

Supplementary Materials: Acute Toxicities of the Saxitoxin Congeners Gonyautoxin 5, Gonyautoxin 6, Decarbamoyl Gonyautoxin 2&3, Decarbamoyl Neosaxitoxin, C-1&2 and C-3&4 to Mice by Various Routes of Administration

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Table S1. Time to onset of symptoms, mortalities, death times and recovery times of mice dosed with the saxitoxin derivatives.

GTX5

Acute toxicity by intraperitoneal injection

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 0.100 | 1 | 6 | 0 | - | 1 | 48 |
| 0.125 | 2 | 2, 3 | 1 | 7 | 1 | 78 |
| 0.158 | 2 | 1, 2 | 2 | 7, 7 | 0 | - |
| 0.199 | 1 | 3 | 1 | 6 | 0 | - |

Acute toxicity by gavage

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 12.6 | 1 | - | 0 | - | 1 | 90 |
| 15.0 | 2 | 8, 10 | 0 | - | 2 | 125, 175 |
| 18.9 | 3 | 13, 15, 20 | 2 | 161, 255 | 1 | 247 |
| 23.8 | 2 | 5, 8 | 2 | 125, 147 | 0 | - |

Acute toxicity by feeding

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 40.0 | 1 | 29 | 0 | - | 1 | 327 |
| 50.0 | 3 | 23, 28, 30 | 1 | 152 | 2 | 142, 305 |
| 64.0 | 2 | 20, 23 | 2 | 77, 74 | - | - |

C1&2

Acute toxicity by intraperitoneal injection

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 0.250 | 1 | 2 | 0 | - | 1 | 46 |
| 0.320 | 2 | 3, 4 | 0 | - | 2 | 103, 105 |
| 0.400 | 2 | 2, 3 | 1 | 11 | 1 | 110 |
| 0.449 | 1 | 3 | 1 | 19 | 0 | - |

Acute toxicity by gavage

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 28.0 | 2 | 26, 31 | 0 | - | 2 | 118 |
| 35.0 | 3 | 16, 19 | 1 | 32 | 2 | 182 |
| 44.0 | 2 | 7, 17 | 2 | 85, 98 | 0 | - |

Acute toxicity by feeding

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 55.0 | 1 | 42 | 0 | - | 1 | 142 |
| 69.0 | 2 | 30, 45 | 0 | - | 2 | 255, 617 |
| 87.0 | 3 | 21, 27 | 3 | 173, 72, 110 | - | - |

GTX6

Acute toxicity by intraperitoneal injection

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 0.119 | 1 | 10 | 0 | - | 1 | 185 |
| 0.150 | 2 | 2, 9 | 0 | - | 2 | 70, 78 |
| 0.189 | 3 | 1, 2 | 2 | 5, 10 | 1 | 181 |
| 0.238 | 1 | 2 | 1 | 4 | - | - |

Acute toxicity by gavage

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 25.0 | 2 | 17, 30 | 0 | - | 2 | >535, > 382 |
| 31.0 | 3 | 15, 22, 25 | 3 | 52, 80, 80 | 0 | - |
| 40.0 | 1 | 21 | 1 | 90 | 0 | - |

Acute toxicity by feeding

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 94.0 | 1 | 85 | - | - | 1 | 303 |
| 119 | 1 | 80 | - | - | 1 | 400 |
| 151 | 1 | 46 | - | - | 1 | 392 |
| 188 | 1 | 53 | - | - | 1 | 347 |

dcGTX2&3

Acute toxicity by intraperitoneal injection

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 0.032 | 1 | 12 | 0 | - | 1 | 123 |
| 0.040 | 3 | 4, 9, 11, | 1 | 9 | 2 | 205, 312 |
| 0.050 | 2 | 2, 3 | 2 | 7, 11 | 0 | - |
| 0.063 | 1 | 4 | 1 | 6 | 0 | - |
| 0.079 | 1 | 2 | 1 | 6 | 0 | - |

Acute toxicity by gavage

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 4.80 | 1 | 62 | 0 | - | 1 | 202 |
| 6.00 | 3 | 10, 15, 53 | 0 | - | 3 | 120, 105, 218 |
| 7.60 | 2 | 9, 10 | 2 | 15, 52 | 0 | - |

Acute toxicity by feeding

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 15.9 | 1 | 34 | 0 | - | 1 | 85 |
| 25.0 | 3 | 34, 55, 113 | 0 | - | 3 | 200, 270, 138 |
| 32.0 | 2 | 31, 72 | 2 | 147, 82 | 0 | - |

dcNeoSTX

Acute toxicity by intraperitoneal injection

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 0.277 | 1 | 8 | 0 | - | 1 | 449 |
| 0.311 | 1 | 6 | 0 | - | 1 | 296 |
| 0.349 | 1 | 10 | 0 | - | 1 | 377 |
| 0.391 | 1 | 7 | 0 | - | 1 | 342 |
| 0.439 | 3 | 4, 8, 16 | 0 | - | 3 | 309, 470, 522 |
| 0.493 | 2 | 2, 3 | 2 | 50, 180 | 0 | - |

Acute toxicity by gavage

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 3.50 | 1 | 105 | 0 | - | 1 | 152 |
| 4.40 | 2 | 95, 181 | 0 | - | 2 | 305, 371 |
| 5.50 | 3 | 53, 87, 132 | 2 | 435, 380 | 1 | 531 |
| 7.00 | 2 | 100, 190 | 2 | 337, 290 | 0 | - |

Acute toxicity by feeding

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 12.8 | 1 | 68 | 0 | - | 1 | 382 |
| 14.3 | 2 | 85, 110 | 1 | 354 | 1 | >443 |
| 16.1 | 2 | 53, 90 | 2 | 425, 518 | 0 | - |
| 18.0 | 1 | 40 | 1 | 250 | 0 | - |
| 20.2 | 1 | 133 | 1 | 219 | 0 | - |

C3&4

Acute toxicity by intraperitoneal injection

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 0.446 | 1 | 8 | 0 | - | 1 | 141 |
| 0.472 | 2 | 8, 9 | 0 | - | 2 | 108, 117 |
| 0.500 | 3 | 3, 3, 5, | 3 | 20, 31, 43 | 0 | - |

Acute toxicity by gavage

| Dose ($\mu\text{mol/kg}$) | Total number of mice | Time to onset of symptoms (minutes) | Number of dead mice | Time of death (minutes) | Number of surviving mice | Time to recovery (minutes) |
|-----------------------------|----------------------|-------------------------------------|---------------------|-------------------------|--------------------------|----------------------------|
| 40 | 2 | 26, 33, | 0 | - | - | 240, 80 |
| 50 | 3 | 10, 12, 17 | 3 | 46, 52, 44 | - | - |