# COMPARISON OF IN-VITRO DESENSITIZATION AT CARDIAC $\beta_1$- AND VASCULAR $\beta_2$ -ADRENOCEPTORS

S.W. Martin, K.J. Broadley, Division of Pharmacology, Welsh School of Pharmacy, UWCC, PO Box 13, Cardiff CF1 3XF.

β-adrenoceptors are known to be desensitized by chronic exposure to β-agonists (Harden 1983). Whether the two subtypes, $\beta_1$ and $\beta_2$, are equally susceptible to desensitization is controversial. Selective down-regulation of $\beta_1$-adrenoceptors occurs in isolated blood vessels after chronic infusion of rats with isoprenaline (ISO) (Cohen & Schenck 1987), although equal desensitization of cardiac $\beta_1$ and vascular $\beta_2$ responses occurred (Hayes et al 1986). Desensitization of cardiac $\beta_1$-responses has been demonstrated by incubation of isolated tissues with ISO (Herepath & Broadley 1990), however, limited data has been obtained with isolated vascular tissues. This study compares the susceptibility to in vitro desensitization of cardiac $\beta_1$- and vascular $\beta_2$- adrenoceptor-mediated responses.
Left atria, pulmonary artery and aorta were removed from rats (male, 250-350g) and immersed in Krebs solution (37°C) gassed with 5% $CO_2$ in $O_2$. Atria were paced at 2Hz while vascular rings (3-5mm) were suspended between wire hangers. Cumulative concentration-response curves for (-)-ISO were constructed, vascular rings being first contracted with noradrenaline (pulmonary, 60nM; aorta, 20nM). A maximum ISO concentration of 30μm was added but replaced by 1μm and left in contact with the tissue for 6h. During this time atria were not paced. The bath was then washed out 6 times over 1h and a second ISO curve constructed. Time-matched control experiments were performed and the mean ($n \geq 4$) changes in tension used to correct the pre-incubation curves.
After incubation with ISO, the concentration-response curve for left atrial tension was displaced to the right and the maximum increase in tension after incubation (0.29±0.19g, n=4) was significantly ($P<0.05$, paired Student's t-test) less than the corrected value before (0.40±0.09g). The pulmonary artery also showed a reduced maximum relaxation after incubation, from 0.37±0.06g (corrected, n=6) to 0.30±0.15g, however this was not significant. The maximum relaxation of the aorta was, in contrast, slightly greater after incubation with ISO (1.38±0.18g, n=4) than the corrected preincubation maximum (1.35±0.38g), but this was not significant.
Thus prolonged incubation with β-agonist induced a significant desensitization of the cardiac $\beta_1$-adrenoceptor-mediated responses, but the $\beta_2$-adrenoceptor-mediated vasorelaxation was either reduced non-significantly (pulmonary artery) or unaffected (aorta). These results suggest that the $\beta_2$-adrenoceptor is less susceptible to in vitro desensitization. However, the roles of agonist concentration and specificity of desensitization are currently under study.

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