The stinging or "burning" sensation from a *Physalia physalis* (Portuguese man-of-war) is caused by a complex venom delivered through specialized stinging cells called nematocysts located in its tentacles. The venom contains a mixture of proteins, peptides, enzymes, and other non-protein compounds. [1]

## Key chemical components of the venom include:

- Physalitoxin: The primary toxic protein, described as a potent hemolytic (blood cell-destroying) and lethal agent. It is a large glycoprotein composed of three different subunits.
- **Enzymes:** The venom contains various enzymes that aid in incapacitating prey, including:
  - Phospholipase A2 and B
  - Collagenase and elastases
- **Neurotoxins:** Some toxins in the venom have neurotoxic effects by disrupting nerve function. Specific neurotoxins have been shown to affect:
  - Nicotinic cholinergic receptors, which impact muscle contractions and nerve signals.
  - o Glutamatergic transmission in neurons and neuromuscular junctions.
- Other bioactive compounds: The venom also contains a range of other components, such as:
  - Purines
  - Quaternary ammonium compounds
  - Biogenic amines, including histamine, which contributes to the inflammatory and painful reaction.
  - o Betaines [1, 2, 3, 4, 5]

## How the venom causes a "burning" sensationThe burning pain is the result of a multi-faceted attack on the victim's cells and nervous system:

- **Neurotoxic effects:** Certain components affect nerve cells, causing the intense and sometimes radiating pain.
- **Inflammatory response:** The presence of histamine and other components triggers a strong localized immune response, which includes pain, redness, and swelling.
- Cytolytic activity: Toxins in the venom create pores in cell membranes, which leads to calcium influx, osmotic swelling, and the destruction of the cells. This cellular damage contributes to the intense and persistent pain. [1, 2, 6, 7, 8]

Al responses may include mistakes.

- [1] https://pmc.ncbi.nlm.nih.gov/articles/PMC11598359/
- [2] http://lists.upstate.edu/pipermail/toxvtc/attachments/20250512/4a853080/attachment-0003.pdf
- [3] https://www.sciencedirect.com/science/article/pii/0005279581900696

- [4] https://pubmed.ncbi.nlm.nih.gov/6111356/
- [5] https://www.sciencedirect.com/science/article/abs/pii/0306452289902066
- [6] http://lists.upstate.edu/pipermail/toxvtc/attachments/20250512/4a853080/attachment-0003.pdf
- [7] https://www.sciencedirect.com/science/article/abs/pii/S0041010199002135
- [8] https://www.sciencedirect.com/science/article/pii/S0041010199001567