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Ex-vivo Perfusion Bioassay: An Excellent Technique to Measure the Bioactivity of Inhalable Insulin Coated Microcrystals

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Purpose. To measure the bioactivity of inhalable insulin coated microcrystals using a perfusion bioassay that measures its vasodilatory effect on smooth muscle arterial tissue. Methods. The bioactivity of an insulin protein coated microcrystal (PCMC), a potential candidate for pulmonary drug delivery and commercial insulin was determined on a Danish Myo Tech P110 pressure myograph system. 12 week old Mesenteric resistance arteries from Male Wistar rats were isolated and immersed in a physiological salt solution (PSS) and attached to 2 opposing hollow glass micro-cannula (outer diameter 80 microns). The PSS was gradually warmed to 37°C (at a pressure less than 5mm Hg) for 1hr. Subsequently the pressure was increased up to 40mm Hg over a period 15 minutes and equilibrated for a further 15 minutes after gassing with 95%O₂ / 5%CO₂ to achieve a pH of 7.4 at 37°C. After normalisation by two washes of 123mM KCl and exposure to 1-10mM noradrenaline the arteries were exposed intraluminally to each insulin preparation by gradual infusion directly into the lumen via a fetal microcannulae inserted to the tip of the glass mounting cannula, at a constant pressure. Results. The preliminary results (full cumulative response curve yet to be determined) demonstrate insulin mediated relaxation to noradrenaline preconstriction. The level of constriction drops from 100% to 42% as the concentration of insulin increases from -11 to -9 Log M for the PCMC compared with a drop from 100 % to 65% for the commercial insulin preparation. However the more potent vasodilatory effect found for the insulin PCMC is more likely to be a result of variance introduced in each dilution step than a real increase in potency. Conclusion. The perfusion bioassay technique provides an excellent method of measuring insulin bioactivity and indicates the insulin loaded on the microcrystal support is fully active.