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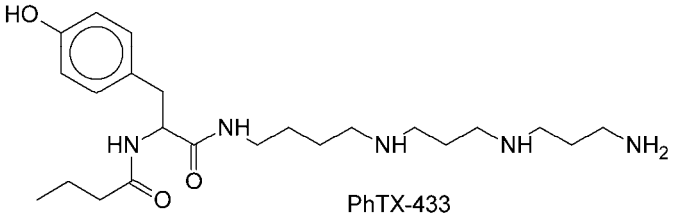
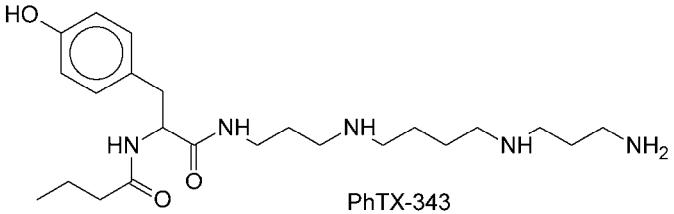
The Actions of Philanthotoxins-343 and -12 on Rat Neuronal Nicotinic Acetylcholine Receptors

Background

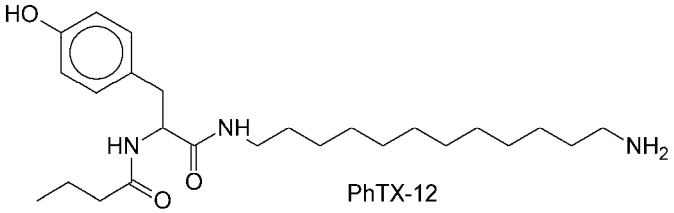
- Philanthotoxin-433 (PhTX-433) is a polyamine-containing active component of Egyptian digger wasp venom.
- It is a strong non-competitive inhibitor of ionotropic receptors such as nicotinic acetylcholine receptors (nAChR).
- Analogues have been generated that have greater selectivity and potency for nAChR.



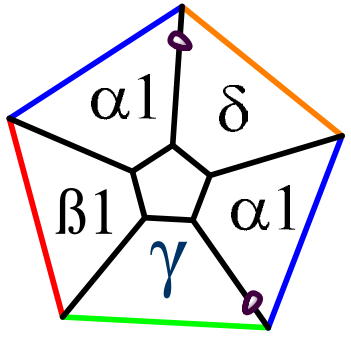
PhTX-433



PhTX-343



PhTX-12



Muscle-nAChRs

Aims

In this project we investigate the impacts of PhTX-433 analogues on the various N-nAChR subunit combination such as α4β2 and α3β4 expressed in Xenopus oocytes and using two-electrode voltage-clamp as recording technique.

PhTX	IC_{50} μM (-100mV)
PhTX-343	**16.6**
PhTX-12	**0.93**

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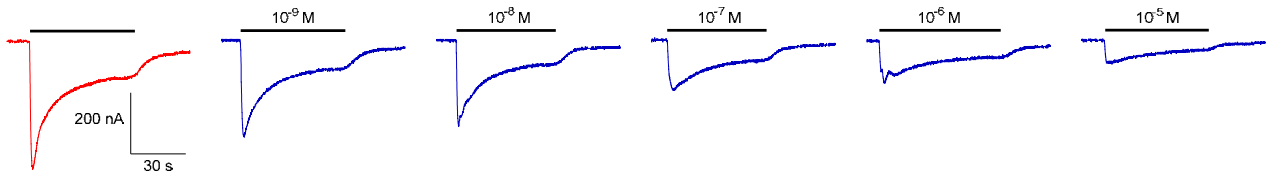
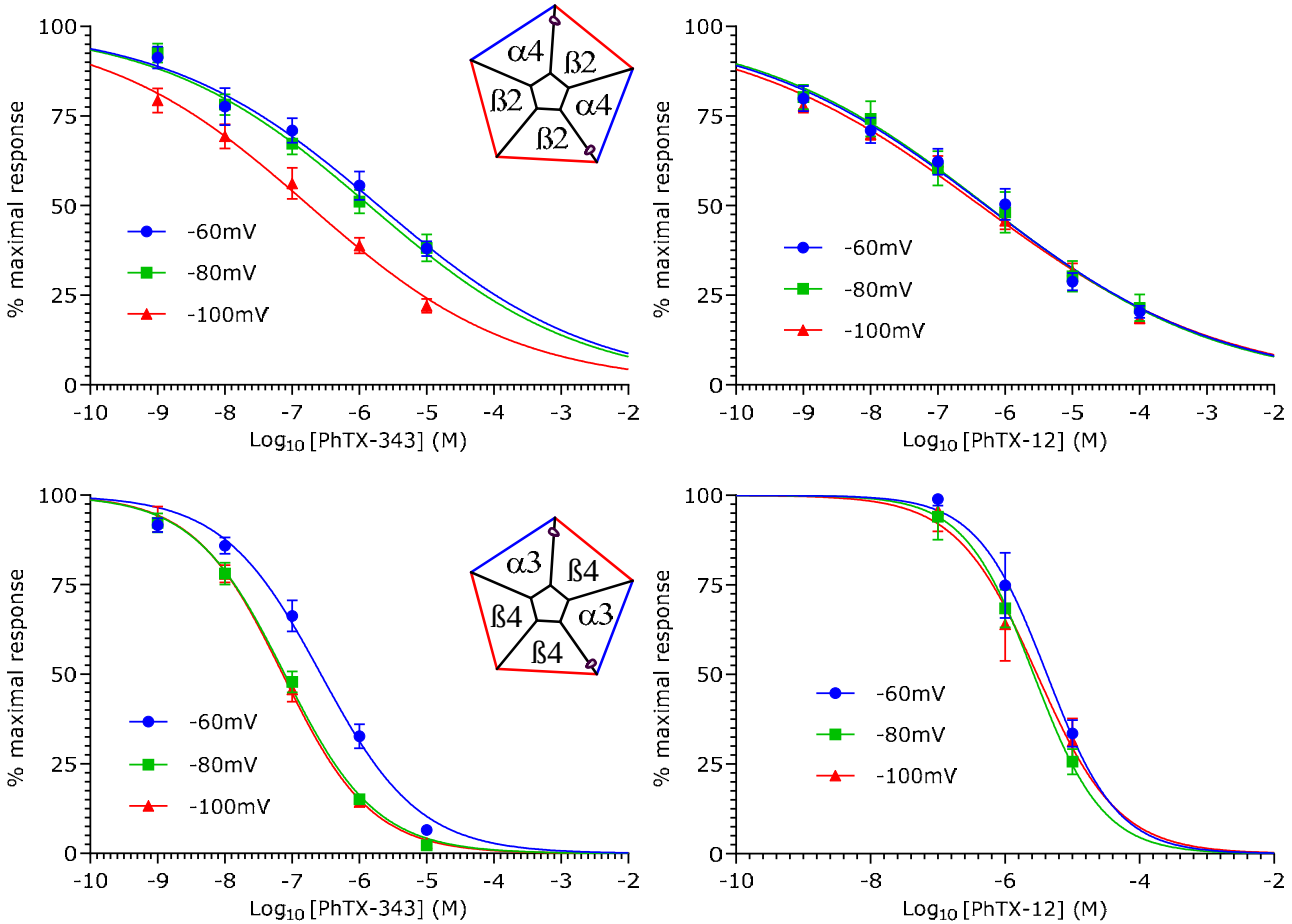
Results





Conclusion

PhTX-343 potency was strongly affected by subunit combination of nAChRs, while PhTX-12 activity was not.

This and previous evidence suggests alternative binding sites for the two analogues.

Philanthotoxin	α4β2 IC_{50} μM (-100mV)	A3β4 IC_{50} μM (-100mV)
PhTX-343	**0.17**	**0.071**
PhTX-12	**0.43**	**3**