An Investigation Into Salbutamol Sulfate Dry Powder Transport Across Calu-3 And Differentiated Human Bronchial Epithelial Cells

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Rationale: Salbutamol is a short acting β_2-adrenergic agonist commonly used to treat airway diseases. Although the characteristics of salbutamol transport across airway epithelial cell line model have been studied, little is known about the permeability of primary epithelial cell model to salbutamol microparticles. The aim of the study is to access salbutamol sulfate dry powder transport through differentiated primary human bronchial epithelial cells and the Calu-3 cell line (HTB-55).
Method: Human primary bronchial epithelial (HBECs) and Calu-3 cells were cultured at an air-liquid interface (ALI) for at least 21 days and 11 days, respectively. Salbutamol sulfate (SS) 200 µg/capsule in dry powder form was deposited on the cell layers using a twin stage impinger (TSI) at a flow rate of 60 L/min for 4 seconds. The transport of the SS was studied over 4 hours. Drug penetration across cell layers was assessed by high performance liquid chromatography (HPLC).
Results: Our results demonstrated that when 9.7 ± 2.9 µg of SS was deposited on epithelial cells, 45.7 ± 19.0% of the deposited dose crossed the Calu-3 ALI model after 240 min, whereas the permeability through the differentiated HBECs model was calculated to be 53.5 ± 16.3% of the deposited dose. In addition, the percentage of transported SS through differentiated HBECs (n=4) at 5, 10, 15, 20, 30, 40, 50, 60, 90, 120, 180, 210 and 240 min had a positive relationship with the amount of SS dry powder deposited on the cell layers ($p<0.05$). However, this relationship was not apparent with Calu-3 cells ($p>0.05$, n=4).
Conclusion: To study the transport of salbutamol sulfate dry powder after deposition on the epithelial cells, differentiated primary HBECs are more representative of the in vivo physiological transport rate of SS than Calu-3. Furthermore, the data suggest that the dose of SS inhaled and deposited in the airways correlates with the transport of SS through the airway epithelium, which in turn would affect the concentration of the drug at the level of the airway smooth muscle.

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