Effect of sodium bicarbonate on rheological properties of Cystic Fibrosis sputum and drug permeation

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Background Cystic Fibrosis (CF) is characterized by a thick and sticky mucus-gel responsible for both airway obstruction and loss of pulmonary function as well as resistance to drug diffusion reducing the effective drug delivery to the lung. Studies on drug–mucus interaction may be a crucial step in therapeutic management of CF.

Aim In the present research, rheological measurements were performed in order to examine the rheological properties of human bronchial mucus obtained from CF patients. Moreover, the effect of saline solution containing a high concentration (100 mM) of sodium bicarbonate on sputum viscosity was evaluated. To understand the mechanisms that occur when inhaled micro- and nano-particles are deposited on the mucus and to check the ability of the drug to penetrate through CF mucus, dissolution and permeation properties of Ketoprofen lysinate (Klys) from a previously developed Dry Powder Inhaler were evaluated.

Methods Rheological measurements were performed using an ARES rotational rheometer (Rheometrics, Inc.) with a parallel plate geometry. The gel fraction, separated from the liquid phase by means of centrifugation, of various mucus samples from CF patients was loaded onto the plate. The elastic (G') and the viscous (G'') moduli, tan δ (ratio of G'' to G') and η* (complex viscosity) were evaluated as parameters frequency-dependent. The experiments were conducted on untreated sputum and on sputum treated with $NaHCO_3$. Drug permeation across CF treated or untreated mucus from dry powders was studied by means of Franz-type vertical diffusion cells.

Results Rheological studies showed that the elastic modulus (G') was always greater than the viscous modulus (G''). Furthermore, viscosity decreased with increasing frequency, as for pseudo-plastic fluids and Tan δ values were sensibly less than 1 (G'>G''), indicating an elastic behaviour higher than a viscous one. Preliminary results indicated that $NaHCO_3$ caused a downward shift of both the elastic and viscous moduli, with a reduction in complex viscosity. As to drug permeation, the untreated sputum, expected to act as a physical barrier, slowed down drug dissolution and

permeation compared to buffer permeability (control). Permeation studies across CF mucus treated with $NaHCO_3$ showed higher Klys dissolution/permeation than untreated mucus.

Conclusions The interesting results confirm the previously reported $NaHCO_3$ effectiveness in CF; this weak base seems to act decreasing high viscosity of the CF bronchial secretion and, potentially, resulting in better mucus clearance and in fighting pulmonary infections.