CADMIUM INHIBITS ENDOTHELIN-INDUCED, BUT NOT ACETYLCHOLINE-INDUCED, CONTRACTION OF THE SHARK (SQUALUS ACANTHIAS) VENTRAL AORTIC VASCULAR SMOOTH MUSCLE

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We have shown previously that cadmium (Cd^{2+}) produces contraction in isolated rings of vascular smooth muscle (VSM) of the ventral aorta of the spiny dogfish shark, Squalus acanthias (Evans and Weingarten, Toxicology 61: 275-281, 1990) and have hypothesized that the heavy metal interacted with muscarinic receptors because atropine blocked the response (Evans et al., Toxicology 62: 89-94, 1990). We have also recently characterized the receptor involved in the contractile response of the same tissue to the peptide endothelin (ET) (Evans and Gunderson, J Comp Physiol, in press, 1996). Wada et al. (Febs Lett 285: 71-74, 1991) have shown that Cd^{2+} displaces ET from receptors on the human placenta, non-competitively displaces ET from solubilized receptors, and inhibits ET-induced contraction of the rat aorta, suggesting that Cd^{2+} is a non-competitive inhibitor of ET receptors. Interestingly, Smith et al. (Environ Health Perspect 102 Suppl 3: 181-189, 1994) have recently proposed that Cd^{2+} interacts with an orphan receptor (no known ligand) which activates IP_3 formation. This proposed orphan receptor shares many characteristics with ET receptors. Thus, we initiated a series of experiments to determine if Cd^{2+} would interfere with either ACh- or ET-induced contraction of shark aortic VSM.

Rings were prepared and mounted as we have described previously (e.g., Evans, J Comp Physiol 162: 179-183, 1992), except that tension was monitored using a 4-channel, Biopac A/D recording system connected to a Macintosh 140 Powerbook. Rings were paired and, after an initial equilibration period at 500 mg tension, one was treated with Cd^{2+} (10^{-5} or 10^{-4} M) for 30 minutes, the other with the same volume of distilled water (10 or 100 µl in 10 ml elasmobranch Ringer's solution), before the addition of 10^{-4} M Ach or 10^{-7} M ET-1.

Incubation of shark aortic VSM rings in 10^{-4} M Cd^{2+} did not inhibit the contraction produced by subsequent addition of 10^{-4} M Ach ($p > 0.10$; $N = 13$), which suggests that, contrary to our previous hypothesis, Cd^{2+} may not interact directly with muscarinic receptors. The response to ET, on the other hand, was diminished significantly when the rings were incubated in 10^{-4} M ACh (Fig. 1). However, a lower concentration (10^{-5} M) of ACh was without effect.

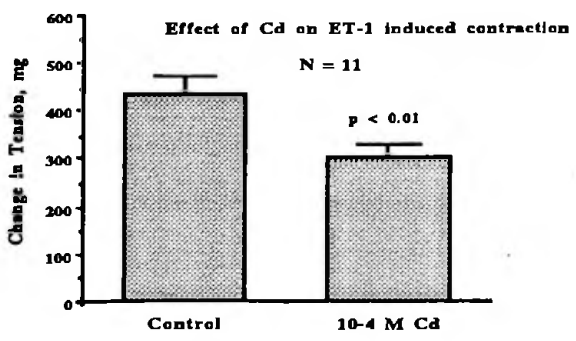

Figure 1

Our data suggest that Cd^{2+} may contract shark aortic VSM by interacting with ET receptors. This may account for the 50% of the Cd^{2+} induced contraction that is insensitive to atropine (Evans et al., Toxicology 62: 89-94, 1990). How Cd^{2+} stimulates atropine-sensitive contraction is still unknown. Supported by NSF IBN-9306997 and a Grant in Aid from the Maine Affiliate of the American Heart Association to DHE, a fellowship from the AHA to MG, and EHS-P30-ESO3828 to the Center for Membrane Toxicity Studies.).