iSPERSE: A Novel Inhaled Dry Powder Delivery Platform for the Delivery of Large Molecule Drugs to the Lung for Local and Systemic Treatments

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RATIONALE: Increased focus has been directed towards the use of inhaled dry powder (DP) formulations in pulmonary drug delivery over conventional metered dose inhalers or nebulizers. The advantages to DP formulations (propellant free, reduced patient coordination) also come with disadvantages (flow rate dependence, inefficient drug delivery, low drug load). We are developing a salt based DP platform (iSPERSE™), that is small, dispersible, flow rate independent and capable of delivering biologically active molecules to the lung and systemic circulation. The aim of this study was to test the delivery of two biologics in the iSPERSE platform: 1) a formulation containing bovine IgG as a model antibody and 2) a formulation containing insulin to ascertain systemic activity following lung delivery.

METHODS: Bovine IgG: C57BL6 mice were exposed to different doses of bovine IgG iSPERSE DP or a placebo DP (98% leucine, 2% NaCl) via whole body exposure. Immediately following DP treatment a serum sample was taken and mice underwent bronchoalveolar lavage (BAL). BAL supernatants and serum samples were assayed for bovine IgG via ELISA. Insulin: Mice were exposed to a DP formulation containing 5% insulin or placebo via whole body exposure. Immediately prior to DP exposure and at 30 minute intervals thereafter blood glucose levels were measured.

RESULTS: Bovine IgG in the BAL was detectable after delivery of two different powder doses and resulted in 32.8 ng and 95.21 ng bovine IgG in lung lavages, respectively. Bovine IgG was undetectable in the serum after the lower dose exposure, however in the group exposed to a higher dose of bovine IgG DP, serum bovine IgG was detected (10.4 ng/ml) demonstrating systemic exposure. To test the activity of a biologic delivered systemically, animals were exposed to a similar DP formulation containing insulin. Treated animals exhibited a significant drop in blood glucose levels 30 minutes post-exposure (44%, $p<0.001$) compared to controls and remained significantly reduced for up to 2 hours.

CONCLUSIONS: Aerosol delivery of bovine IgG and insulin utilizing iSPERSE, a novel DP delivery platform, resulted in lung deposition and systemic delivery of biologically active molecules, demonstrating the utility of the platform for both pulmonary and systemic drug delivery. Furthermore, iSPERSE may provide a framework for future work looking at the delivery of high drug loads or large molecules to the lung for a variety of indications.