162P

THE EFFECT OF MONO AND DIVALENT CATIONS ON THE IN-VITRO HYDRATION KINETICS OF PURIFIED PORCINE GASTRIC MUCUS GEL

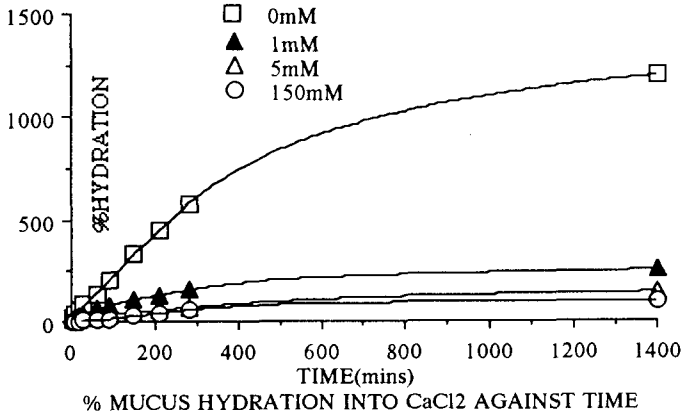
G.J. Phillips, M.I.Lethem, T.A.Paget, S.L. James, Pharmaceutical Sciences Research Group, Dept. of Pharmacy, Brighton Polytechnic, Brighton, BN2 4GJ

The control of the rheological properties of mucus is of paramount importance in mucociliary transport, and abnormal rheology is symptomatic of many obstructive airways diseases including cystic fibrosis (CF).

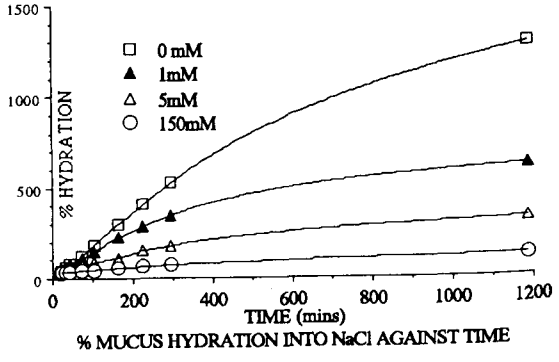
It has been suggested that the excessively thick and sticky mucus characteristic of CF may result from deficiencies in the control of the swelling of the mucus granules immediately after secretion. This may be due to an ionic abnormality in the fluid into which the mucus swells and/or the polyionic composition of the secreted mucus causing it to remain permanently unswollen (Tam & Verdugo 1981).This work investigates the effects of altering the ionic composition of the swelling media on the hydration potential and kinetics of purified porcine gastric glycoproteins in vitro. It may thus lead to a novel and rational approach to the treatment of the pulmonary clinical manifestations of CF and other obstructive airway diseases.

0.1ml samples of purified pig gastric mucus gel adjusted to 6% dry weight and a range of NaCl or $CaCl_2$ concentrations was placed onto a 0.45 µm poresize microporous membrane filter of a 12mm Millicell insert and covered with a layer of silicone oil to prevent mucus dehydration.The insert was placed on a sponge saturated with swelling media equilibrated with the NaCl or $CaCl_2$ concentration in the mucus.This was to avoid initial water flux due to Na^+ or Ca^{2+} movement down a concentration gradient.

Hydration of the mucus was monitored by weighing the inserts at intervals.The following results have been obtained:



% MUCUS HYDRATION INTO CaCl2 AGAINST TIME



% MUCUS HYDRATION INTO NaCl AGAINST TIME

These results indicate that mucus hydration is predominantly a charge dependent process. It is thus suggested that, due to charge shielding, charged groups on the glycoproteins are not available for attracting water of hydration.The prediction that divalent Ca^{2+} is twice as effective as monovalent Na^+ in reducing hydration rate and final hydrated volume, is verified by the results.Thus the ionic composition of the hydration fluid in the respiratory tract must be considered just as important as the glycoprotein and protein content of the mucus when investigating obstructive airway diseases.

Tam,P.Y.,Verdugo,P.(1981) Nature.292:340-342