Why scorpion stings are so painful

3 August 2017, by Bob Yirka

Mesobuthus martensii, also known as the Chinese golden scorpion. Credit: Dr. Shilong Yang

(Phys.org)—A combined team of researchers from the U.S. and China has figured out why scorpion stings are so painful. In their paper published on the open access site *Science Advances*, the team explains how scorpion venom containing a variety of toxins and is mildly acidic, causing a lot of pain.

Scorpions have stingers on the ends of their tails that pierce the skin of victims and inject venom. Prior research has suggested the purpose of the venom is not to kill, but to cause pain so that predators will leave them alone. In this new effort, the researchers studied the venom and revealed why it is so painful.

They focused on a peptide called BmP01, previously identified as the most likely pain-causing ingredient in the fluid mixture of more than 100 toxins. Prior research has shown that it activates a pain signal carrying pathway in the brain called TRPV1. But what has confused prior researchers is why the peptide causes so much pain—on its own, it would not seem that the minuscule amount would be able to cause much pain. To find out what might be boosting its pain potential, the researchers looked at other ingredients and characteristics of the venom.

They noticed that the venom was mildly acidic. Looking even closer, they found that BmP01 tends to bind with proton-binding sites on TRPV1. Also, more importantly, the acid in the venom resulted in donations of protons that worked with BmP01 to heighten the amount of pain it could cause. Together, the researchers found, the two were able to unlock the gate that led to the TRPV1 pathway, which allowed more pain signals to pass through. That meant that the pain signals generated by the introduction of BmP01 into the body were magnified due to the acidity of the venom.

A scorpion faces its natural enemy. Although legendary for their toxicity, scorpion stings are also known to be extremely painful, apparently to deter larger predators that cannot be overpowered. Credit: Dr. Shilong Yang

The researchers note that inflicting pain as a survival mechanism by the scorpion suggests that there may be more than one toxin in the venom that is being enhanced by donated protons, adding up to the very painful experience reported by victims.

More information: Shilong Yang et al. A bimodal activation mechanism underlies scorpion toxin–induced pain, *Science Advances* (2017). DOI: 10.1126/sciadv.1700810 , advances.sciencemag.org/content/3/8/e1700810

Abstract
Venomous animals use peptide toxins for hunting and self-defense. To achieve these goals, toxins need to bind to their targets with high affinity due to the small amount that a single bite or sting can deliver. The scorpion toxin BmP01 is linked to sting-induced excruciating pain; however, the reported minimum concentrations for activating TRPV1 channel or inhibiting voltage-gated potassium (Kv) channels (both in the micromolar range) appear too high to be biologically relevant. We show that the effective concentration of BmP01 is highly pH-dependent—it increases by about 10-fold in inhibiting Kv channels upon a 1-U drop in pH but decreases more than 100-fold in activating TRPV1. Mechanistic investigation revealed that BmP01 binds to one of the two proton-binding sites on TRPV1 and, together with a proton, uses a one-two punch approach to strongly activate the nociceptive channel. Because most animal venoms are acidic, proton-facilitated synergistic action may represent a general strategy for maximizing toxin potency.

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