**Abstract**

*Clostridium botulinum*, which causes Botulism, is a bacterium found in soil and in improperly processed foods. Botulism causes neuromuscular diseases, where paralysis results in a part of the body because the nerves that supply it are diseased. Common symptoms of Botulism usually appear 12 to 36 hours after consumption and include a dry mouth, difficulty swallowing, slurred speech or difficulty speaking, muscle weakness, blurred or double vision, and drooping eyelids. Botulism works by blocking the release of neurotransmitters – chemicals which trigger neighboring nerves or activate muscle cells – through the action of Cofidal Neurotxins (CTNs) that break down soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) proteins, which are essential for fusion of the vesicle carrying the neurotransmitters with the cell membrane, thus releasing the neurotransmitters. If the neurotransmitters are not released, communication between nerve and muscle cells is halted, thus leading to paralysis. Botulism Toxins (BoNTs) are composed of three domains: receptor, translocation, and catalytic. The receptor domain of BoNTs binds to receptors in the surface of neurons and enters the neuron by receptor-mediated endocytosis. Once inside the neuron, the catalytic domain is translocated across the membrane of the vesicle by the translocation domain, into the cytosol, where the catalytic domain cleaves SNARE proteins. This blocks the release of neurotransmitters and leads to paralysis.

**Molecular Structure of Botulism Serotype-A**

**Light Chain**
- **Catalytic**
- **Receptor**
- **Translocation**

**Heavy Chain**
- **Catalytic**
- **Receptor**
- **Translocation**

**Botulinum Neurotoxin serotype A**

**PBD:3BTA**

**How BOTOX® cleaves SNAP25**

- **a)** SNAP25 is attached to a presynaptic membrane
- **b)** Binding of BoNT/A with SNAP25
- **c)** Complex leading to cleavage of SNAP25

**Conclusion**

Botulism causes (limp) paralysis by blocking the release of neurotransmitters. It breaks down SNARE proteins responsible for transmission between nerve and muscle cells. There are seven serotypes of the botulism neurotoxin: A-G. BoNT/A (the serotype used in BOTOX®) can be used to treat muscle spasms. This treatment results in normal control.

**Therapeutic Uses**

Botulinum Endotoxin (BOTOX®) has been approved by the Food and Drug Administration to treat: Strabismus (lazy eye), blepharospasm (uncontrolled blinking), cervical dystonia (involuntary muscle contractions in the neck), focal dystonia (the misfiring of nerves resulting in an undesirable muscle contraction), and severe primary axillary hyperhidrosis (excessive underarm sweating). BOTOX® is used for cosmetic treatments of wrinkles and frown lines. In the future, BOTOX® may be used for treating tinnitus (ringing in the ears), urinary incontinence, and excessive scarring.

**References**


**Introduction**

**Avian Botulism:**
- Ducks with footed paralysis in the neck
- Clostridium botulinum, a bacteria found in the soil, produces a toxin which targets neurons, causing paralysis.
- This toxin cleaves SNAP25 proteins, resulting in inhibited vesicle fusion (the muscle can no longer communicate with the nerve).
- Botulism is the most toxic protein to humans!
- However, Botulism is also the most commonly used protein in medicine.
- The Botulinum Neurotoxin has three domains: Receptor Binding, Catalytic, and Translocation.
- There are seven serotypes of Botulinum Neurotoxin (A-G). Serotype A is used in BOTOX®.

---

**Blepharospasm:**
- (uncontrolled blinking) Before and After Botox Treatment

---

**How SNAP25’s Role in Vesicle Fusion**

In a normal neuron, SNAP25 fuses with the v-SNARE protein to allow the release of a neurotransmitter into the synapse. The muscle cell can then respond to stimuli.

When the botulinum toxin is present, the light chain (the catalytic domain) cleaves SNAP25 and SNAP 25 can no longer fuse with the v-SNARE protein; therefore, the neurotransmitters cannot be released, and the muscle cell cannot respond.

**Before and After Botox**


---

**Botulism Neurotoxin (BOTOX®)** has been approved by the Food and Drug Administration to treat: Strabismus (lazy eye), blepharospasm (uncontrolled blinking), cervical dystonia (involuntary muscle contractions in the neck), focal dystonia (the misfiring of nerves resulting in an undesirable muscle contraction), and severe primary axillary hyperhidrosis (excessive underarm sweating). BOTOX® is used for cosmetic treatments of wrinkles and frown lines. In the future, BOTOX® may be used for treating tinnitus (ringing in the ears), urinary incontinence, and excessive scarring.

---

**References**
