Bile salt enhancers for inhalation: correlation between in vitro and in vivo lung effects - DTU Orbit (31/03/2019)

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The lungs have potential as a means of systemic drug delivery of macromolecules. Systemic delivery requires crossing of the air-blood barrier, however with molecular size-dependent limitations in lung absorption of large molecules. Systemic availability after inhalation can be improved by absorption enhancers, such as bile salts. Enhancers may potentially interfere with the different constituents of the lungs, e.g. the lung surfactant lining the alveoli or the lung epithelium. We used two in vitro models to investigate the potential effects of bile salts on lung surfactant function (with the constrained drop surfactometer) and on the epithelium in the proximal airways (with the MucilAir™ cell system), respectively. In addition, we measured direct effects on respiration in mice inhaling bile salt aerosols. The bile salts inhibited lung surfactant function at different dose levels, however they did not affect the integrity of ciliated cells at the tested doses. Furthermore, the bile salt aerosols induced changes in the breathing pattern of mice indicative of pulmonary irritation. The bile salts were ranked according to potency in vitro for surfactant function disruption and in vivo for induction of pulmonary irritation. The ranking was the same, suggesting a correlation between the interference with lung surfactant and the respiratory response.

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