

THE EFFECT OF STARCH DERIVATIVES ON THE ANTIBACTERIAL ACTIVITY OF VARIOUS PARABENS AND BENZOIC ACID AGAINST ESCHERICHIA COLI

K.Sabra and P.B.Deasy, Department of Pharmaceutics,
School of Pharmacy, Trinity College, University of Dublin, Ireland.

Derivatives of starch are used in the formulation of pharmaceutical preparations as thickening agents, fillers, binders and disintegrants. Farley and Lund (1976) reported that Instant Clearjel, an esterified pregelatinized maize starch, and Primojel, a sodium starch glycollate of potato starch, were effective suspending agents for chalk and sulphadimidine mixtures. This study is concerned with the influence of these polymers on the antibacterial activity of preservatives of the parabens type and benzoic acid, which are used in such mixtures.

Escherichia Coli NCTC 5233 was used as the test organism because of its frequent occurrence as a contaminant of pharmaceutical suspensions. Elevated temperatures were used to hasten bacterial inactivation. Viable count determinations were made using a surface spread technique having first established the suitability of the recovery conditions of incubation on nutrient agar (Oxoid) at 37°C for 24 h containing a fixed carryover concentration of preservative. Log survival-time plots constructed from the count data were approximately linear and their slopes were determined by a least squares regression fit.

When E.coli was heated at 50°C for 2 h with 0.1% methyl, ethyl or propyl hydroxybenzoate it was shown that the rate of inactivation increased with increasing length of alkyl substitution. However addition of either 1% Instant Clearjel or 1% Primojel significantly reduced the antibacterial activity of the parabens. A similar effect was also noted when 0.1% benzoic acid was used as preservative.

The reduction in antibacterial activity of the parabens and benzoic acid caused by addition of either starch derivative was also evident when the pH was varied over the range 5-9 and the temperature over the range 30-60°C. However the preservatives were more active at low pH and higher temperature. Increase in concentration of Instant Clearjel and Primojel over the range 1-3% progressively reduced the antibacterial activity of 0.1% methyl hydroxybenzoate.

Binding studies confirmed the formation of a reversible complex between each preservative and starch derivative employed. When concentrations of preservatives corresponding to the unbound amount were used in the absence of starch derivatives they gave survival curves which were intermediary in slope between those obtained using total concentrations of preservatives with or without starch derivative present. These results indicate that the reduction in preservative activity by the starch derivatives is only partially due to the complex formation but is probably also due to a direct protective effect of the starch derivatives on the test organism.

Overall these findings suggest that preservation of pharmaceutical suspensions with normal use concentrations of parabens and benzoic acid may be ineffective if cold-water dispersible starch derivatives like Instant Clearjel and Primojel are used as suspending agents.