ACTION OF TRACE AMINE *P*-TYRAMINE ON ADRENERGIC RECEPTORS IN ISOLATED PORCINE CORONARY ARTERY

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The trace amine *p*-tyramine can increase blood pressure (Premont *et al.*, 2001; Vaughan, 1994), and elevated levels of *p*-tyramine can be detected in hypertensives (Andrew *et al.*, 1993). Conventional thinking assumes that this amine exerts its pharmacological effects by releasing noradrenaline (NA) from sympathetic nerve endings which in turn acts on adrenoceptors, in other words it is an indirectly acting sympathomimetic amine (ISA). This study investigates whether the action of *p*-tyramine, on isolated porcine coronary vessels, can be attributed to ISA.

Fresh porcine hearts obtained from a local abattoir were immediately placed on ice. Left anterior descending coronary arteries were dissected from the myocardium and cut into 5mm rings. For endothelium denuded studies, endothelium was removed by gentle rubbing. Arterial rings were mounted on wires in an organ bath filled with Krebs solution at 37°C, aerated with 95% O_2 and 5% CO_2. An initial resting tension of 5g was applied after equilibration for 1 hour. Removal of endothelium was confirmed by absence of a relaxation by 10µM bradykinin of vessels pre-contracted with U46619 (5nM). Cumulative concentration-response curves (CRCs) to *p*-tyramine (0.1-3000 µM) and NA (0.1-100 µM) were then obtained. Adrenoceptor subtypes involved in the responses to NA and *p*-tyramine were evaluated using 3 µM DL-propranolol (non-selective β-adrenoceptor antagonist) and 1µM prazosin (α_1-adrenoceptor antagonist). α_2-Adrenoceptors on the endothelium, were eliminated by denuding endothelium. Isometric tension was recorded on a PowerLab/4SP computer system and plotted as % response to 60mM isotonic KCl added at the end of the experiment. Statistical comparisons used one way ANOVA and Dunnett post-test.

NA produced a concentration-dependent relaxation in both endothelium denuded and endothelium intact coronary artery (-35.5±5.9%, n=6 and -8.2±3.1%, n=5 respectively at 0.1mM). Propranolol eliminated the relaxation in endothelium-intact tissue (-0.3±0.1%, n=4 at 0.1mM), and exposed dose-dependent contractions in endothelium denuded vessels (21.8±4.5%, n=6 at 0.1mM). The contraction observed to NA in endothelium denuded vessels pre-treated with propranolol was eradicated by prazosin (-1.8±0.8%, n=4 at 0.1mM). *p*-Tyramine caused concentration-related constriction reaching a maximum of 63.4±3.8% (n=14) at 3mM. Removal of the endothelium had no effect on *p*-tyramine CRCs (75.8±17.9%, n=5 at 3mM). Endothelial α_2-adrenoceptors do not therefore play a significant role in the response to *p*-tyramine. Propranolol increased the contraction at the highest dose (3mM) to 92.3±16.8% (n=6), however this was non-significant. The contraction to the maximum concentration of *p*-tyramine in the presence of prazosin alone (52.8±13.0%, n=5) and in the presence of prazosin with propranolol (71.8±10.5%, n=5) did not significantly differ ($P>0.05$) from *p*-tyramine alone and in the presence of propranolol respectively.

Indirect sympathomimetic activity involving α-adrenoceptors is not responsible for the contractions of coronary artery to *p*-tyramine, which must therefore be via non-adrenoceptor-mediated mechanisms.

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