POLYMER HYDRATION AND DRUG DISTRIBUTION WITHIN THE GEL LAYER OF HYDROPHILIC MATRIX DEVICES DURING DRUG RELEASE

C.D.Melia, J.S.Binns, M.C.Davies. Department of Pharmaceutical Sciences, University of Nottingham, Nottingham,UK

Hydrophilic matrix (HM) devices, widely-utilised as sustained release drug delivery systems, comprise drugs and excipients within a compressed polymer matrix which, on hydration, rapidly forms a gel or pseudogel surface layer. Drug release is critically dependent on the properties of the gelling polymer (Alderman 1985) with the gel layer acting as a rate-controlling barrier both to the ingress of water and to outward drug release. This work reports preliminary findings using cryogenic scanning electron microscopy (CSEM) in combination with energy dispersive X-ray microanalysis (EDX) to examine the internal structure, the degree and evenness of polymer hydration, and the spatial distribution of drug within the gel layer of a typical HM system undergoing hydration and drug release.

Simple hydrophilic matrices were prepared by dry compression of sodium alginate with or without calcium sulphate 10% or diclofenac sodium 25%w/w (all 90-125 um particle size), and were hydrated in a USP dissolution apparatus 1 at 100rpm in pH 7.4 phosphate buffer. After 1 hour they were removed, rapidly frozen in nitrogen slush (-210°C), freeze fractured, etched (-80°C) under vacuum, gold coated and transferred to the cold stage of the electron microscope (-180°C). Electron micrographs were obtained at a typical accelerating voltage of 25 kV and magnification of x400. EDX maps of chlorine (diagnostic for the drug) were obtained where appropriate.

Two distinct regions and considerable detail were discernible within the gel layer of the pure alginate matrix. There was a clear boundary between the outer 20% of the gel, which was evenly and more highly hydrated, than the main body of the gel which exhibited a lower degree of hydration. The latter showed a progressively more uneven hydration pattern with increasing depth, with "islands" of poorly hydrated regions increasingly predominating the surrounding more hydrated areas, thereby forming a reticular network of channels through which (presumably) dissolved drug must pass to be released. The gel/dry core interface was remarkably distinct, although higher magnifications showed some surface hydration of particles in the core. Gel structure was not discernibly different in the drug-containing matrices and EDX maps of drug distribution confirmed high concentrations of drug within the dry core diminishing towards the outer edge of the gel layer. Undissolved drug crystals were observed (and confirmed by EDX) extending outwards from the core into the centre of the gel. Calcium, which ionically cross-links alginate at a molecular level, gave rise to observable changes in the structure of the hydrated gel. There was a dramatic layering of hydration channels parallel to the gel surface in the outer hydrated region, a structural feature which was reflected to a lesser extent within the main body of the gel. These results indicate that for HM devices based on sodium alginate, the hydrated surface gel layer appears to have a complex internal structure, which may be further modified by excipients that interact with the polymer. This has important ramifications for our understanding and modelling of drug release mechanisms in these systems.

Alderman, D.A. (1985) Int.J.Pharm.Tech.Prod.Manuf. 5: 1-9