

Synergism between food toxicants acting on sodium channels

Ciguatera fish poisoning (CFP) is one of the most frequent poisonings related to fish consumption. It is caused by the ingestion of fish contaminated with ciguatoxins (CTXs) produced by microalgae of the genus *Gambierdiscus* and *Fukuyoa*. The characteristic symptoms of the intoxication include gastrointestinal, cardiovascular and neurological disturbances. CTXs act on voltage-gated sodium channels (VGSC) by their binding to the site 5 of their alpha subunit, shifting the activation voltage towards more negative membrane potentials. This effect is enhanced by the coexistence of CTXs with other VGSC modulators which are also food contaminants as pyrethroid compounds, widely used in agriculture. Nowadays, an increasing presence of ciguatoxins in European Coasts and similarly, the increasing use of phytosanitary products for control of food plagues had raised the concerns regarding human health. In this work, the effects of ciguatoxins and pyrethroids in human sodium channels were investigated. The results presented in this study indicate that both types of compounds have a remarkable synergistic effect in voltage-dependent sodium channels. Exposure of human cells to these compounds elicited a decrease in the maximum peak inward sodium currents and hyperpolarized the activation voltage of sodium channels, effects that were boosted by the simultaneous presence of both toxicants. Since the regulatory levels in food for these components are set separately, this study highlights the need to re-evaluate their limits in feedstock considering that they act on the same cellular target.