J. Pharm. Pharmacol. 1998, 50 (Supplement): 89

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Investigation of a drug–polymer interaction using Raman spectroscopy

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Raman spectroscopy is an analytical technique that may be conveniently employed to characterise pharmaceutical systems. For example Davies et al. (1990) described the use of Fourrier Transform Raman spectroscopy to quantify drugs in polymeric systems. In this study we report the use of a simpler dispersive Raman method with far red excitation to evaluate possible interactions between chlorhexidine and the polymeric constituents of semi-solid multicomponent, bioadhesive formulations described for topical application to the oral cavity (Jones et al, 1998).

Raman spectra were recorded for solid CHX and for CHX (5%w/w) dispersed in polymer matrices consisting of one or more of the polymers dissolved / suspended in phosphate buffered saline. The polymers are hydroxyethylcellulose (HEC, 3%w/w), polyvinylpyrollidone (PVP, 3%) and polycarbophil (PC, 3%).

Spectra were recorded using 785 nm excitation (100 mw at sample) using a 180° backscattering geometry, the laser line focused (<100 mm x 10 mm) onto the sample using a cylindrical lens. Scattered light was collected, passed through a holographic notch filter and then dispersed by single stage spectrograph onto a CCD detector. Spectra were typically accumulated for 360 s. Due to the opalescent nature of the samples all the spectra were superimposed on a smooth background of stray light which was removed from all the spectra shown by digitally subtracting a similar stray light signal generated by placing a rough aluminium plate in the sample position.

The figure shows Raman spectra of CHX as solid and in a series of aqueous polymer systems. The spectrum of each of the polymer systems without CHX is significantly weaker than that for solid CHX, so the spectra are dominated by bands from CHX. It is clear that the spectra of CHX in HEC and in HEC/PVP are indistinguishable from that for solid CHX This is to be expected as CHX is insoluble in water, forming a suspension of microcrystalline particles. This is unaffected by the presence of HEC and/or PVP. However, with the addition of PC to either system there is a shift in the strongest band from 1564cm^{-1} to 1608cm^{-1}.

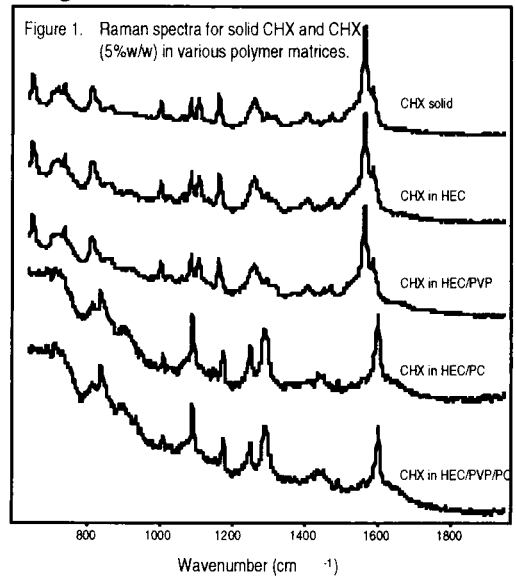

Figure 1. Raman spectra for solid CHX and CHX (5%w/w) in various polymer matrices.

The most obvious explanation for this shift, is protonation of the basic CHX by the numerous carboxylic acidic groups on the PC molecule. Identical shifts in the band positions were observed when this protonation was modelled using acetic acid, supporting the view that there is a simple acid base reaction between PC and CHX. However, small but reproducible differences in the band intensities observed with acetic acid suggest that some more specific interaction may be present.

The interaction between CHX and PC will have an effect on the clinical performance of both the drug and the polymer. For CHX, the solubility and hence the rate of drug release will be affected. For PC, interaction with the cationic agent may reduce its capacity for mucoadhesive interaction.

Here, we have successfully illustrated the use of Raman spectroscopy for the analysis of drugs in polymers without the need for Fourrier Transform technology or a near IR light source.

The Authors thank Andor Technology Limited for the loan of a RamanSpec instrument.

Davies, M.C. et al. (1990) Int.J.Pharm 66, 223-232.
Jones, D.S. et al. (1998) Pharm.Res. In press.