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1 Snake Venomics Display: An online toolbox for visualization of snake
2 venomics data

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24 Abstract

25 With the introduction of powerful mass spectrometry equipment into the field of snake venom
26 proteomics, a large body of venomics data is accumulating. To allow for better comparison between
27 venom compositions from different snake species and to provide an online database containing this
28 data, we devised the Venomics Display toolbox for visualization of venomics data on linear scales.
29 This toolbox is freely available to be used online at [https://tropicalpharmacology.com/tools/snake-](https://tropicalpharmacology.com/tools/snake-venomics-display/)
30 [venomics-display/](https://tropicalpharmacology.com/tools/snake-venomics-display/) and allows researchers to visualize venomics data in a Relative Abundance (%)
31 visualization mode and in an Absolute Abundance (mg) visualization mode, the latter taking venom
32 yields into account. The curated venomics data for all snake species included in this database is also
33 made available in a downloadable Excel file format. The Venomics Display toolbox represents a
34 simple way of handling venomics data, which is better suited for large data sets of venom
35 compositions from multiple snake species.

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39 **Keywords:** Venomics; Snake venom; Venom proteomics; Snake Venomics Display; Visualization
40 of venomics data, Snake venomics

41 **Introduction**

42 Venom proteomics has gained increasing attention in the last decade due to scientific interests in
43 venom compositions, venom/toxin evolution, and elucidation of pathophysiological mechanisms of
44 envenomings, as well as technological advances within proteomics and mass spectrometry that have
45 allowed researchers to perform ever more in-depth investigations. In addition to venomics (Calvete,
46 2014), new fields have recently emerged, such as quantitative venomics, antivenomics, and functional
47 venomics/toxicovenomics (Calvete, 2010; Calvete et al., 2017, 2009; Calvete and Lomonte, 2015;
48 Laustsen, 2016; Laustsen et al., 2015a, 2015b; Lomonte and Calvete, 2017). Particularly within snake
49 venomics, this has created a wealth of data that allows researchers to obtain a deeper understanding
50 of venom function(s), evolutionary strategies for defense and prey subduction, and for developing
51 improved antivenoms (Laustsen, n.d.; Laustsen et al., 2015a). However, with increasing complexity,
52 a need for better structure and visualization of data presents itself. Inspired by how DNA and protein
53 sequences are often visualized by linear alignment, and to alleviate the need for a database containing
54 snake venomics data (Tasoulis and Isbister, 2017), we gathered all reported snake venomics data and
55 created an Open Access visualization toolbox that is freely available to be used online. This toolbox,
56 coined Snake Venomics Display, may help researchers obtain an overview of venom compositions
57 within snake families, genera, and species, as well as guide scientist and physicians to quickly
58 determine which toxin families are abundant in a given snakebite. This may be useful in the
59 interpretation of large sets of venomics data, and it may aid the development of new antivenoms.
60 Additionally, we have made all the venomics data included in our online database freely available in
61 an Excel format by direct download via a link in the Snake Venomics Display toolbox.

62 **Methods**

63 **Data collection**

64 Data on toxin abundances was retrieved for 232 venom proteomes and for 10 venom gland
65 transcriptomes (identified by a superscripted asterix in the snake name) from 143 snake species
66 characterized in 103 original articles reviewed by Calvete (Calvete, 2013), Laustsen et al. (Laustsen
67 et al., 2016), and Tasoulis & Isbister (Tasoulis and Isbister, 2017), and an online database was created.
68 Abundances for trace toxins were consistently set to the maximum value of the interval (e.g. an
69 abundance reported as <0.1% was set to 0.1% in our database). Venom yields were obtained from
70 <http://snakedatabase.org/> for the 83 species for which this information was available. In cases where
71 the total venom abundance (in %) exceeded 100%, the data was normalized. All included venomics
72 data is available in an Excel format by direct download in the Snake Venomics Display toolbox.

73

74 **Building the program**

75 The program was designed using the WordPress plugin: “wpDataTables”. This plugin is widely used
76 for its table-generation feature, and it possesses highly customizable charting functionalities used for
77 the Snake Venomics Display toolbox. The venomics database described above was loaded into the
78 plugin, and filters were specified with user-friendliness and functionality in mind. The data was then
79 loaded in the plugin’s “HighCharts” rendering software to display an interactive horizontal bar chart.
80 Important functions, like responsiveness and setting the chart to follow the filter, were activated. A
81 color scheme was manually defined so that colors express the protein family of the toxins. Visual
82 specifications for the chart, such as units for axes and numbers, size, and credits link, were set, and
83 the chart was embedded on the webpage. The same procedure was executed for both Snake Venomics
84 Display visualization modes (Relative Abundance and Absolute Abundance).

85

86 **Results and discussion**

87 **How to use the Snake Venomics Display toolbox**

88 Upon loading the Snake Venomics Display toolbox at [https://tropicalpharmacology.com/tools/snake-](https://tropicalpharmacology.com/tools/snake-venomics-display/)
89 [venomics-display/](https://tropicalpharmacology.com/tools/snake-venomics-display/), a small description of the two currently available visualization modes (Relative
90 Abundance and Absolute Abundance) is displayed together with buttons to access these modes
91 (Figure 1). By clicking on one of these buttons, the user can use a tool in the Snake Venomics Display
92 toolbox. The toolbox is by default filtered to display all venomics data available. However, the
93 displayed snakes can be modified using the filtering system below the chart. Here, seven settings can
94 be modified: "Snake" (name in Latin), "Common names" (in English), "Genus", "Family", "Country",
95 "Region", and "Venom yield". The latter allows the user to only display data on snake venoms that
96 have venom yields in a specified range (in mg). Venom yield data was retrieved from
97 <http://snakedatabase.org/>. "Region" allows the user to select a region from which a desired snake or
98 group of snakes are endemic. The snakes have been put into regions according to
99 <http://www.toxinology.com/>. Searching for a country in the "Country" filter will display all snakes
100 endemic in that specific country. "Family" allows the user to define which snake family to look at.
101 "Genus" allows for filtering on the genus level, while "Latin name" can both filter for genus as well
102 as a specific snake species. The "Common names" filter will display the venom compositions for
103 snakes with a given common name. The common names have been acquired from
104 <http://www.toxinology.com/>. The "Snake" filter is modified by typing the desired snake species or
105 genus using Latin names, while "Common names" is modified by typing the desired common name
106 of a species in English. "Country" and "Region" are applied similarly by typing the desired region
107 and/or country. "Genus" and "Family" are specified using a drop-down menu. To remove the current
108 filter and display all snakes in the database, the "CLEAR FILTERS" button is clicked. By clicking
109 on the snake name, the user will be taken to the PubMed entry of the original publication from which

110 the data was collected. Finally, an “add data by request” button is provided to allow users to submit
111 their own published venomics data to help keep the database up to date.

112

113 **Relative venom compositions**

114 The Snake Venomics Display toolbox enables easy comparison of snake venoms by linear
115 visualization of venomics data. By selecting the Relative Abundance Display, the user will be able to
116 compare relative venom compositions (toxin family abundances expressed as percent of whole
117 venom) for families, genera, and species of snakes from different regions of the world. This can be
118 useful for quickly obtaining an overview of which toxin families are dominant in a given snake venom
119 and how this compares with closely and/or distantly related species. It is envisioned that this may be
120 particularly useful for researchers who wish to compare venoms from many snake species in relation
121 to snake venom evolution.

122 As an example, the relative abundance of toxin families present in venoms from the
123 *Bitis* genus can be seen in [Figure 2](#). From this visualization, it quickly becomes evident that the *Bitis*
124 venoms share a similar relative venom composition, although *Bitis caudalis* distinguishes itself by
125 having a much higher proportion PLA₂s (purple).

126 In comparison with the similar, yet clearly different venom compositions of the *Bitis*
127 genus, the venom compositions for four selected *Naja* venoms are clearly more similar in terms of
128 relative abundance of toxin families ([Figure 3](#)). However, as these snake species are reported to
129 deliver very different venom yields when milked, the clinical manifestations may differ between bites
130 from different species within the genus. To visualize venom compositions in closer relation to the
131 possible medical impact that a bite from a given snake species may have, the Absolute Abundance
132 visualization mode was developed.

133

134 **Absolute venom compositions**

135 The Absolute Abundance visualization mode was developed to take venom yields into account when
136 displaying venomics data. This represents a simple way of observing venom compositions, which
137 may possibly provide a slightly more reliable indication of which toxin families are most medically
138 relevant for a given envenoming case. As an example of this visualization mode, the same venoms
139 from the *Bitis* genus are displayed in [Figure 4](#). Here, it quickly becomes evident that even though *B.*
140 *caudalis* venom is dominated by PLA₂s, this toxin family is more likely to have an actual medical
141 impact in bites from the *Bitis gabonica* species due to the insignificant venom yields delivered by *B.*
142 *caudalis* and the high venom yields delivered by *B. gabonica*.

143 Similarly, a very different picture emerges when comparing the previously selected
144 *Naja* venoms in the Absolute Abundance visualization mode ([Figure 5](#)). Although bites from all four
145 snake species should be handled as critical medical emergencies, it seems evident that severe bites
146 from *Naja mossambica* can be more serious than bites from the other species.

147 A word of caution needs to be highlighted. Although the Absolute Abundance
148 visualization mode may seem useful for evaluating the medical impact of bites from different snake
149 species, this should in no case be used uncritically. Snakebites differ significantly, not only between
150 species, but also between different specimens, with larger specimens being able to deliver larger
151 amounts of venom in a bite. The Absolute Abundance visualization mode should thus mainly be used
152 to provide a general overview of the *possible* severity of bites from different snake species –
153 conceivably in introductory educational settings.

154 **Conclusions**

155 Snake Venomics Display is a toolbox for linear visualization of snake venomics data, which allows
156 for better comparison of large sets of snake venom proteomes. This toolbox will be continuously
157 improved for user-friendliness, as well as it will be updated with venomics data as this becomes

158 available. We invite researchers in the field to submit both such data as well as comments and
159 feedback, which we can use to make the Snake Venomics Display toolbox even more useful.

160

161 **Acknowledgments**

162 We thank Professor Juan Calvete, Instituto Biomedicina Valencia (Spain) for fruitful scientific
163 discussion. Thanks also go to the Novo Nordisk Foundation for financial support
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165

166 **Author contributions**

167 A.H.L. conceived the study. S.D.P. collected the data. S.H.D., R.U.W.F., and A.M.E. designed and
168 developed the program. S.H.D. and R.U.W.F. analyzed the case data presented in the manuscript.
169 A.H.L., S.D.P., S.H.D., and R.U.W.F. wrote the manuscript. All authors reviewed the manuscript.

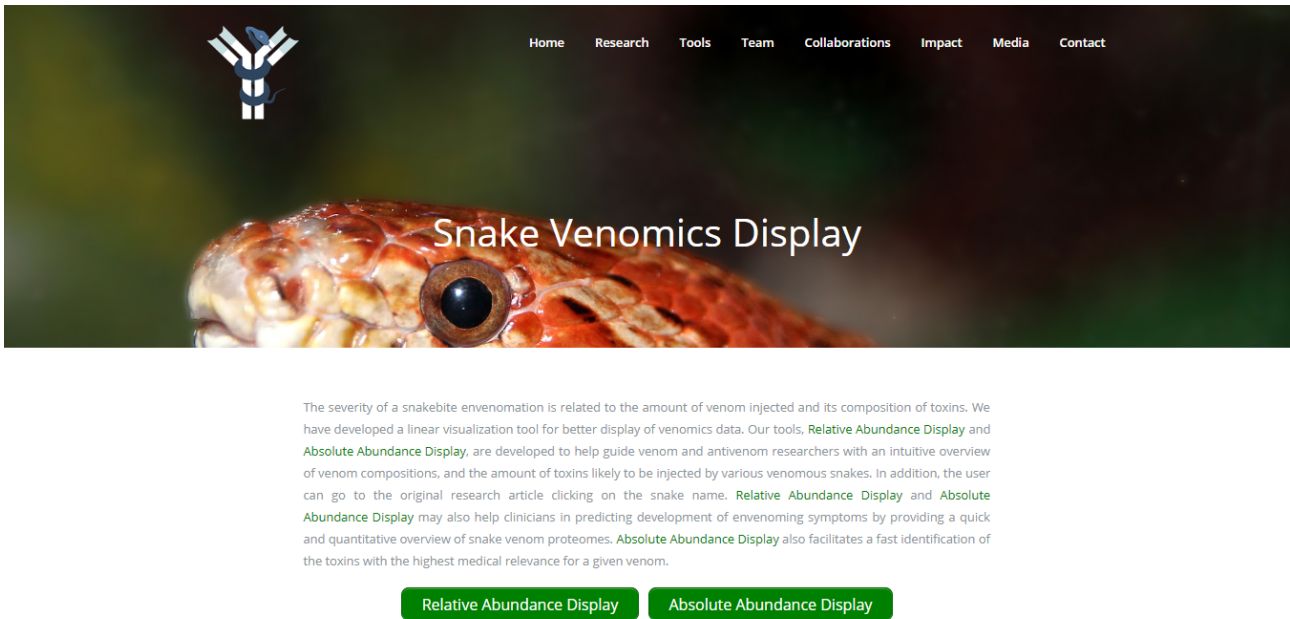
170 **References**

- 171 Calvete, J.J., 2014. Next-generation snake venomomics: protein-locus resolution through venom
172 proteome decomplexation. *Expert Rev. Proteomics* 11, 315–329.
173 <https://doi.org/10.1586/14789450.2014.900447>
- 174 Calvete, J.J., 2013. Snake venomomics: From the inventory of toxins to biology. *Toxicon*, Special
175 Issue: Toxins: from Threats to Benefits 20th Meeting of the French Society of Toxinology
176 (SFET) 75, 44–62. <https://doi.org/10.1016/j.toxicon.2013.03.020>
- 177 Calvete, J.J., 2010. Antivenomics and venom phenotyping: A marriage of convenience to address
178 the performance and range of clinical use of antivenoms. *Toxicon*, Highlights in
179 Toxinology: Biodiversity in Toxins - Tools for Biological Research and Drug Development
180 56, 1284–1291. <https://doi.org/10.1016/j.toxicon.2009.12.015>
- 181 Calvete, J.J., Lomonte, B., 2015. A bright future for integrative venomomics. *Toxicon*, Omic
182 perspectives of the toxin universe 107, Part B, 159–162.
183 <https://doi.org/10.1016/j.toxicon.2015.10.024>
- 184 Calvete, J.J., Petras, D., Calderón-Celis, F., Lomonte, B., Encinar, J.R., Sanz-Medel, A., 2017.
185 Protein-species quantitative venomomics: looking through a crystal ball. *J. Venom. Anim.*
186 *Toxins Trop. Dis.* 23, 27. <https://doi.org/10.1186/s40409-017-0116-9>
- 187 Calvete, J.J., Sanz, L., Angulo, Y., Lomonte, B., Gutiérrez, J.M., 2009. Venoms, venomomics,
188 antivenomics. *FEBS Lett.*, Prague Special Issue: Functional Genomics and Proteomics 583,
189 1736–1743. <https://doi.org/10.1016/j.febslet.2009.03.029>
- 190 Laustsen, A.H., 2016. Recombinant antivenoms, 1st ed. University of Copenhagen, Copenhagen,
191 Denmark.
- 192 Laustsen, A.H., n.d. Guiding recombinant antivenom development by omics technologies. *New*
193 *Biotechnol.* <https://doi.org/10.1016/j.nbt.2017.05.005>
- 194 Laustsen, A.H., Engmark, M., Milbo, C., Johannesen, J., Lomonte, B., Gutiérrez, J.M., Lohse, B.,
195 2016. From Fangs to Pharmacology: The Future of Snakebite Envenoming Therapy. *Curr.*
196 *Pharm. Des.* 22, 5270–5293. <https://doi.org/10.2174/1381612822666160623073438>
- 197 Laustsen, A.H., Lohse, B., Lomonte, B., Engmark, M., Gutiérrez, J.M., 2015a. Selecting key toxins
198 for focused development of elapid snake antivenoms and inhibitors guided by a Toxicity
199 Score. *Toxicon* 104, 43–45. <https://doi.org/10.1016/j.toxicon.2015.07.334>
- 200 Laustsen, A.H., Lomonte, B., Lohse, B., Fernández, J., Gutiérrez, J.M., 2015b. Unveiling the nature
201 of black mamba (*Dendroaspis polylepis*) venom through venomomics and antivenom
202 immunoprofiling: Identification of key toxin targets for antivenom development. *J.*
203 *Proteomics* 119, 126–142. <https://doi.org/10.1016/j.jprot.2015.02.002>
- 204 Lomonte, B., Calvete, J.J., 2017. Strategies in “snake venomomics” aiming at an integrative view of
205 compositional, functional, and immunological characteristics of venoms. *J. Venom. Anim.*
206 *Toxins Trop. Dis.* 23. <https://doi.org/10.1186/s40409-017-0117-8>
- 207 Tasoulis, T., Isbister, G.K., 2017. A Review and Database of Snake Venom Proteomes. *Toxins* 9.
208 <https://doi.org/10.3390/toxins9090290>
- 209

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212 **Figure legends**

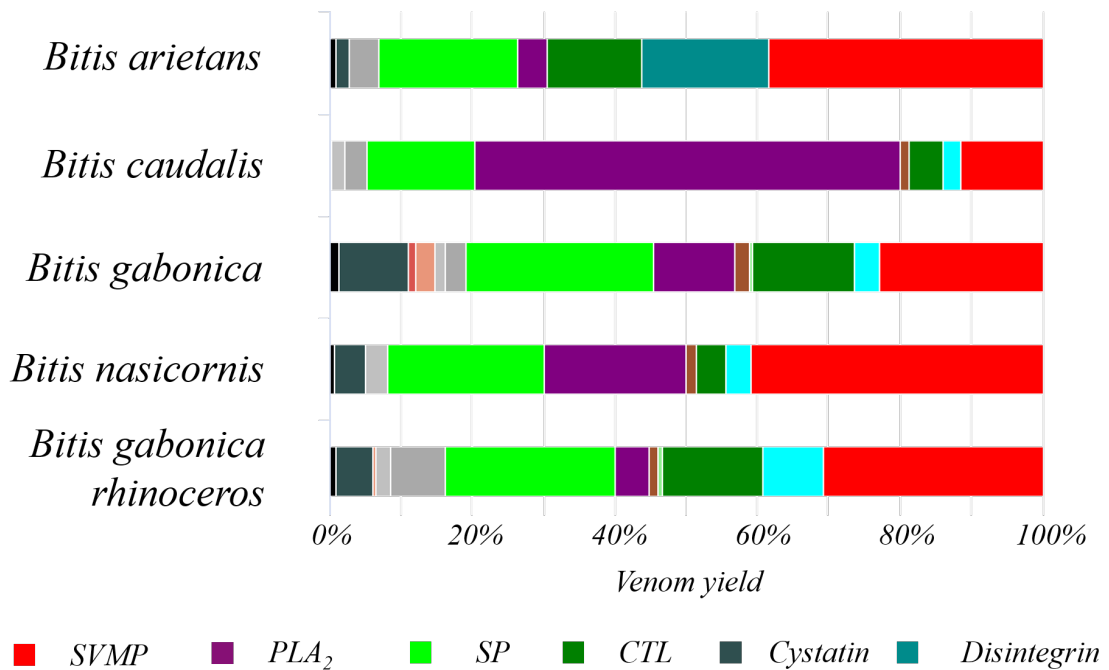


213

214 **Figure 1.** Initial view upon loading the Snake Venomics Display toolbox

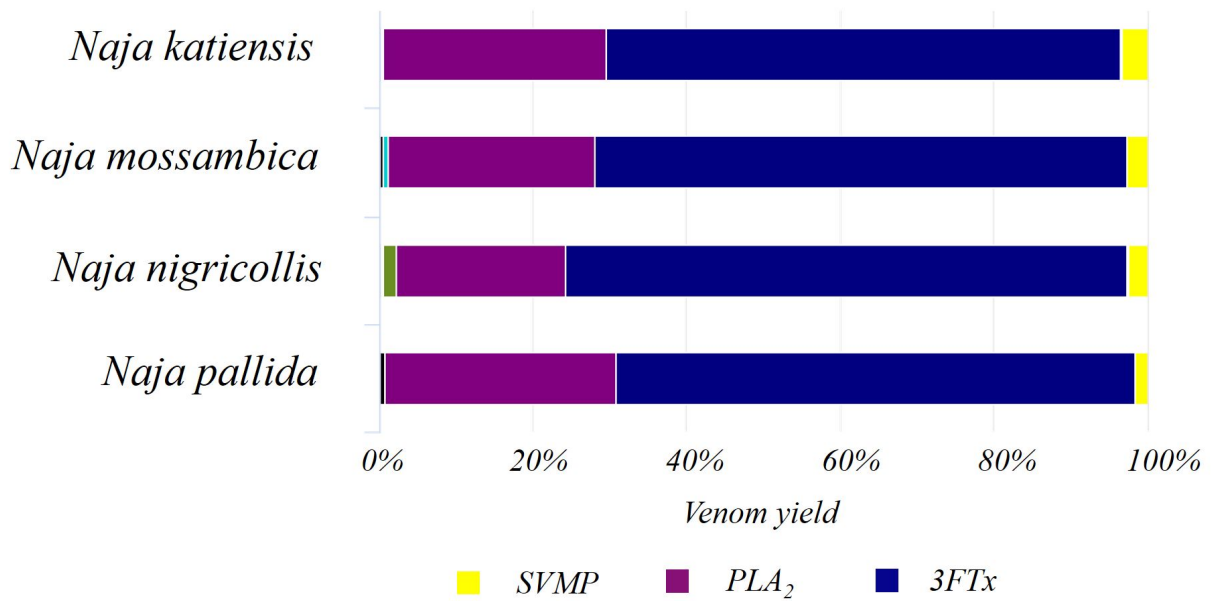
215 (<https://tropicalpharmacology.com/tools/snake-venomics-display/>).

216

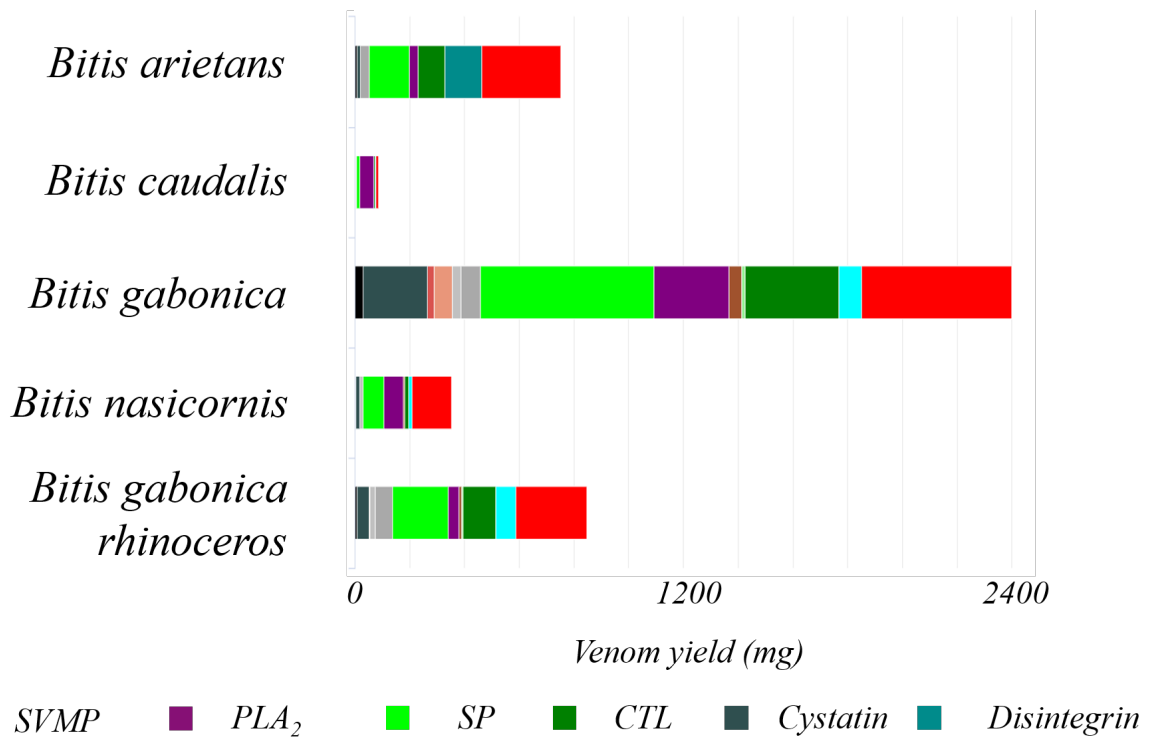


217

218 **Figure 2.** Display of the relative composition of selected venoms from the Bitis genus. Abbreviations:
 219 SVMP: Snake Venom MetalloProteinase. PLA₂: PhosphoLipase A2. SP: Serine Proteinase. CTL: C-
 220 Type Lectin.
 221



222
 223 **Figure 3.** Display of the relative compositions of selected venoms from the Naja genus.
 224 Abbreviations: SVMP: Snake Venom Metalloproteinases. PLA₂: Phospholipases A₂. 3FTx: Three-
 225 Finger Toxins.
 226



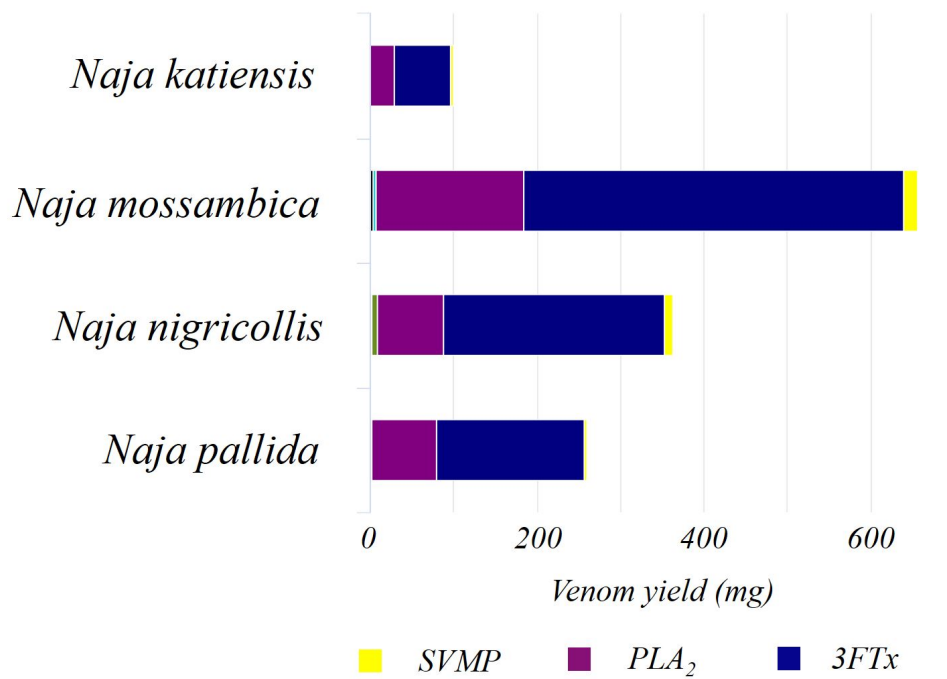
227

228 **Figure 4.** Display of the absolute compositions of selected venoms from the *Bitis* genus.

229 Abbreviations: SVMP: Snake Venom Metalloproteinase. PLA₂: Phospholipases A₂. SP: Serine

230 Proteinases. CTL: C-Type Lectins.

231



232

233 **Figure 5.** Display of the absolute compositions of selected venoms from the *Naja* genus.

234 Abbreviations: SVMP: Snake Venom Metalloproteinases. PLA₂: Phospholipases A₂. 3FTx: Three-
 235 Finger Toxins.

236

237