A mucin model for the *in vitro* evaluation of mucolytic agents

S. S. DAVIS, A. INGLIS, D. MCNEIL AND S. SCOBIE

Pharmaceutics Research Group, Pharmacy Department, University of Aston in Birmingham, Birmingham B4 7ET, U.K.

The sputum produced in asthma and chronic bronchitis is a viscoelastic gel. Potential mucolytic agents are usually assessed by their action on sputum samples collected from patients. Such samples are variable in their properties and meaningful data are difficult to derive. Consequently, we have developed an *in vitro* mucin model based on hog gastric mucin (Sigma). It comprises 10% mucin, which is allowed to hydrate for 12 h at 4°, and the pH is adjusted to 8·0 using tris buffer. Biorheological studies have been conducted using the Ferranti-Shirley cone and plate viscometer and a new stress relaxation method based on a micro-force balance (Davis, 1973). The relative mucolytic activities of a range of commercially available drugs and potential compounds are shown in Table 1.

The reduction in consistency, as compared to a control with water, varied with the agent and its concentration. The relative mucolytic activities found with the model were in agreement with reported *in vitro* and *in vivo* studies using sputum samples (Sheffner & Lish, 1970). The potential mucolytic agent dithiothreitol was ten times more effective than *N*-acetyl cysteine at the same molar concentration. It has been suggested that these two compounds break disulphide bonds in mucoprotein by means of a disulphide-sulphydryl interchange reaction. However, thiourea (also containing a sulphydryl group) is ineffective as a mucolytic agent. The consistency of the mucus model can be increased by small quantities of added disodium tetraborate. This is due to cross-linking of mucoprotein chains.

Table 1. In vitro *reduction in consistency of mucin model compared to control with water (37°).*

Compound	Concn %	% fall in consistency (60 min)	Compound	Concn %	% fall in consistency (60 min)
N-Acetyl cysteine	0·5	39	Superinone	0·0125	—2
	1·0	55	Urea	2·4	—2
	2·0	63	Thiourea	1·0	—1
Dithiothreitol	0·2	62	Disodium Tetraborate	0·1	—45
	2·0	73			
Ascoxal	3·0	18			
Trypsin	0·1	31			

REFERENCES

DAVIS, S. S. (1973). *Bull. Physio. Path. Resp.*, **9**, 47–90.

SHEFFNER, A. L. & LISH, P. M. (1970). *In Antitissive Agents* vol III, Editors: Salem, H. and Aviado, D. M., pp. 785–833. Pergamon Press, Oxford.

Effect of mucin on the bioavailability of tetracycline from the gastro-intestinal tract: *in vivo*, *in vitro* correlations

B. W. BARRY AND M. P. BRAYBROOKS

School of Pharmacy, Portsmouth Polytechnic, Portsmouth PO1 2QQ, U.K.

Functions of the mucus film lining the G.I. tract are poorly understood. This work employed four techniques to investigate the influence of a mucus model (porcine crude mucin) upon the bioavailability of tetracycline from the small intestine. (1) *In vivo* rat intestine perfusion/absorption technique—perfused with tetracycline phosphate (a) in phosphate buffer pH 6·3 and (b) in 1% mucin in buffer, samples taken at 20, 40 and 60 min and analysed for tetracycline. (2) Everted gut method—solutions (a) and (b) analysed as in (1). (3)