THE INFLUENCE OF SOME STRUCTURALLY RELATED PLURONICS ON THE HYDROLYSIS OF ASPIRIN

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Several workers have reported that micellar concentrations of non-ionic surface-active agents decrease the rate of hydrolysis of esters in aqueous solution. Increased protection against hydrolysis was seen when molecular modification, in an ester series, favoured micellar entrapment (Smith and others, 1974). However, there is little information on the effect of change of surfactant structure on the protection of esters. This report describes the influence of structurally related polyoxyethylene-polyoxypropylene block polymers (PLURONICS) on the hydrolysis of aspirin. The Pluronics used were L63, L64, P65 and F68, having a common hydrophobe and an increasing hydrophilic content.

Degradation and solubility studies were carried out at 37° and at pH 1.0 and 5.0. Density measurements for partial molar volumes and volume fraction calculations were made using an Anton Paar density meter.

The aqueous solubility of aspirin at pH 1.0 was 5.85 mg ml^{-1}. No increase in aspirin solubility was seen in concentrations of Pluronics L63, L64 and P65 up to 10% w/v. In the case of F68 a two-fold increase in solubility was seen in a 4% w/v solution.

Hydrolysis of aspirin in aqueous solution and in solutions containing different concentrations of Pluronics proceeded as a first order reaction at pH 1.0 and pH 5.0. At pH 5.0, the maximum protection seen was 3% in the presence of 7% w/v F68. At pH 1.0 reaction rate constants were linearly related to Pluronic concentrations up to 10% w/v in the case of F68, whereas non-linearity was observed above 7% w/v in L63, L64 and P65. The results are summarised in Table 1.

Table 1. First order rate constants (min^{-1} x 10^4) in aqueous Pluronic solutions at pH 1.0.

% w/v	L63	L64	P65	F68
1	1.602	1.628	1.638	1.843
3	1.214	1.253	1.258	1.687
5	1.058	1.050	1.051	1.589
7	0.890	0.909	0.932	1.503

On a weight basis, L63 provided greatest protection against hydrolysis, but on a molar basis the trend indicated that F68 was more efficient. As expected the protection per equivalent of oxyethylene decreased with increasing oxyethylene content. In contrast, protection as a function of mole fraction hydrophobe and of volume fraction of Pluronic were of the same order for L63, L64 and P65, whereas there was a three-fold enhancement in the presence of F68. These results indicate that two separate protective mechanisms are operating in the Pluronic series. From a consideration of solubility data it is probable in the case of F68 that micellar solubilisation protects the aspirin molecule. Rate constants for hydrolysis of aspirin in aqueous ($2.07 \times 10^{-4} min^{-1}$) and micellar phases ($1.17 \times 10^{-4} min^{-1}$) of F68 have been calculated from plots of observed rate constants against a function of volume fraction of F68 and micellar:aqueous partition coefficient for aspirin (Mitchell & Broadhead, 1967). The protective mechanisms operating with L63, L64 and P65 are less obvious.

Mitchell, A.G. & Broadhead, J.F. (1967) J. Pharm. Sci. 56, 1261-1266
Smith, G.G., Kennedy, D.R. & Nairn, J.G. (1974) Ibid. 63, 712-715

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