5**	**GF6**	**GF7**	**GF8**	**GF9**	**GF10**
Plasma clotting activity (U/mg) ($\times 10^4$) [a]	12.3 ± 0.21	11.8 ± 0.14	8.4 ± 0.12	3.4 ± 0.09	18.8 ± 0.57	13.1 ± 0.38	0.7 ± 0.01	5.8 ± 0.11	ND	ND
Coagulant / Anticoagulant	C	C	C	C	AC	AC	AC	C	-	-
PT (U/mg) ($\times 10^2$) [a]	7.2 ± 0.19*	6.2 ± 0.20*	4.8 ± 0.23*	2.5 ± 0.14*	2.2 ± 0.10*	1.4 ± 0.05*	0.1 ± 0.01	1.5 ± 0.02*	0.1 ± 0.01	0.3 ± 0.01
APTT (U/mg) ($\times 10^3$) [a]	2.1 ± 0.07*	2.1 ± 0.05*	1.6 ± 0.04*	1.5 ± 0.04*	0.9 ± 0.04*	0.7 ± 0.03*	0.2 ± 0.01*	0.1 ± 0.01	-	0.1 ± 0.01
Direct haemolysis (%) [b]	1.3 ± 0.04	-	1.8 ± 0.05	2.0 ± 0.07	0.7 ± 0.02	-	-	-	-	-
Indirect haemolysis (%) [b]	26.1 ± 0.9*	1.2 ± 0.05	3.2 ± 0.09	8.8 ± 0.07*	41.3 ± 1.2*	38.8 ± 1.1*	6.1 ± 0.12*	3.0 ± 0.05	4.1 ± 0.08	1.0 ± 0.01
Reduction in platelet count (%) [c]	52.6 ± 1.5*	51.3 ± 1.1*	49.1 ± 1.8*	47.8 ± 1.2*	1.7 ± 0.1	-	-	-	-	-
Platelet modulation (%) [d]	(+) 36.8 ± 1.2*	(+) 31.7 ± 0.9*	(+) 29.4 ± 1.0*	(+) 23.3 ± 1.1*	(-) 28.9 ± 1.2*	(-) 19.2 ± 1.0*	(-) 10.5 ± 0.3*	ND	ND	ND

[a] One unit of pro-coagulant activity was defined as a decrease in 1 s of clotting time of PPP incubated with RVV samples, compared to control PPP (1X PBS, pH 7.4). [b]Haemolytic activity was assayed against 5% (v/v) mammalian (goat) erythrocytes. [c] Platelet count of control was $5.2 \pm 0.21 \times 10^6$ cells/ml. [d] Platelet modulation was assessed using goat PRP. The (+) and (-) sign represent platelet aggregation and deaggregation activities, respectively. ND: not detected

Table 4.10c. Some pharmacological properties of EI RVV (N) (40 µg/ml) and its GF fractions (10 µg). Values are mean ± SD of triplicate determinations. Significance of difference with respect to negative control (1X PBS, pH 7.4), *p<0.05.

Pharmacological property	**GF1**	**GF2**	**GF3**	**GF4**	**GF5**	**GF6**	**GF7**	**GF8**	**GF9**	**GF10**
Plasma clotting activity (U/mg) ($\times 10^4$) [a]	12.1 ± 0.23	11.0 ± 0.13	8.9 ± 0.11	6.6 ± 0.19	19.8 ± 0.47	14.7 ± 0.51	0.5 ± 0.01	0.4 ± 0.01	ND	ND
Coagulant / Anticoagulant	C	C	C	C	AC	AC	AC	AC	-	-
PT (U/mg) ($\times 10^2$) [a]	7.0 ± 0.14*	6.1 ± 0.21*	4.6 ± 0.17*	3.4 ± 0.10*	3.3 ± 0.12*	1.6 ± 0.05*	0.2 ± 0.01	0.5 ± 0.01	0.3 ± 0.02	0.1 ± 0.01
APTT (U/mg) ($\times 10^3$) [a]	2.1 ± 0.07*	2.0 ± 0.05*	1.5 ± 0.02*	1.2 ± 0.04*	1.0 ± 0.02*	0.8 ± 0.02*	0.1 ± 0.01*	-	0.1 ± 0.01	-
Direct hemolysis (%) [b]	1.4 ± 0.04	-	1.5 ± 0.05	1.8 ± 0.06	0.6 ± 0.02	-	-	-	-	-
Indirect hemolysis (%) [b]	28.2 ± 1.1	0.8 ± 0.02	1.5 ± 0.04	5.9 ± 0.18	44.8 ± 1.18	43.3 ± 1.51	8.4 ± 0.21	3.9 ± 0.09	3.7 ± 0.11	2.8 ± 0.09
Reduction in platelet count (%) [c]	53.0 ± 1.2*	52.6 ± 1.8*	50.0 ± 0.8*	48.3 ± 1.4*	-	-	-	-	-	-
Platelet modulation (%) [d]	(+) 34.9 ± 1.1*	(+) 34.8 ± 0.8*	(+) 34.7 ± 1.2*	(+) 25.9 ± 1.0*	(-) 30.0 ± 1.2*	(-) 22.2 ± 0.8*	(-) 10.8 ± 0.3*	ND	ND	ND

[a] One unit of pro-coagulant activity was defined as a decrease in 1 s of clotting time of PPP incubated with RVV samples, compared to control PPP (1X PBS, pH 7.4). [b] Hemolytic activity was assayed against 5% (v/v) mammalian (goat) erythrocytes. [c] Platelet count of control was $5.2 \pm 0.21 \times 10^6$ cells/ml. [d] Platelet modulation was assessed using goat PRP. The (+) and (-) sign represent platelet aggregation and deaggregation activities, respectively. ND: not detected

4.1.6 Neutralization of enzyme activities and pharmacological properties of WI, EI, and SI RVV samples by commercial PAV manufactured in India

The *in vitro* neutralization potency of commercial Indian PAVs towards enzymatic and some pharmacological properties of WI, EI, and SI RVV samples was found to vary significantly. The enzymatic and pharmacological activities of SI RVV were well neutralized (>80%) by PAVs with exception of PLA_2 activity, while the PAVs failed to neutralize several activities such as PLA_2, fibrin(ogen)olytic, TAME, BAEE (Figs. 4.14a-d, 4.15), indirect haemolysis and pro-coagulant properties of WI and EI RVV samples (Figs. 4.16a-d, 4.17). Further, platelet aggregation property and reduction in platelet count induced by WI and EI RVV samples were moderately (~50%) neutralized by all the tested PAVs (Figs. 4.16a-d). Nevertheless, the neutralization of enzymatic activities and pharmacological properties of WI RVV by MAV was found to be superior to PAV (Figs. 4.15, 4.17). However, due to the unavailability of reliable snakebite detection kit in India, physicians prefer to administer PAV for treating snakebite. As a result, not enough MAV raised against RVV was available for performing the neutralization as well as immuno cross-reactivity studies against RVV samples from EI and SI.

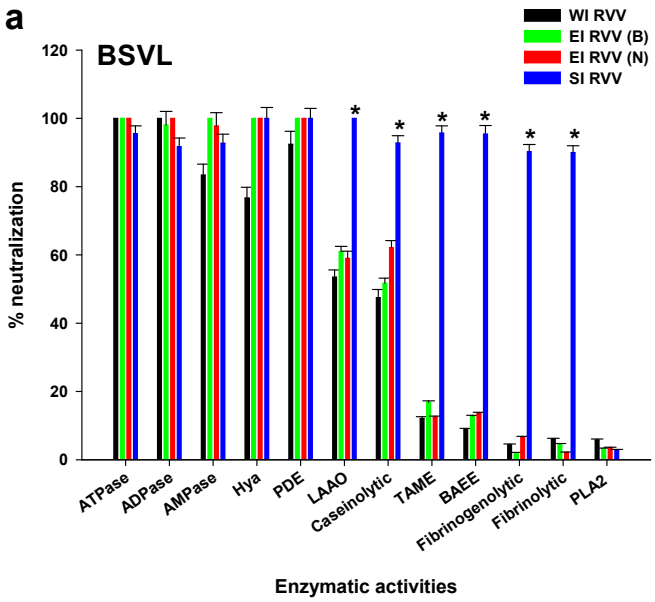
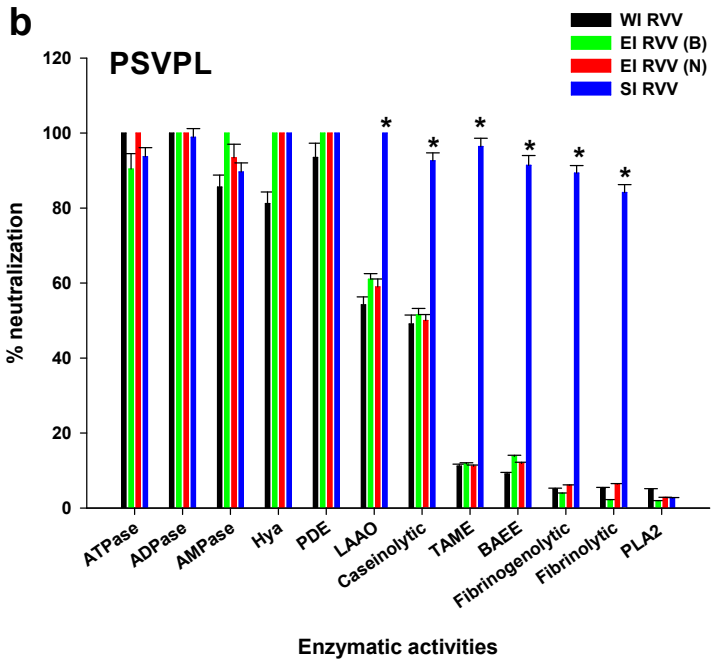


Fig. 4.14. Neutralization of enzyme activities of WI RVV, EI RVV (B), EI RVV (N), and SI RVV by **a.** Bharat Serums and Vaccines Ltd. (BSVL) PAV at 1:10 (venom: antivenom; protein: protein) ratio. Values are mean ± SD of triplicate determinations.

Significance of difference of SI RVV with respect to WI RVV, EI RVV (B), and EI RVV (N), *p<0.01.



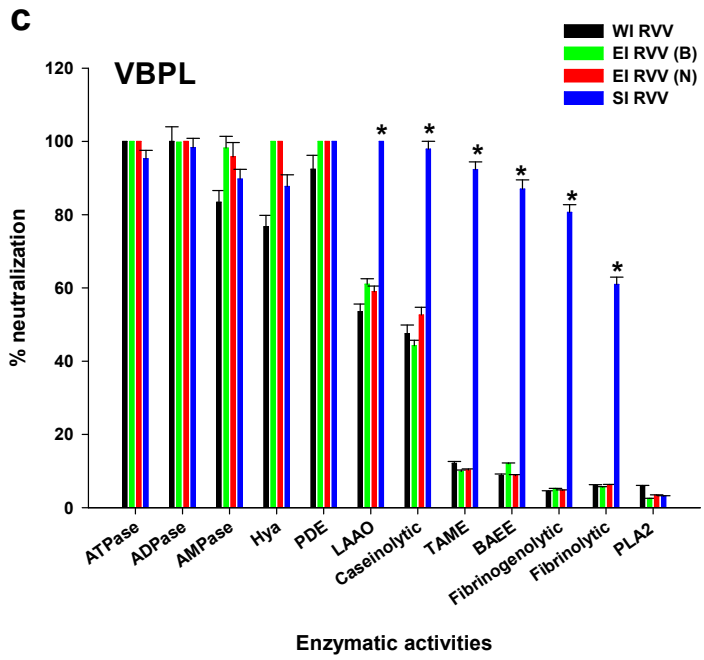


Fig. 4.14. Neutralization of enzyme activities of WI RVV, EI RVV (B), EI RVV (N), and SI RVV by **b.** Premium Serums and Vaccines Pvt. Ltd. (PSVPL) PAV and **c.** Virchow Biotech Pvt. Ltd. (VBPL) PAV at 1:10 (venom: antivenom; protein: protein) ratio. Values are mean ± SD of triplicate determinations. Significance of difference of SI RVV with respect to WI RVV, EI RVV (B), and EI RVV (N), *p<0.01.

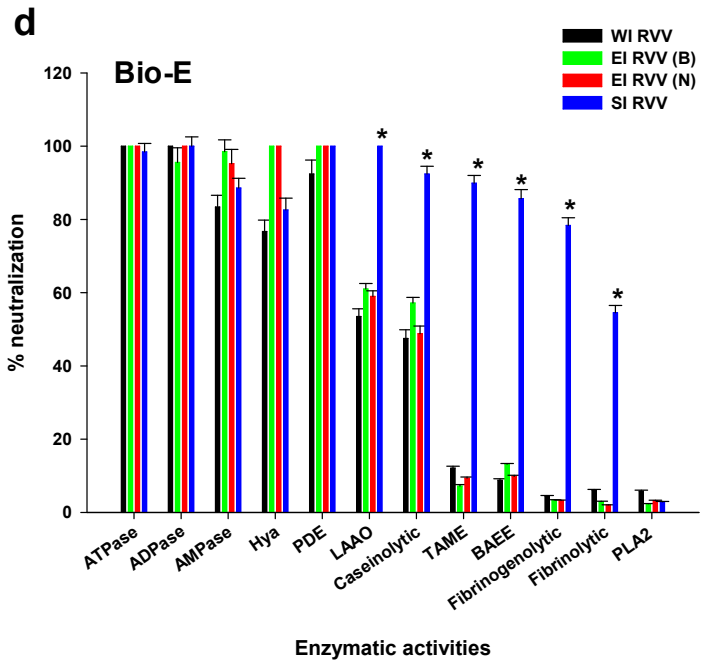


Fig. 4.14. Neutralization of enzyme activities of WI RVV, EI RVV (B), EI RVV (N), and SI RVV by **d.** Biological-E Ltd. (Bio-E) PAV at 1:10 (venom: antivenom; protein: protein) ratio. Values are mean ± SD of triplicate determinations. Significance of difference of SI RVV with respect to WI RVV, EI RVV (B), and EI RVV (N), *p<0.01.

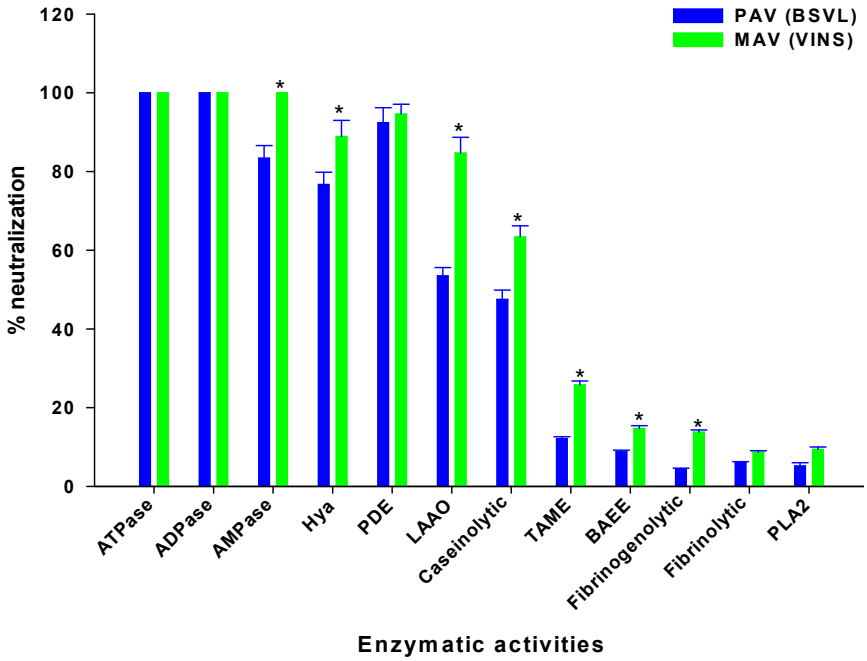


Fig. 4.15. Neutralization of enzyme activities of WI RVV by Bharat Serums and Vaccines Ltd. (BSVL) PAV and Vins BioProducts Ltd. (VINS) MAV at 1:10 (venom:

antivenom; protein: protein) ratio. Values are mean ± SD of triplicate determinations. Significance of difference with respect to PAV, *p<0.05.

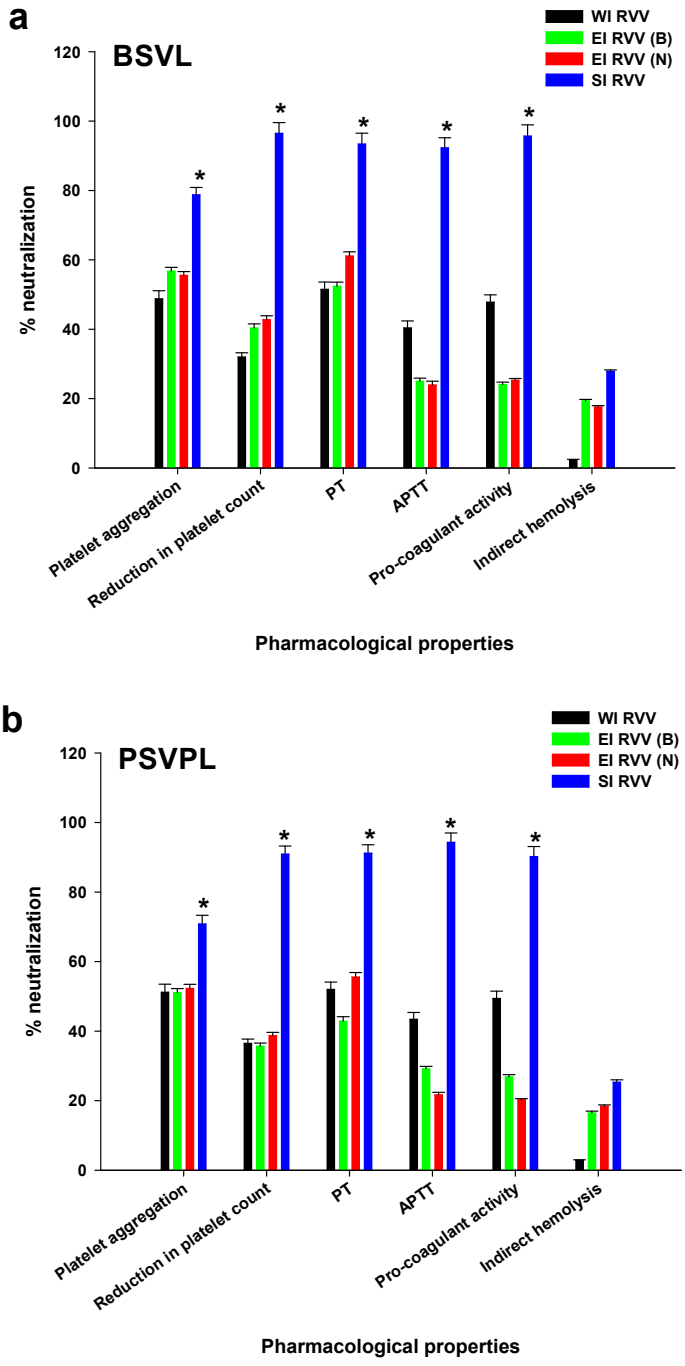


Fig. 4.16. Neutralization of pharmacological properties of WI RVV, EI RVV (B), EI RVV (N), and SI RVV by **a.** Bharat Serums and Vaccines Ltd. (BSVL) PAV and **b.** Premium Serums and Vaccines Pvt. Ltd. (PSVPL) PAV at 1:10 (venom: antivenom; protein: protein) ratio. Values are mean ± SD of triplicate determinations. Significance of difference of SI RVV with respect to WI RVV, EI RVV (B), and EI RVV (N), *p<0.05.

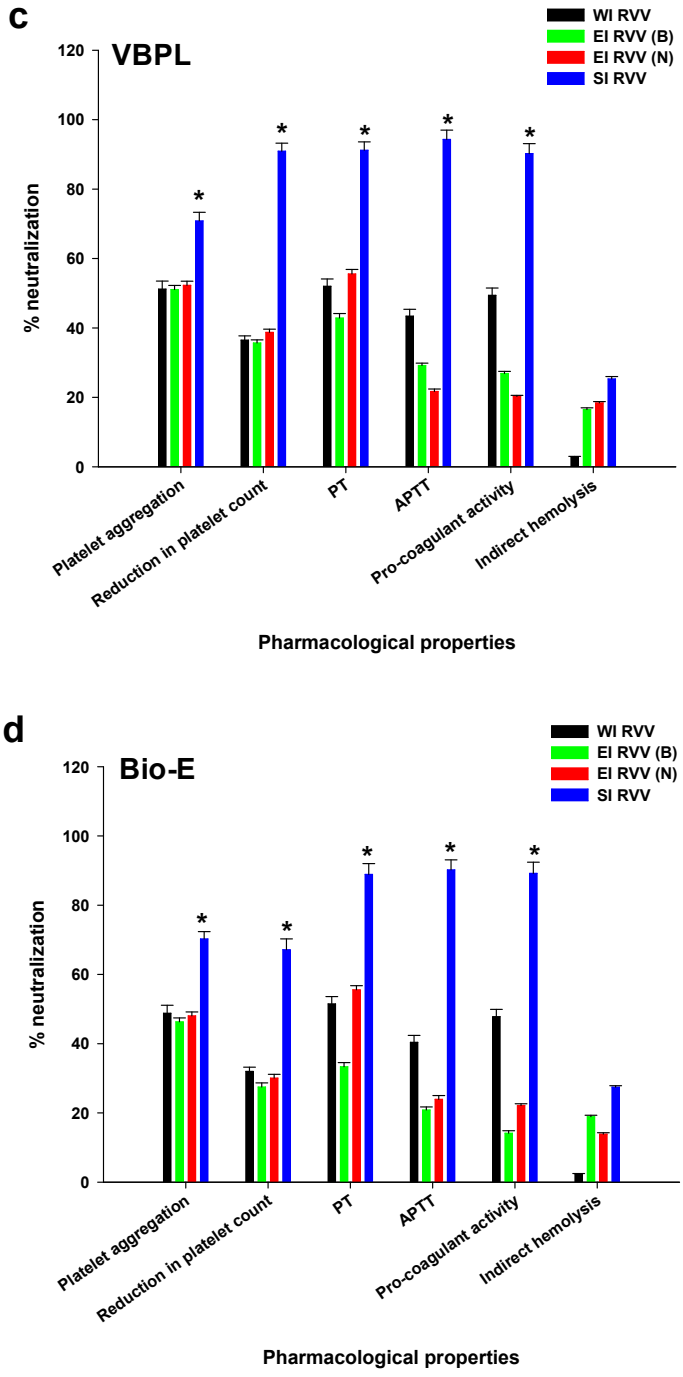


Fig. 4.16. Neutralization of pharmacological properties of WI RVV, EI RVV (B), EI RVV (N), and SI RVV by **c.** Virchow Biotech Pvt. Ltd. (VBPL) PAV and **d.** Biological-E Ltd. (Bio-E) PAV at 1:10 (venom: antivenom; protein: protein) ratio. Values are mean ± SD of triplicate determinations. Significance of difference of SI RVV with respect to WI RVV, EI RVV (B), and EI RVV (N), *$p<0.05$.

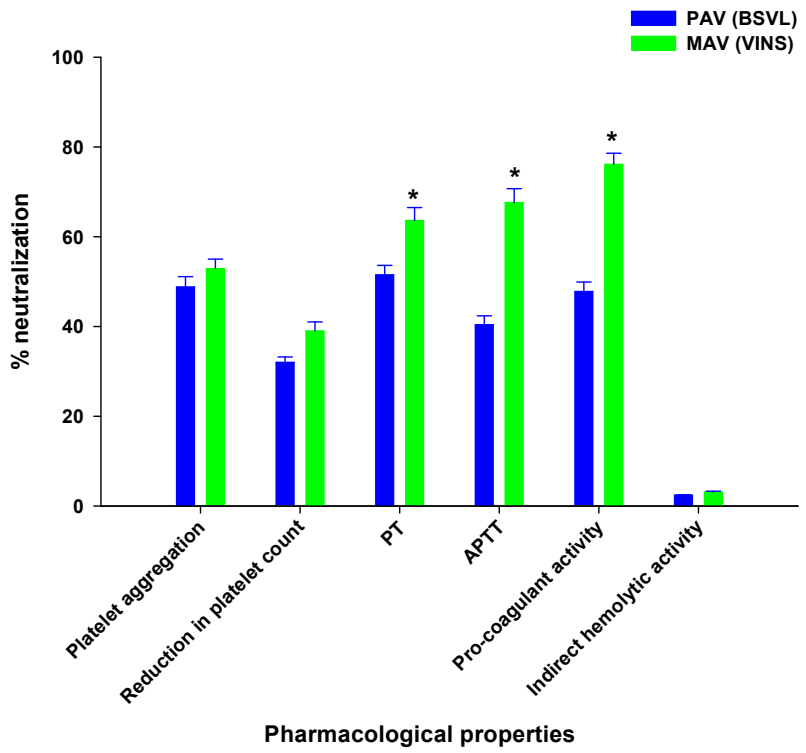


Fig. 4.17. Neutralization of pharmacological properties of WI RVV by Bharat Serums and Vaccines Ltd. (BSVL) PAV and Vins BioProducts Ltd. (VINS) MAV at 1:10 (venom: antivenom; protein: protein) ratio. Values are mean ± SD of triplicate determinations. Significance of difference with respect to PAV, *$p<0.05$.

4.1.7 Assessment of immunological cross-reactivity of RVV samples against commercial polyvalent (PAV) and/or monovalent (MAV) antivenom by ELISA and immunoblot analysis

4.1.7.1 ELISA

All the PAVs under the study demonstrated immuno cross-reactivity with WI, EI, and SI RVV samples; however, to a significantly different extent (Figs. 4.18a-d). Nevertheless, recognition of WI RVV proteins by MAV was superior to PAV (Figs. 4.18a). The high (>50 kDa) and mid molecular mass venom toxins (~20 to 50 kDa) eluted in fractions GF1 to GF4 of WI and EI RVV were better recognized than their low molecular weight counterparts (<20 kDa) eluted through fractions GF5 to GF10 (Figs. 4.18a-c).

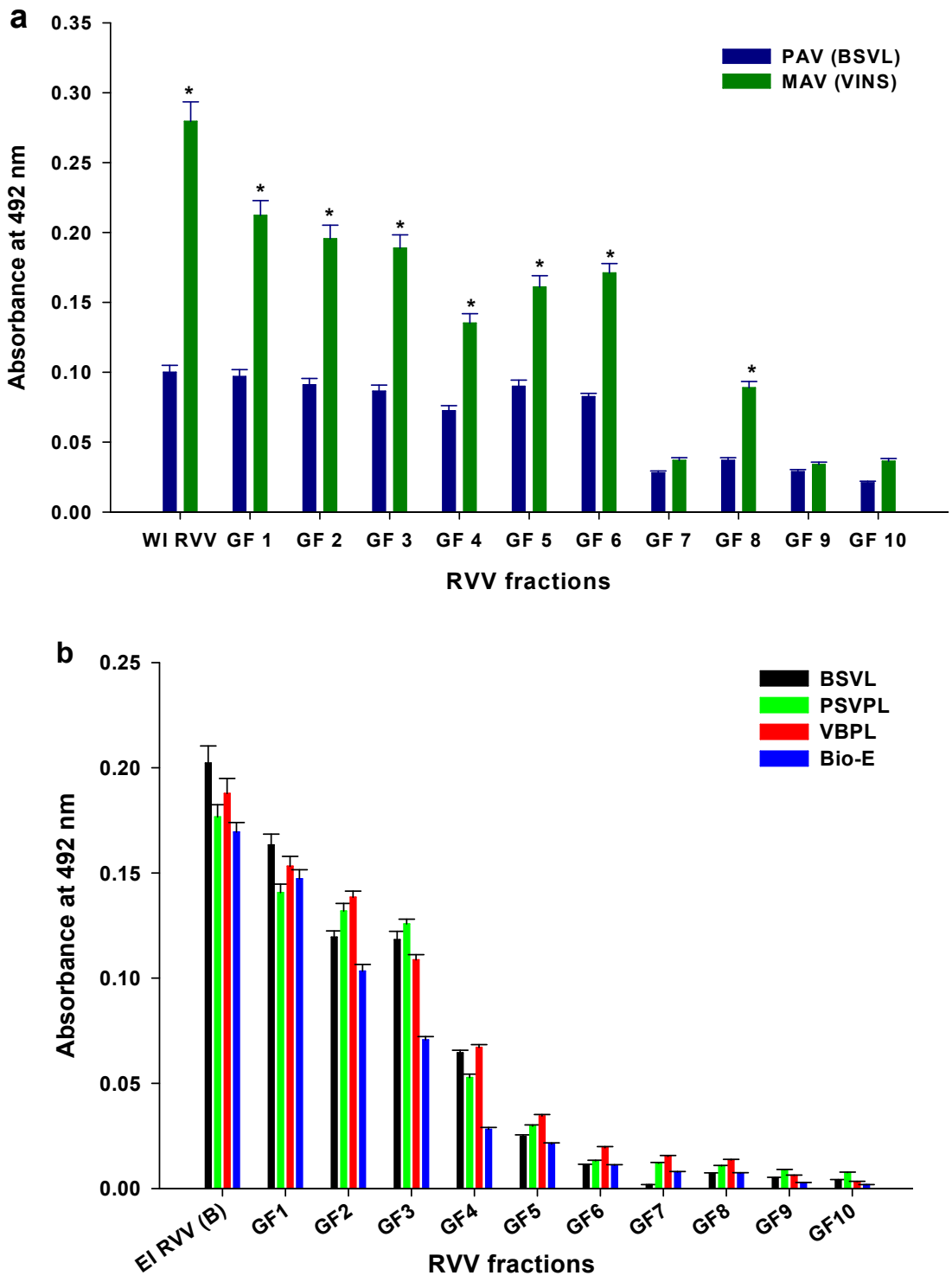


Fig. 4.18. Immunological cross-reactivity of **a.** WI RVV and its GF fractions, **b.** EI RVV (B) and its GF fractions with commercial PAV and/or MAV by ELISA. Values are mean ± SD of triplicate determinations. Significance of difference with respect to cross-reactivity of PAV, *$p < 0.05$.

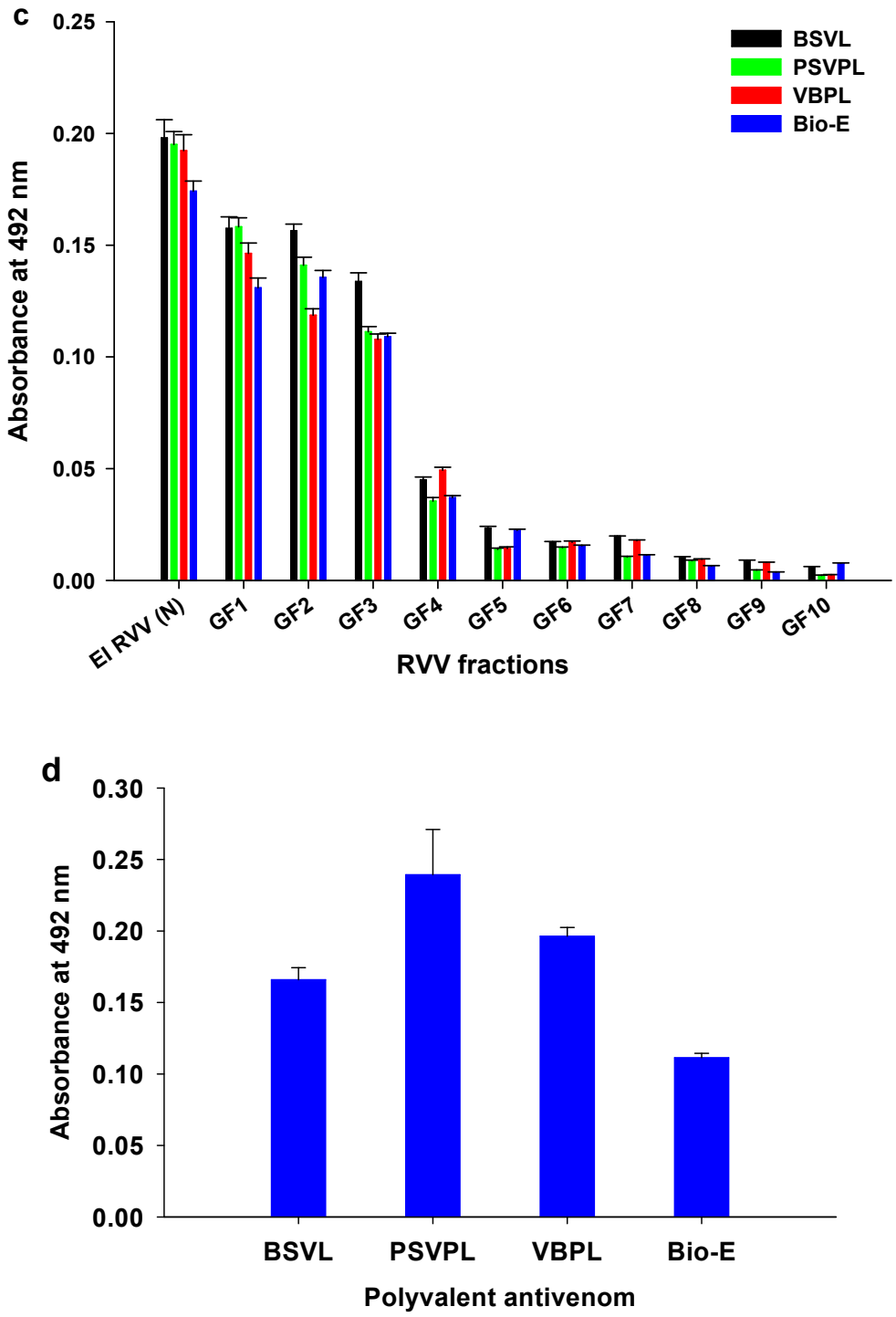


Fig. 4.18. Immunological cross-reactivity of **c.** EI RVV (N) and its GF fractions, and **d.** SI RVV with commercial PAV by ELISA. Values are mean ± SD of triplicate determinations.

4.1.7.2 Immunoblot analysis

Immunoblot analysis also demonstrated better immuno-recognition of high (>50 kDa) and mid-molecular weight RVV toxins (~20 to 50 kDa) by PAV compared to the low molecular weight counterparts (<20 kDa) (Figs. 4.19a-d). Further, in accordance with the ELISA results, MAV exhibited better immuno recognition of WI RVV proteins compared to PAV (Fig. 4.19a). In addition, densitometry analysis of the crude RVV blots probed independently with four Indian commercial PAVs suggested that SI RVV, compared to RVV samples from WI, and EI exhibited better immuno cross-reactivity against PSVPL PAV, while there was no significant difference in the immuno cross-reactivity of the RVV samples against BSVL, VBPL, and Bio-E PAVs (Fig. 4.20).

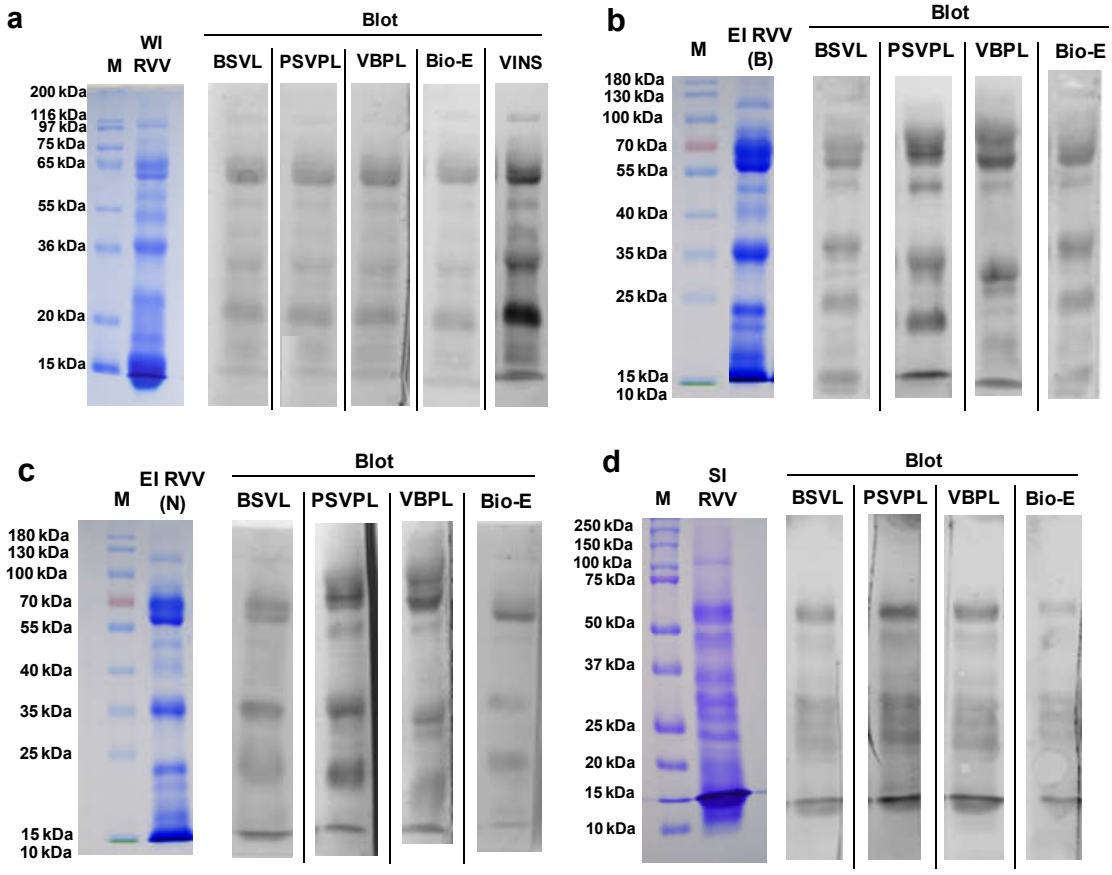


Fig. 4.19. Immunological cross-reactivity of **a.** WI RVV, **b.** EI RVV (B), **c.** EI RVV (N), and **d.** SI RVV with commercial PAV and/or MAV by Western blot analysis. The blots were probed with respective PAV or MAV, developed using BCIP/NBT substrate, and scanned on an Epson scanner (section 3.2.4.2).

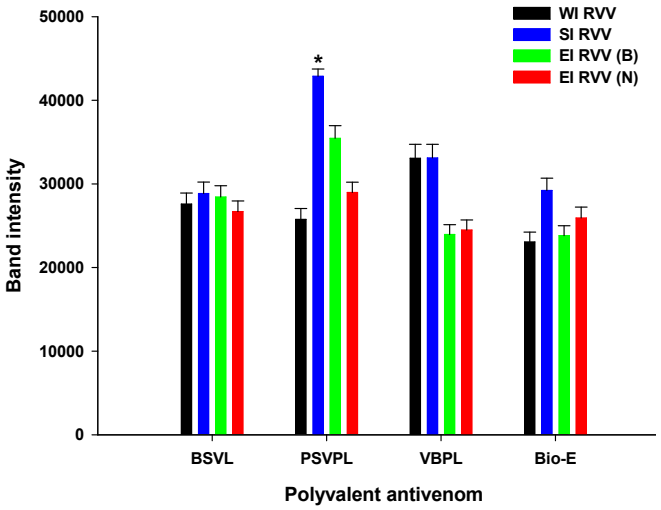


Fig. 4.20. Densitometry analysis of the immunoblots of RVV samples detected by commercial PAVs. The analysis was done using ImageQuant TL software (GE Healthcare, Sweden). Significance of difference of SI RVV with respect to WI RVV, EI RVV (B), and EI RVV (N), *p<0.05.

Further, in accordance with the results of ELISA, immunoblot analysis of the GF fractions of WI and EI RVV also suggested the better immuno recognition of the high (>50 kDa) and mid molecular mass RVV toxins (~20 to 50 kDa) eluted in fractions GF1 to GF4 of WI and EI RVV compared to their low molecular weight counterparts (<20 kDa) eluted through fractions GF5 to GF9 (Figs. 4.21a-c).

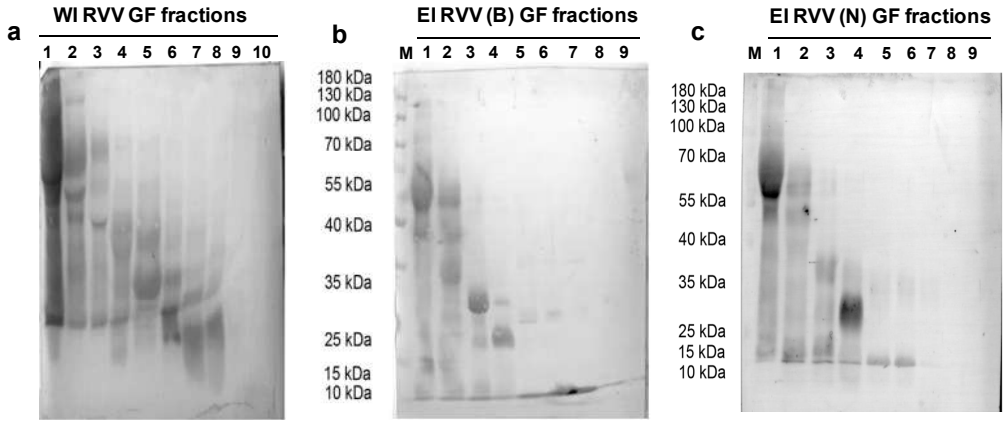


Fig. 4.21. Immunological cross-reactivity of GF fractions of **a.** WI RVV, **b.** EI RVV (B), and **c.** EI RVV (N) with commercial PAV (BSVL) by Western blot analysis as described in section 3.2.4.2.

4.1.8 Second generation antivenomics of RVV samples against commercial PAVs to identify partial/least immune recognized proteins of RVV

SDS-PAGE analyses of the PAV unbound fractions of WI, EI and SI RVV samples suggested that most of the non-retained proteins were in the molecular weight range of ~10 - 15 kDa (Figs. 4.22-4.25). The in-gel trypsin digestion and subsequent LC-MS/MS analysis of partial/least immunogenic RVV proteins present in the SDS-PAGE bands of PAV unbound fractions indicated that these proteins belong to PLA_2, SVSP, SVMP, LAAO, KSPI, snaclec, VEGF, CRISP, and NGF protein families (Figs. 4.22b, 4.24a,b, 4.25b). Further, the label-free quantitative analysis suggested that PLA_2 followed by KSPI were the least recognized proteins among all the RVV samples (Figs. 4.22b, 4.24a,b, 4.25b). In addition, quantitative proteomics analysis also showed that PAVs do not contain sufficient antibodies against proteases (SVMP and SVSP) of WI and EI RVV samples (Figs. 4.22b, 4.24a,b).

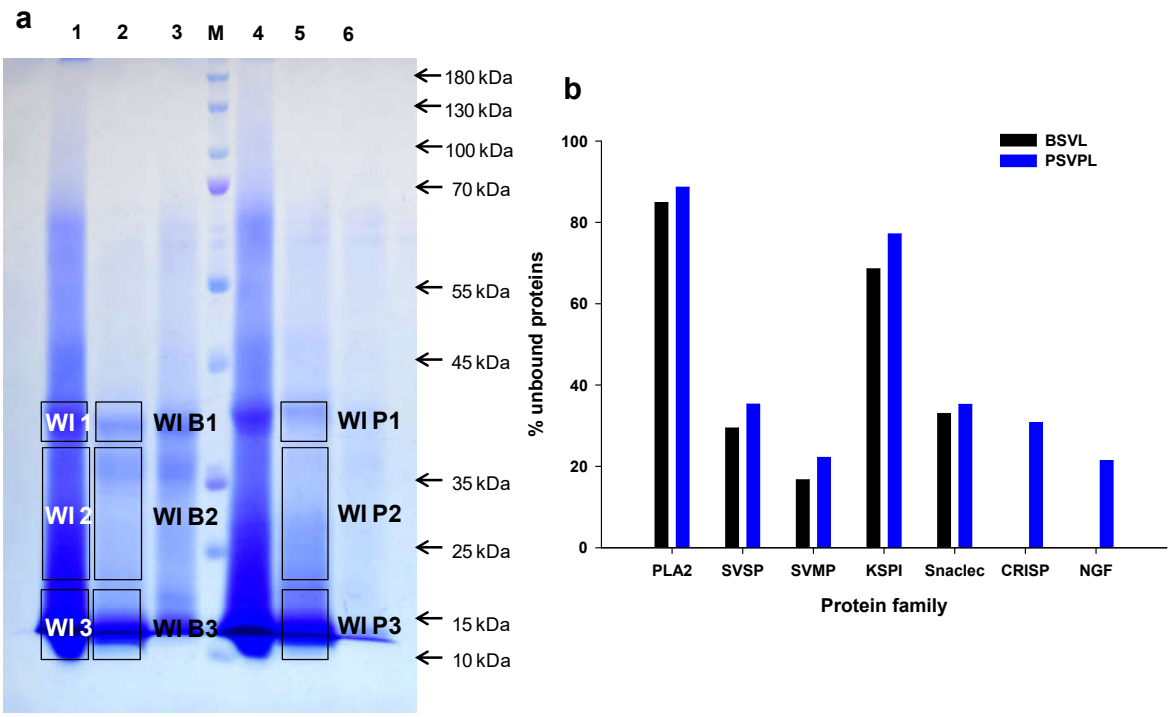


Fig. 4.22a. 12.5% SDS-PAGE analysis of WI RVV, PAV-immuno-affinity column unbound and bound fractions of WI RVV. Lane M contains protein molecular markers. Lanes 1 and 4 represent crude WI RVV (500 µg proteins, reduced). Lanes 2 and 5 represent WI RVV unbound proteins (representing partial or least immunogenic proteins) eluted from immuno-affinity column coupled with PAV manufactured by BSVL and PSVPL, respectively. Lanes 3 and 6 represent WI RVV bound proteins

eluted from immuno-affinity column coupled with PAV manufactured by BSVL and PSVPL, respectively. WI B1 to WI B3 and WI P1 to WI P3 represent the excised protein bands subjected to in-gel trypsin digestion and subsequent LC-MS/MS analysis for protein identification. **b.** Percentage of unbound proteins of WI RVV eluted from immuno-affinity columns coupled with PAV (BSVL and PSVPL) as calculated from MS2 based label-free quantification method.

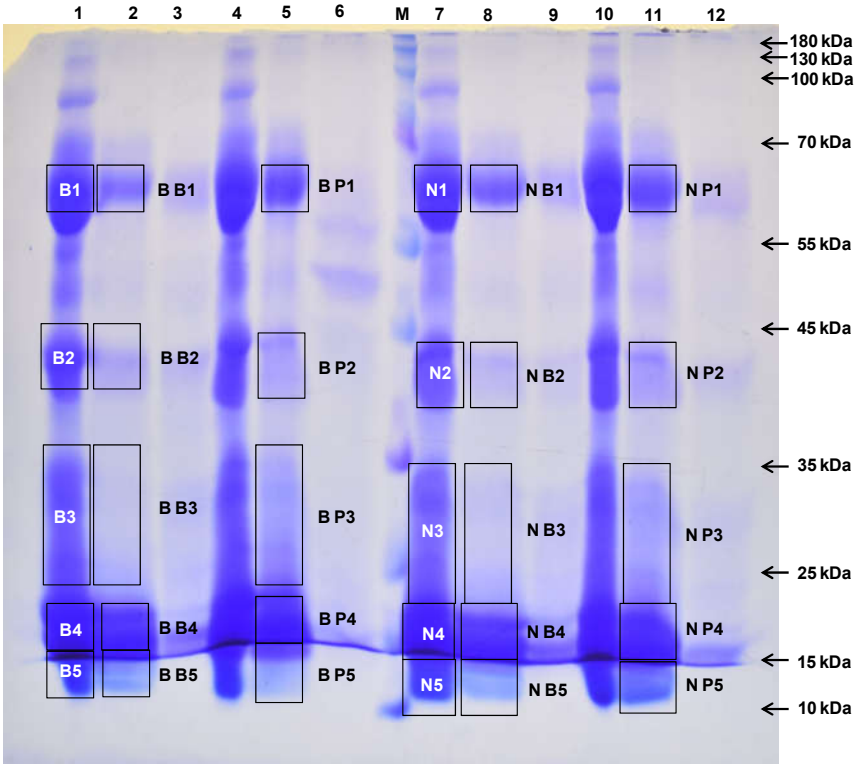


Fig. 4.23. 12.5% SDS-PAGE analysis of EI RVV samples and their PAV-immuno-affinity column unbound and bound fractions. Lane M contains protein molecular markers. Lanes 1 and 4, and 7 and 10 represent crude EI RVV (B), and EI RVV (N) (500 µg proteins, reduced), respectively. Lanes 2 and 5, and 8 and 11 represent EI RVV (B), and EI RVV (N) unbound proteins (representing partial or least immunogenic proteins) eluted from immuno-affinity column coupled with PAV manufactured by BSVL and PSVPL, respectively. Lanes 3 and 6, and 9 and 12 represent EI RVV (B), and EI RVV (N) bound proteins eluted from immuno-affinity column coupled with PAV manufactured by BSVL and PSVPL, respectively. B B1 to B B5, B P1 to B P5, N B1 to NB5, and N P1 to NP5 represent the excised protein bands subjected to in-gel trypsin digestion and subsequent LC-MS/MS analysis for protein identification.

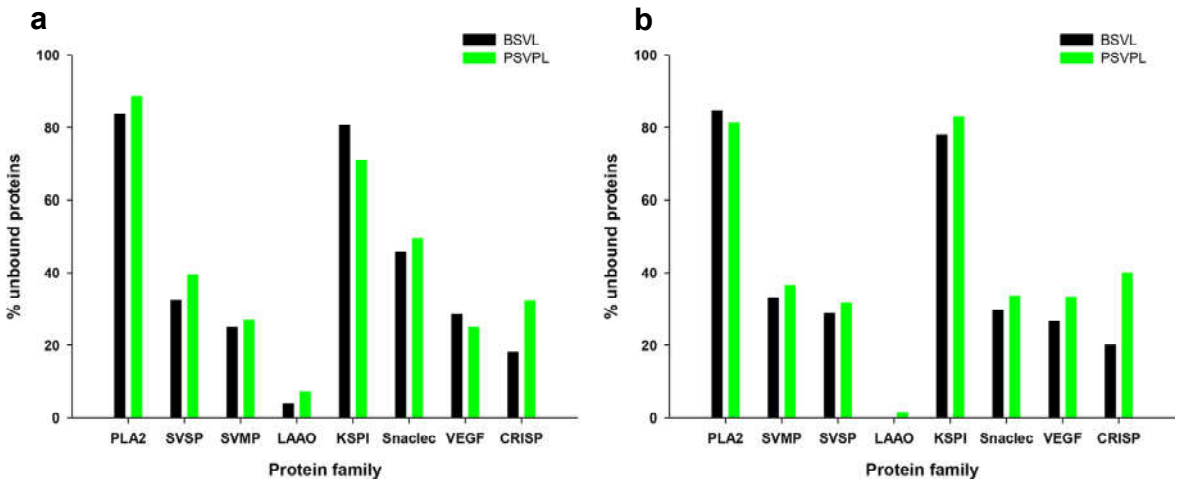


Fig. 4.24. Percentage of unbound proteins of **a.** EI RVV (B), and **b.** EI RVV (N) eluted from immuno-affinity columns coupled with PAV (BSVL and PSVPL) as calculated from MS2 based label-free quantification method.

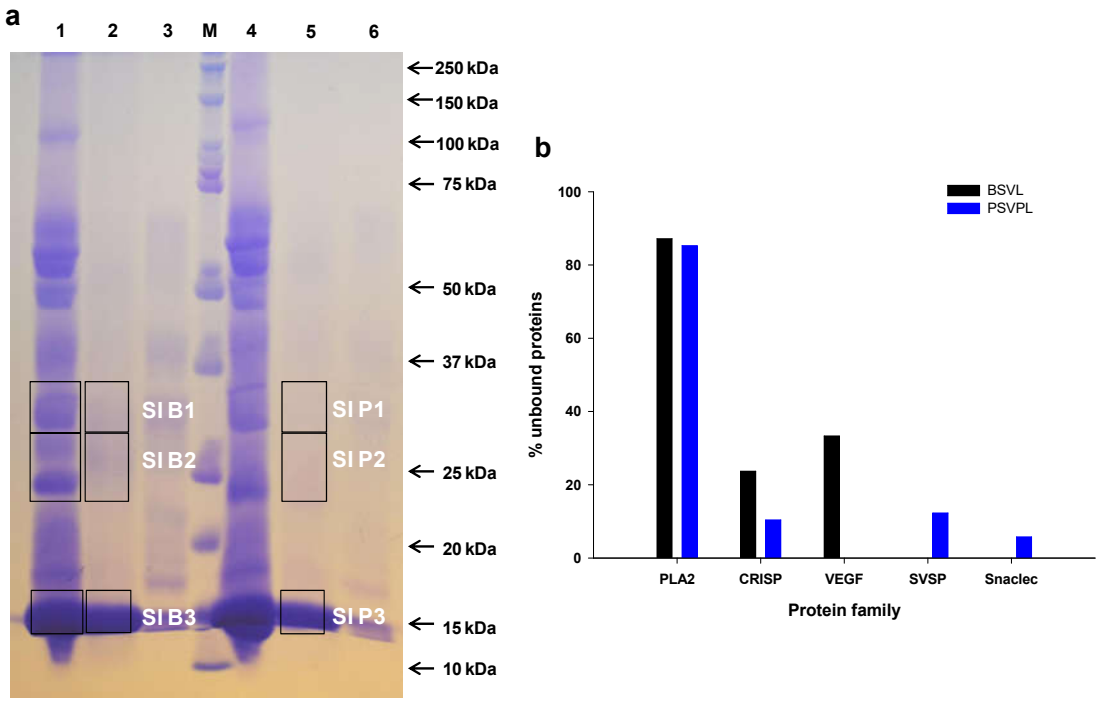


Fig. 4.25a. 12.5% SDS-PAGE analysis of SI RVV, PAV-immuno-affinity column unbound and bound fractions of SI RVV. Lane M contains protein molecular markers. Lanes 1 and 4 represent crude SI RVV (500 µg proteins, reduced). Lanes 2 and 5 represent SI RVV unbound proteins (representing partial or least immunogenic proteins) eluted from immuno-affinity column coupled with PAV manufactured by BSVL and PSVPL, respectively. Lanes 3 and 6 represent SI RVV bound proteins eluted from immuno-affinity column coupled with PAV manufactured by BSVL and PSVPL, respectively. SI B1 to SI B3 and SI P1 to SI P3 represent the excised protein bands

subjected to in-gel trypsin digestion and subsequent LC-MS/MS analysis for protein identification. **b.** Percentage of unbound proteins of SI RVV eluted from immuno-affinity columns coupled with PAV (BSVL and PSVPL) as calculated from an average of MS1 (Summed Peptide-Spectrum Match Precursor Intensity) and MS2 (NSAF) based label-free quantification methods.

4.2 Discussion

4.2.1 Densitometry of SDS-PAGs and its correlation with proteomic data

Densitometry analysis of the SDS-PAGs of crude RVV samples under reduced condition suggested the predominance (56.1% to 62.1%) of RVV proteins in the mass range of ~6 to 25 kDa, which is primarily represented by PLA_2, RVV-X light chain, KSPI, NGF, snaclec, disintegrins, CRISP, and VEGF [1-9]. This is in good accordance with a previous proteomic study on Pakistan RVV that was found to contain abundant (64.5%) low-molecular-mass (5 to 15 kDa) proteins in its venom [9]. Notably, the molecular masses of WI and EI RVV proteins eluted in different GF fractions, were found to be different by SDS-PAGE analyses under reduced and non-reduced conditions. Several low molecular weight proteins bands (~15 to 20 kDa) were observed along with high molecular weight RVV components (>50 kDa) in GF1 and GF2 fractions of WI and EI RVV, which is consistent with the findings on Pakistan RVV [9]. These findings unambiguously suggest the occurrence of multiple subunits, self-aggregation of proteins, non-covalent oligomers (multimeric forms), and/or interactions among the RVV proteins [10-12]. Notably, the proteins present in GF7 of WI RVV showed a broad band in the range of ~15 to 28 kDa under non-reduced condition, while under reduced condition, they migrated at a molecular weight range of ~6 to 10 kDa which indicates self-aggregation of proteins in native state. A similar observation was also reported for the Rusvikunin complex, previously isolated and characterized from Pakistan RVV [11], which suggest the occurrence of such protein complexes in WI RVV. However, such aggregation of proteins could not be identified in EI RVV samples.

Further, the relative abundance of RVV proteins determined by MS-based label-free protein quantification was well correlated with the densitometry analysis of SDS-PAGE protein bands (reduced). For example, the percent band intensity of RVV

proteins in the molecular mass range of 10 to 22 kDa representing PLA_2, snaclec, VEGF, NGF, and KSPI was found to be 56.1%, 62.1%, 57.4%, and 60.7% in WI RVV, SI RVV, EI RVV (B), and EI RVV (N), respectively, whereas, the cumulative relative abundance of the above RVV proteins by MS-based quantitative proteomics was determined at 58.3%, 64.8%, 58.4%, and 62.0% in WI RVV, SI RVV, EI RVV (B), and EI RVV (N), respectively. Similarly, the cumulative relative abundance of RVV proteins in the molecular mass range of >45 kDa, represented by SVMP, LAAO, NT, PDE, PLB, and carboxypeptidase (CP), determined by LC-MS/MS analysis (26.7%, 16.4%, 23.7%, and 20.2% in WI RVV, SI RVV, EI RVV (B), and EI RVV (N), respectively) and by SDS-PAGE analysis (27.5%, 17.8%, 24.0%, and 21.2% in WI RVV, SI RVV, EI RVV (B), and EI RVV (N), respectively) was found to be nearly identical. This method of correlation of proteomic data with percent SDS-PAGE band intensity of crude venom should be considered as a 'Gold Standard' for quantitative proteomic analysis of venom.

4.2.2 Venom proteome composition of RV from WI, SI, and EI

With the advent of biochemical assays including purification and characterization of enzymes, RVV complexity was gradually determined [13,14]. However, this approach has a major limitation for the identification and quantification of the non-enzymatic and minor components of snake venom, which is often crucial since these components may dictate the differences in severity of pathogenesis and clinical symptoms following envenomation [15]. These constraints have now been overcome by the recent advancements in the field of mass spectrometry coupled with robust database search algorithms, and the development of powerful venom de-complexing strategies that have become integral to biological research and have helped the evolution of the field of venom proteomics [2,16-18].

Generally, prior to mass spectrometric analysis, venom de-complexation, the first step of proteomic workflow is achieved by either 1D or 2D SDS-PAGE, or liquid chromatography (gel-filtration, ion-exchange and/or reversed-phase high-performance liquid chromatography), or a combination of liquid chromatography and 1D SDS-PAGE techniques [16]. The choice of a particular workflow depends on several factors, such as the aims and objective of the study, the quantity of available starting material (snake venom), analytical facilities, and database status. Nevertheless, every chromatography method has its own advantages and limitations. For example, RP-HPLC followed by

gel-based identification strategies are often limited by the staining of proteins in low abundance and glycoprotein, and by the loss of smaller peptides (<5 kDa) in SDS-PAGE [16]. Further, organic solvents like acetonitrile, used for the elution of venom proteins in RP-HPLC can cause their denaturation, thereby disrupting the native state of venom proteins and protein-protein complexes of snake venoms that play an important role in venom-induced lethality and toxicity. Therefore, the enzymatic and pharmacological properties of RP-HPLC fractions may not be well correlated to the protein(s) composition of that venom fraction, which would hinder the toxicovenomic study. Fractionation of venoms by gel-filtration (GF) and/or ion-exchange (IE) chromatography can circumvent these difficulties [9]; however, subsequent in-solution trypsin digestion and the mass spectrometry analysis of GF or IE fractions have additional hurdles. First, it is difficult to draw a relationship between the identified peptides and their parent protein [16]. Second, a shotgun proteomics approach for analyzing complex venom proteomes often faces the problem of low peptide coverage, possibly because generally, 10 - 30% of the acquired spectra are successfully matched to protein sequences in the target database [19]. To circumvent the above problem, some stringent identification criteria, for example, a -10logP value ≥ 30 and 20, for protein and peptide, respectively, the presence of at least one unique peptide and overlapping distinct peptide were adopted in this study. Further, semi-tryptic peptides were also considered to improve the protein identification and coverage [20].

Quantification of identified components through proteomic analysis (quantitative proteomics) is another important way to understand the variation in snake venom composition. However, without isotope labeling methods this can be very challenging. Nevertheless, toxinologists have represented the relative abundance of the venom proteome components by using various strategies. For example, determination of the area under RP-HPLC peaks at 215 nm (AUC) provides a surrogate measure of the peptide bonds [16,21-25] and therefore relative areas provides a measure of relative abundance of the venom components. However, these absorbance values may be influenced by the side chain composition of the toxins, where the aromatic side chains (present in tyrosine, tryptophan, phenylalanine, and histidine) contribute significantly and thus can be biased towards the composition of different proteins eluted in the RP-HPLC peaks [26]. On the contrary, MS-based label-free quantification strategies have become popular due to the relative ease of experimentation and the small amount of

sample needed [8,9,27], but which is still limited by database dependency. Further, the paucity of relevant entries in the target database is an inevitable drawback associated with shotgun mass spectrometry-based protein identification, and several important components of snake venoms, such as ATPase and ADPase enzymes, may be overlooked because they have yet to be documented in the databases [9] (present study). Thus, every proteomic workflow has its own pros and cons, and the use of a particular strategy depends on the major objective of the study. In our particular study, correlation of mass spectrometry data with biochemical and pharmacological properties of RVV proteins and its protein complexes was the major objective and therefore, we preferred venom fractionation by gel filtration chromatography. Nevertheless, due to the availability of a very small amount of SI RVV sample we opted for venom de-complexation by 1D SDS-PAGE.

RVV is primarily haemotoxic, affects the blood coagulation cascade of the victims, and is predominated by protein classes inducing consumption coagulopathy and blood anticoagulation [13,14]. Notably, the occurrence of enzymatic proteins in RVV samples from WI, Burdwan, Nadia, and SI was determined at 67.5%, 59.9%, 56.5% and 70.0%, that clearly suggests that RVV is predominated by enzymatic classes of proteins. Here is a brief account of the enzymatic proteins identified in RVV from different geographical locales of India.

4.2.2.1 Enzyme toxins in RVV

Irrespective of the geographical location, the most abundant class of protein identified in RVV is PLA_2, a multi-functional toxin that exhibits diverse pharmacological effects including neurotoxicity, cardiotoxicity, myotoxicity, necrosis, anticoagulant, hypotensive, haemolysis, haemorrhage, edema, platelet modulation, and membrane damage [5,14,28-35]. Their molecular weight ranges from 10 to 15 kDa and they are classified under Groups I and II of the secretory PLA_2 ($sPLA_2$) [3]. Although PLA_2s are predominant in RVV samples from WI, EI, and SI, their relative abundance as well as number of PLA_2 isoforms vary dramatically. Such a great discrete difference in relative abundance of a major RVV toxin class obviously signifies the role of geographical variation in determining the disparities in venom composition. Further, similar to the previous observation on Pakistan RVV [9], PLA_2 enzyme was detected through all the GF peaks of WI and EI RVV, advocating interaction of this enzyme with other RVV proteins to augment the toxicity of interacting components [36].

Another striking difference was the occurrence of variable amounts of neurotoxic PLA_2 isoforms among different venom samples. Three isoforms of neurotoxic PLA_2s in WI RVV (Daboiatoxin, gi|149241831; VRV-PL-VIIIa, gi|24638087; and RV-4 gi|400713) and SI RVV (VRV-PL-VIIIa, P59071.1; Basic phospholipase A_2 chain HDP-1P, Q1RP79.1; and Daboiatoxin, Q7T3T5.1) contributing 3.2% and 19.1%, respectively were identified by LC-MS/MS analyses, while EI RVV completely lacked this sub-class of PLA_2 toxin.

RVV is reported to constitute substantial quantities of proteolytic enzymes [10,37-42]. These are the primary components of RVV that dictates the *in vitro* pro-coagulant nature of this venom and thus they play a crucial role in the pathophysiological effects of RV envenomation [14,37]. Snake venom proteases are broadly classified as serine proteases and metalloproteases [37,43], and both groups are found in significant amounts in RVV. They accomplish their task by the proteolytic cleavage of a number of blood coagulation factors such as Factor X and V, prothrombin, fibrinogen, fibrin, etc., thereby rendering a state of imbalance in the haemostatic system in victims or prey [10,37-39].

Based on their size and domain structure SVMPs are grouped to PI, PII, and PIII classes [41,43]. PIII-SVMPs are high molecular weight components (>60 kDa) of RVV and they represent the second, and fourth most abundant enzymatic class of protein in WI and EI RVV, and SI RVV, respectively. In addition to affecting the haemostatic system in victims, SVMPs induce hemorrhage, edema, necrosis or muscular degeneration [37,38,42,44,45]. Among the identified isoforms, RVV-X, which can potentially activate blood coagulation factor X, was identified in all the RVV samples. It is a heterodimer of a heavy chain of molecular weight 59 kDa and heterogeneous light chains of molecular weights 18 and 21 kDa [41]. In addition, isoforms of α and/or β-fibrinogenase were also detected in the RVV samples. These SVMPs can cleave α and/or β chains of the fibrinogen molecules, thereby contributing to consumption coagulopathy [10,37,38].

SVSPs are fibrin(ogen)olytic enzymes with molecular mass typically in the range of ~23-33 kDa [39,46-49]; however, Russelobin is a high molecular mass serine protease reported from Pakistan RVV [40]. They are associated with RV-induced coagulopathy by virtue of their ability to cleave a wide range of blood coagulation factors. Some of the SVSPs demonstrate fibrinogen clotting activity and they are termed

"snake venom thrombin-like enzymes" (SVTLEs) [40,50,51], while others can cleave kininogen (kallikrein-like proteases) [52], Protein C, and plasminogen [46,53]. In addition, RVV-V, a ~30 kDa monomeric serine protease that activates blood coagulation factor V [39], was identified in all the venom samples. SVSPs represent the second, and third most abundant enzymatic class in SI RVV, and EI and WI RVV, respectively.

LAAO are homodimeric and thermolabile enzymes with a molecular weight in the range of 60-150 kDa [54,55]. The characteristic yellow color of RVV is due to the presence of FAD, a cofactor of LAAO enzymes [55,56]. They can catalyze the oxidative deamination of an L-amino acid to an α-keto acid, liberating ammonia and hydrogen peroxide; the latter is particularly detrimental to cells [57]. This class of proteins is reported to induce edema, apoptosis, platelet modulation, haemolytic activity, anticoagulant effects, and hemorrhagic effects [55,58,59]. LAAO is the second most abundant enzymatic class of toxin in SI RVV (7.5%); however, they were identified as minor venom components (<2%) in EI and WI RVV (Fig. 4.12b) which again highlights the geographical variation in venom composition of RV.

NT (AMPase, ADPase, and ATPase) is another group of high molecular weight enzymes which can cleave a wide range of nucleotide molecules in presence or absence of divalent metal ions [60,61]. In their native state, they usually occur as bulky multimers of ~260 kDa, while the molecular mass of their monomeric sub-units ranges from 60-70 kDa [62,63]. Due to their low relative abundance (0.4% to 1.8%) in all the investigated RVV samples (Fig. 4.12b) and transient stability, these snake venom enzymes are poorly characterized [9,64]. However, some of the studies reported their role in modulation of platelet function via the action of adenosine released upon enzymatic cleavage of nucleotides [63,65].

PDE can affect blood coagulation and modulation of platelet function in victims by cleavage of phosphodiester bond from the 3' terminus of polynucleotides or endonucleolytic cleavage of both double and single-stranded RNA and DNA, thereby releasing 5'-mononucleotides [66]. These enzymes are single subunit high molecular mass venom proteins with molecular mass ranging from 100 to 140 kDa [67,68]. The relative abundance of this minor component of RVV was found to be comparable (0.5% to 1.4%) among the RVV samples under study (Fig. 4.12b).

Hya, a class of endo-β-glycosidases, is known as 'spreading factor', and their molecular weight ranges from 33 kDa to 110 kDa [69]. The wide range in their molecular mass is attributed to either their structural heterogeneity due to post-translational modification or to faulty characterization [70]. They can degrade hyaluronic acid (endo-β-N-acetyl-D-hexosamine) present in the extracellular matrix of local tissue, thereby promoting local hemorrhagic effects as well as aiding in the distribution of venom following injection [69,71]. Therefore, these enzymes likely have a significant contribution to RV-induced toxicity, however, until now there is no report on the purification and characterization of Hya from RVV.

In addition to Hya, the relative abundance of other minor enzymatic classes of RVV, such as GC, PLB, APase, and CP, was found to be comparable in RVV samples from EI, WI, and SI (Fig. 4.12b); however, proteomic analysis could not detect some of these enzymes in all RVV samples, perhaps consistent with their probable roles as housekeeping proteins, rather than venom toxins. In addition, because of their extremely low contribution to total venom composition (<1%), variation in the relative abundance of these enzymes in a particular RVV sample is not likely to influence the toxicity of venom.

4.2.2.2 Non-enzyme toxins in RVV

KSPI binds to the active site of serine proteases via 6 conserved cysteine residues, termed as the Kunitz motif (P3, P2, P1, P1', P2' and P3') [2,72]. They are low molecular weight proteins (~6 to 10 kDa) comprising of 50-60 amino acids. Apart from their inhibitory activity on serine proteases, they are also reported to block ion-channels and act on coagulation, fibrinolysis, and inflammation [6,11,73-75]. KSPI is the most abundant non-enzymatic component of WI and EI RVV; however, they were detected in minor amounts in SI RVV reflecting geographical variation in RVV composition.

Snaclecs are comprised of larger quaternary structures of disulfide-linked homo- or hetero-dimers, the molecular weight of the monomers being in the range of 8 to 16 kDa [7,76]. They target blood coagulation factors, cell membranes, and platelet receptors and thereby trigger haemostatic imbalance in victims [7,77-80]. They represent the most and second most abundant non-enzymatic class of protein in SI RVV and EI RVV, respectively. On the contrary, their relative abundance in WI RVV was significantly lower compared to the other two RVV samples (Fig. 4.12c).

CRISP consist of a single polypeptide chain of 20-30 kDa with 16 conserved cysteine residues [1]. They are reported to inhibit smooth muscle contraction and cyclic nucleotide-gated ion channels [81,82]. With a relative abundance of 6.8%, CRISP is the second most abundant non-enzymatic protein class in WI RVV, while they are minor venom components (<5%) in EI and SI RVV (Fig. 4.12c).

VEGF (~23-33 kDa) are reported to bind to the cellular receptors like KDR and Flt-1 and exhibit potent hypotensive effect and enhancement of vascular permeability [83]. NGF belongs to a family called "neurotrophic factors" and their molecular weight ranges from 25 kDa to 54 kDa [4]. They are a class of poorly characterized venom protein, and their pharmacological effect in victims or rationale of existence in snake venoms is yet to be deciphered. However, a few preliminary studies have reported the role of NGF in apoptosis, vascular permeability and wound healing [84]. Dis, the cysteine-rich low molecular weight (4 to 15 kDa) RVV component, is generated by the proteolytic cleavage of Class P II metalloproteases [85]. They are reported to bind platelet integrin receptors via a conserved arginine-glycine-aspartic acid (RGD) motif [85-87]. This binding inhibits or interferes with integrin-ligand interactions, eventually leading to haemostatic imbalance in the victims [85,86]. VEGF, NGF, and Dis are minor RVV components and their relative abundance was found to be comparable in all the RVV samples (Fig. 4.12c). An in-depth study is required to explore the actual pharmacological effects of these non-enzymatic toxins of RVV in RV-bite patients or experimental animals.

4.2.3 The venom compositions of RV from WI, SI, and EI correlates well with their biochemical properties

The enzymatic activities exhibited by WI, EI, and SI RVV were consistent with the proteomic analyses of the RVV samples with exception to ATPase, and ADPase enzymes. The presence of these enzymes in RVV could not be ascertained by proteomic analysis owing to the lack of a comprehensive species-specific database [9,20,88] (present study). SVMP, LAAO, ATPase, ADPase, AMPase, Hya, and PDE are primarily higher molecular weight enzymatic proteins (>50 kDa) in RVV and thus were eluted near the void volume (GF1) of the GF column. SVSPs are mid-molecular weight (~23 to 33 kDa) RVV enzymes that exhibit TAME and BAEE-esterase and fibrinolytic activities, and according to their molecular weight these activities were predominant in GF2 to GF4 of WI and EI RVV. Further, the highest specific PLA_2 activity was

observed in fractions GF5 and GF6 which is in accordance with the molecular weight of these enzymes (~10 to 15 kDa) [32, 34].

SI RVV exhibited higher PLA_2, LAAO, and AMPase activities compared to the RVV samples from other regions of India which is consistent with the higher relative abundances of these enzymes in SI RVV. On the contrary, the lower SVMP, fibrinogenolytic, TAME and BAEE esterase activities of SI RVV compared to other RVV samples is in accordance with the lower amounts of proteases present in this venom. Further, WI RVV, containing relatively higher amounts of proteases compared to SI and EI RVV, was characterized with superior SVMP, fibrinogenolytic, phosphodiesterase, and TAME and BAEE esterase activities. Further, SVMP, fibrinogenolytic, and TAME and BAEE esterase activities of EI RVV were superior to these activities displayed by SI RVV; however, was significantly lower compared to WI RVV. EI RVV was characterized with highest hyaluronidase activity and relatively poor ATPase, ADPase and AMPase activities compared to RVV samples from other parts of India. Interestingly, although the relative abundance of proteases in WI and EI RVV samples was found to be comparable (32.0 to 33.7%) by proteomic analysis, albeit the WI RVV sample demonstrated significantly higher ($p<0.05$) fibrinogenolytic specific activity compared to EI RVV samples. This finding unambiguously indicates that it is not only the relative abundance of the protease enzymes found in a venom, but the potency or enzymatic strength (in terms of specific activity) of individual toxin may also determine the extent of pharmacological activity exhibited by RVV. Additionally, SVMPs have wide substrate specificity and all of them may not display fibrinogenolytic activity [43,89]. Further, this activity may also be attributed to SVSPs; therefore, a direct correlation between fibrinogenolytic activity and content of SVMP may not always be expected. Nevertheless, SI RVV was characterized with least fibrinogenolytic activity which is well correlated with proteomic analysis showing lower relative abundance of protease enzymes in this venom (17.5%).

Therefore, qualitative as well as quantitative differences in enzyme activity in RVV samples from different locales indicate geographical variation in venom composition of RV. Further, the toxicity of venom samples depends on the qualitative and quantitative distribution of different enzymes and toxins in the venom [14,90]; therefore, these disparities in enzymatic properties of RVV may also be responsible for

the differences in severity of pathogenesis and clinical symptoms following RV envenomation.

4.2.4 Pharmacology and clinical manifestations of RV envenomations and their correlation with RVV proteome composition determined by proteomic analysis

An adult RV possesses approximately 200-225 mg of venom in its glands, and therefore, bites can result in large amounts of venom being injected to prey or a victim [29]. The LD_{50} of RVV (in mice) is reported in the range of 0.7 (*i.v.*) to 10 mg/kg (*i.p.*) depending upon the geographic source of the venom and the EI sample was found to be the most lethal compared to RVV samples from western, southern and northern India [13,14,91]. This indicates that in addition to geographic differences in RVV composition, acute toxicity of venom also varies across the Indian sub-continent. RVV samples from all the three regions of India were found to be pro-coagulant under *in vitro* conditions, the potency being dictated by the distribution and abundance of SVMP and SVSP, more specifically, RVV-X and RVV-V. In addition, the venom samples induced indirect hemolysis of erythrocytes (exhibited primarily by PLA_2 enzymes), aggregation of platelets and reduction in platelet count (thrombocytopenia).

The variation in pharmacological properties exhibited by RVV from different parts of India was well corroborated by the proteomic findings. For example, the lower pro-coagulant activity displayed by SI RVV, compared to RVV samples from WI and EI, was consistent with the lower cumulative abundance of SVMP and SVSP in the former RVV. The exceptionally low relative abundance of KSPI in SI RVV (compared to EI and WI RVV) was well correlated with its low trypsin inhibitory activity [13]. Further, platelet aggregation by RVV components such as snaclec, LAAO, and SVTLE is yet another mechanism of provoking haemostatic disturbance in prey/victim [92-94]. The cumulative relative abundance of these components in SI RVV (23.7%) surpassed that of WI (2.4%) and EI (13.6-13.8%) RVV samples which explains the greater platelet aggregation activity demonstrated by SI RVV [92-94]. Therefore, the proteomic analyses of these venoms provided sufficient evidence to account for the observed differences in pharmacological property exhibited by RVV samples from different localities on the Indian sub-continent.

At the onset of RV envenomation, a victim experiences extreme pain at the bite site and its proximal lymph nodes which is accompanied by rapid swelling, local

ecchymosis and intense blebs over the affected extremities that may extend to abdominal or chest wall within 6 to 8 h post envenomation [95-97]. These clinical manifestations are primarily due to the action of abundance of SVMPs in RVV that causes lysis of basement membranes of blood vessels followed by plasma extravasation and leukocyte infiltration thereby initiating an inflammatory response ultimately leading to swelling [45,98,99]. Subsequently, there is development of wet gangrene or non-healing ulcers and if untreated, the bitten part usually toe or finger results in auto-amputations [95]. Gradually, the venom starts its effect on the blood vascular system by provoking haemostatic disturbances, including rapid thrombosis and hypofibrinogenemia that ultimately results in consumption coagulopathy and incoagulable blood [95]. This is steered by the concerted action of the serine proteases and some metalloproteases (FX activator) that activate prothrombin, Factor X and V, and fibrin(ogen)olytic enzymes that catalyze hydrolysis of fibrinogen and/or fibrin [39,40,100,101]. Subsequently, abundant anti-coagulant RVV proteins such as PLA_2, KSPI, and snaclec exert anti-coagulant action by inhibiting various blood coagulation factors such as thrombin, and/or Factor Xa, thereby resulting in incoagulable blood [5-7,102-104]. These ailments further progress to compartment syndrome, characterized by increased pressure within one of the body's compartments resulting in insufficient blood supply to tissues within its vicinity, and loss of sensation over the nerve areas passing through the compartment [95]. Further, RV-envenomed patients also develop hypovolemia due to blood loss by either external bleeding or accumulation in compartments, acute kidney injury (previously termed as acute renal failure or ARF), intravascular haemolysis, haematemesis (blood vomiting), haematuria (blood in urine), haemoptysis, hypotension, and enhanced capillary permeability [14,95-97,105]. Intravascular haemolysis and bleeding complications are primarily inflicted by PLA_2 isoenzymes that can cause lysis of phospholipids of erythrocyte membranes thereby leaving the cells vulnerable to dissolution [29]. While RVV X activators, LAAO, and PLA_2 isoforms are responsible for acute kidney injury [106-108], VEGF exhibits potent hypotension and enhancement of vascular permeability thereby resulting in overall bleeding complications [83].

The above major clinical symptoms are manifested by RV-envenomed patients throughout the country; however, RV-bite patients from SI and a few victims from WI are also reported with ptosis, bulbar palsy, inter-nuclear ophthalmoplegia, and

respiratory paralysis due to pre-synaptic neuromuscular block [95,96,109,110]. While the neurological symptoms are very frequent and severe in SI, they are very rarely reported in WI. These differences in severity of neurological symptoms can be well explained on the basis of variable amounts of neurotoxic PLA_2 isoforms in RVV samples from SI (19.1%) and WI (3.2%) as determined by proteomic analyses. RV-envenomed patients from EI neither exhibit neurotoxic symptoms [14] nor any such PLA_2 isoform was identified in EI RVV.

4.2.5 Potency of commercial polyvalent antivenom in the treatment of RV-envenomed patients in India

Parenteral administration of equine antivenom is the only adequate choice of treatment for snake envenomation. However, the safety and efficacy of equine antivenom are of immense concern for successful hospital management of bite victims [111-113]. Due to the frequency and severity of envenomation by the 'Big Four' snakes (*N. naja*, *D. russelii*, *E. carinatus*, and *B. caeruleus*), the Indian commercial PAV is raised against a cocktail of venoms of these four species. However, several other species of venomous snakes such as *N. kaouthia*, *B. sindanus*, *B. walli*, *B. niger*, *Hypnale hypnale*, *Trimeresus malabaricus,* and *T. gramineus* are also reported to cause a significant number of fatalities [113-118]. Therefore, the inclusion of venom from some of these medically relevant snake species in the immunizing mixture might also be considered to render the Indian PAV effective against a wide range of medically relevant snake species.

Several studies have raised concerns regarding the efficacy of commercial Indian PAVs to recognize and neutralized the low molecular weight (<20 kDa) toxins of RVV [9,11,23,119]. These findings correlated well with the results of the present study. While poor immunogenicity of low molecular mass RVV toxins clearly seems to be the bottleneck for generating sufficient antibodies against these toxins in horses, poor recognition of heterologous RVV toxins with respect to disparities in RVV composition owing to geographical location is also a major concern [14,120]. In India, the venoms collected from snakes inhabiting a small area around Mahabalipuram in Tamil Nadu, SI by the Irula Snake Catchers Industrial Cooperative Society (ISCICS) is the primary source of snake venoms for raising commercial PAV [113]. However, there are reports stating the inefficacy of Indian PAV against snakebite in areas distant from the source of immunizing venoms. In particular, clinical reports suggest relatively poor

effectiveness of Indian PAV in the treatment of RV envenoming in Maharashtra and northern Kerala [113]. Further, for better hospital management of snakebite victims, development of three new regional antivenoms in India was also proposed. For example, in addition to the 'Big Four' species, venoms of *N. kaouthia, B. walli*, *B. niger* and one of the pit-vipers in north-east PAV, *N. oxiana, B. sindanus, E. c. sochureki* and *Macrovipera lebetina* in north-west PAV, and *B. sindanus*, *H. hypnale*, *T. malabaricus,* and *T. gramineus* in south-west PAV might be included in the respective immunizing cocktails [113]. However, the design of such region-specific PAVs is yet to be implemented and one of the major reasons may be the cost factor and scarcity of sufficient amount of venom for raising antivenom in horses.

ELISA and western blotting are widely used to determine the immuno-reactivity of venom components against commercial PAV [9,23,24,88,121]. Both these analyses of crude WI, EI, and SI RVV, and GF fractions of WI and EI RVV unequivocally pointed towards the poor immunogenicity of low molecular mass components (<20 kDa) of these venom samples. Further, the swamping of abundant better immunogenic high-molecular mass RVV proteins, as well as antibodies against the other three species of 'Big Four' snake present in PAV, might be a possibility for the observed poor immuno recognition of low molecular mass RVV proteins. In addition, WI RVV and its GF fractions exhibited better immuno cross-reactivity towards MAV compared to PAV, thereby indicating that MAV is a better choice of antivenom treatment against RV bites. However, due to a lack of reliable snakebite detection kits in India, the species of snake responsible for envenomation cannot be identified with certainty and therefore, physicians prefer administration of PAV for treating snakebite. This also necessitates the development of a reliable snakebite detection kit.

Although widely employed due to ease of operation, however, ELISA and western blotting methods are associated with certain limitations. Assessment of immuno-reactivity by western blot analysis provides a Yes/No response and thus is primarily a qualitative technique [122]. Further, preparation of samples for separation by SDS-PAGE analysis under reduced conditions may denature the proteins thereby leading to loss of conformational epitopes [122]. On the contrary, although ELISA can quantify the antibody binding levels, however, the proteins that lack recognizing antibodies in the antivenom cannot be identified [122]. Antivenomics analysis provides the necessary qualitative as well as quantitative information on the immunological

profile of venoms in which immuno-reactivity is coupled to proteomic identification of the reacting and non-reacting venom components [21,25]. The method relies on the principle of either immunodepletion of venom toxins by antivenom (1st generation) or immunoaffinity chromatography (2nd generation) followed by the LC-MS/MS identification of the antivenom unbound and bound venom components [21,25,88,122]. Identification of poorly immunogenic components of venom can provide valuable insights for designing immunizing protocols specifically against these toxins so as to develop improved antivenom that will deliver more extensive protection against all venom toxins.

Antivenomics studies suggested that PLA_2 and KSPI are the major PAV unbound toxins in WI, EI, and SI RVV samples. All the major PLA_2 isoforms of the RVV samples from WI (gi|400714), EI (AAZ53180.1) and SI (P86368) were found to be poorly immuno-reactive to Indian PAVs. In addition, the tested PAVs could not recognize the major neurotoxic PLA_2 isoform (P59071) of SI RVV. Further, several SVMP and SVSP were also identified in PAV unbound fractions of EI RVV. As already described, these are haemostatically active proteins in RVV that play a pivotal role in RVV-induced toxicity and exhibit diverse pharmacological effects in bite victim. Therefore, poor recognition of these RVV toxins by commercial PAVs can be major hurdle for effective antivenom therapy [9,23].

RVV is predominated by enzymatic proteins that play a profound role in its pharmacological effects; therefore, the neutralization potency of antivenom against a wide array of enzymatic activities and pharmacological properties of RVV also provides valuable information on the efficacy of the tested antivenom. Interestingly, the neutralization potency of PAVs toward various properties of WI, EI, and SI RVV was found to vary significantly. Nevertheless, MAV exhibited better neutralization of enzymatic activities and pharmacological properties of WI RVV. All the enzymatic activities and pharmacological properties exhibited by SI RVV were well neutralized by PAVs with exceptions of PLA_2 and indirect hemolytic activity. Therefore, the poor inhibition of PLA_2 activity of RVV is well corroborated with the poor recognition of PLA_2 enzymes established by antivenomics studies. On the contrary, PAVs were found to be extremely poor in neutralizing several enzymes such as fibrin(ogen)olytic, TAME, BAEE, and pro-coagulant properties of WI and EI RVV. This discrepancy in neutralization potency of PAVs against the venom of same species of snake further

demonstrates the role of geographic location and its influence on RVV composition, leading to the differential efficacy of the same antivenom against different populations of RV. Further, the better neutralization of SI RVV toxins compared to those from EI and WI correlates well with the findings of the western blot as well as antivenomics studies. The use of snake venoms primarily from Irula Snake Catchers' Industrial Cooperative Society, SI for raising equine antivenom [113] explains the observed differential neutralization potency of commercial PAVs against RVV samples from different locales of the country. Therefore, there is an urgency in devising improve immunization schemes to include venom pools from wide geographical locations to render the existing PAV effective throughout the country. Alternatively, efforts can also be made to develop region-specific antivenoms for better hospital management of RV bite patients [113]. Moreover, our study also suggests the development of species-specific snakebite detection kit for better treatment of snakebite patients using MAV instead of PAV.

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