The Inhibition of Neuronal Calcium Channels with Anthranilamide- and Aminobenzothiazole-Derived Compounds

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Neuropathic pain can result from nerve damage resulting from disease, surgery or trauma. It has been proposed that at least 3% of the world’s population suffer from this incapacitating condition and unfortunately symptoms often do not respond to existing therapies. For these reasons new drugs to treat neuropathic pain are of key importance. Due to N-type calcium channels (Ca,2.2 channels) being associated with neuropathic pain, we and others have been interested in the development of inhibitors of this channel. ω–Conotoxin GVIA (Figure 1), a 27 residue peptide present in the venom of the cone snail Conus geographus, is known to inhibit N-type calcium channels and hence we have developed small molecule type-III peptidomimetics. Two of the most active compounds from this endeavour, the anthranilamide 1 and the aminobenzothiazole 2 (Figure 1), have been previously reported.

In this presentation, our very recent investigations of the SARs for both compound classes, measured by the inhibition of Ca,2.2 channel activity in a SH-SY5Y neuroblastoma FLIPR assay, will be presented.

Figure 1. The 3D-structure of ω–Conotoxin GVIA with the relevant residues highlighted and the structure of the anthranilamide 1 and the aminobenzothiazole 2.

References