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Analysis of *Botulinum* Neurotoxin A (BoNT/A) in pharmaceutical products using MALDI-TOF and LC-MS/MS

Yiu-chung Wong

Hong Kong Government Laboratory, Hong Kong

Botulinum neurotoxins (BoNT) are produced by the anaerobic bacterium *Clostridium botulinum* and are one of the most lethal known poisons ($LD_{50} = 0.8 \mu\text{g}$ for a 70 kg human by inhalation). Despite its high lethal toxicity, BoNT have been used to treat spasms and other muscle problems. Most recently, BoNT serotype A (BoNT/A) gains its worldwide popularity in cosmetic surgery to prevent development of facial wrinkles. Clinical testing of BoNT/A is conventionally relied on *in vivo* mouse lethality assay in accordance with pharmacopieal and AOAC methods. In response to increased public pressure to the inhumane testing, sensitive non-animal assays are of urgent need. Identification of BoNT/A in pharmaceutical products by chemical means is always a challenge due to its complex structure, ultra-trace level and the interference from excipients. This work reported a mass spectrometry study on BoNT/A in pharmaceutical injection samples. BoNT/A was isolated using magnetic beads immunoprecipitation, followed by on-beads digestion and was characterized by peptide mass finger printing using high-resolution tandem mass spectrometry coupled with ion mobility and Q-ToF in MS^E mode. The activity of the toxin was confirmed by its proteolytic activity towards specially designed synthetic SNAP-25 substrate. The specific cleaved peptide fragments obtained from SNAP-25 substrate correlated well with its proteolytic activity in linear range from 10 – 100 $MLD_{50}/\mu\text{L}$ ($r^2 > 0.99$). Proteolytic activities of BoNT/A in different excipient matrices were also investigated. The method has been validated across few brands of BoNT/A pharmaceutical injections commonly available in the Asia Pacific and was found to produce reliable results.

Biography

After working in the industry and academia, Dr. Wong joined the Hong Kong Government Laboratory in 1999 and is presently the Head of the Pharmaceutical Chemistry Section in the Laboratory. He is interested in the measurement of trace organic and inorganic toxicants in environment, food, dietary supplement and pharmaceutical matrices. Dr. Wong has organized a number of international proficiency testing programmes and developed several certified reference materials for food and herbal medicine. He has published more than 60 scientific papers and chapters. One of his papers has been awarded the Best Paper in analytical chemistry by CITAC in 2015. He is also the co-author of the book "Toxins and Toxicants in Food", which will be published by Wiley in late 2016.

ycwong@govtlab.gov.hk

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