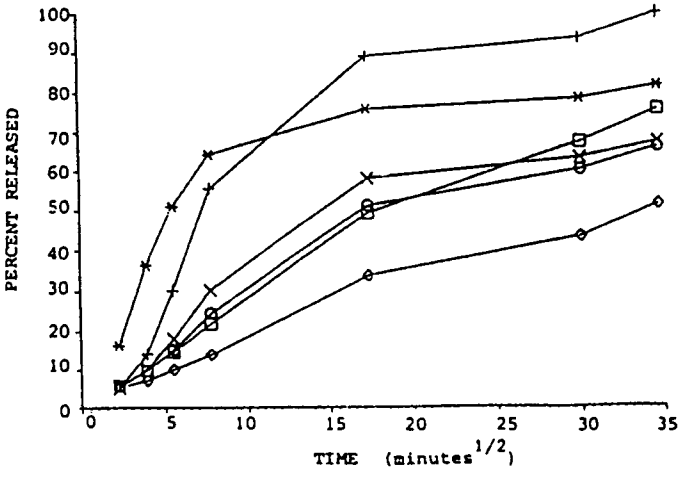
CHARACTERIZATION OF ALGINATES BY CIRCULAR DICHROISM AND ITS CORRELATION WITH RELEASE FROM ALGINATE FILMS

B. Oraceska[1], J.R. Nixon[1], M.C. Solomon[2]. [1] King's College London, Dept. of Pharmacy, Manresa Road, London SW3 6LX, [2] DDSA Pharmaceuticals.

The objective in using alginate films for the delivery of highly skin permeable drugs is to use diffusion from the films as the rate controlling step. The device consists of a monolithic matrix containing nicotine base and a rate controlling membrane, both of which are alginates. Alginates are block copolymers of L-guluronic and D-mannuronic acid, joined by 1,4 glycosidic linkages. Differences in release behaviour are the result of the different proportions of the mannuronic and guluronic acid residues. Stoichiometry, investigated by C.D. shows that various polyvalent metals can be firmly bound to each of the four L-guluronic residues, changing the viscosity and gel characteristics of the algin solution due to cross-linking. Ca, Cu and Cr were used for cross-linking the alginate whether this was subsequently used as a monolithic matrix or a rate-controlling membrane. A rapid method for the determination of the block structure of alginates by C.D. spectra, with a total sample requirement of 10mg, was described by Morris at al (1980), who had previously (1975) demonstrated an empirical correlation between the C.D. of alginate and the overall proportions of D-mannuronate and L-guluronate residues present. The ratio of peak height to trough depth shows appropriate linearity with respect to the ratio of mannuronate to guluronate residues present, up to values ~1 and thereafter varies linearly to the mannuronate content. Commercial samples of Manucol DH and DM were studied and their M/G ratio was determined according to the formula : $M/G=2(x-y)/x$ where x=trough and y=trough-peak.
The mechanism and release profiles of nicotine base from and through different cross-linked formulations were investigated in-vitro using an automated system of modified Franz-type diffusion cells connected to a UV spectrophotometer and computer. A linear relationship of % drug released v $\sqrt{t}$ was obtained after an initial lag period. A faster release was found with higher M/G ratio after swelling (Fig. 1).



*M/G=1.34,Ca-alginate
×M/G=1.34,Cu-alginate
◇M/G=1.34,Cr-alginate
+M/G=1.65,Ca-alginate
□M/G=1.65,Cu-alginate
○M/G=1.65,Cr-alginate

Fig 1. Profiles of the amount of % drug released at 37°C as a function of $\sqrt{t}$ from 7% alginate cross-linked films.

Morris, E. R. et al (1975) J. Chem. Soc. 2: 1418-1425
Morris, E. R. et al (1980) Carbohydr. Res. 81: 305-314