136P

INTERACTION OF NON-IONIC BLOCK CO-POLYMERIC (POLOXAMER) SURFACTANTS WITH POLY (ACRYLIC ACID) AND THE APPLICATION IN THE STABILISATION OF MULTIPLE EMULSIONS

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The application of water in oil in water (w/o/w) multiple emulsions as drug delivery systems has been impeded by their lack of stability. Several approaches have been used to stabilise w/o/w multiple emulsions e.g. interfacial polymerisation of modified poloxamers; interfacial complexation of proteins and poloxamer surfactants and interfacial complexation between poly (acrylic acid) (PAA) and poloxamer surfactants (Law et al., 1986). In order to understand the mechanism of interaction between poloxamer surfactants and PAA a more detailed study has been undertaken involving a range of poloxamer surfactants with varying HLB values, hydrophile to hydrophobe ratios and molecular weights. Such an understanding of these interactions should enable the most appropriate combinations to be chosen to stabilise the initial primary w/o emulsion in w/o/w multiple emulsions.

The interactions between poly(ethylene oxide) and PAA have been widely studied: the complexes can form pH sensitive membranes useful in drug delivery. However, the interaction of PAA with poloxamer block copolymeric surfactants, containing both PEO and PPO, has not been studied previously.

Poly(acrylic acid) (PAA) was Carbopol 907 (molecular weight 450,000). Poloxamer surfactants used were Pluronic^{TM} F127, P104, P103, F68, P75, P85 (equivalent poloxamers 407, 334, 333, 188, 215, 235). Photon correlation spectroscopy was performed on mixtures of the filtered components at known pH values and at 25°C and 90° scattering angle using the standard cumulants method of data analysis and presentation.

Initial addition of small amounts of the poloxamers to PAA solutions (e.g. µl volumes of 5 x 10^{-3}M poloxamers to 1 ml of 1 x 10^{-6}M PAA both at pH2) results in turbidity and/or formation of a precipitate. However, further addition of poloxamer results in dissolution of these large complexes and formation of clear solutions. The volume of poloxamer (5 x 10^{-3}M) required to produce clear solutions with PAA (1 ml of 1 x 10^{-6}M) are shown in Table 1.

Table 1

Poloxamer	Volume (µl)	Number of PPO Units	Number of PEO Units	Particle size (nm)
407	20	67	98 x 2	110
334	60	54	31 x 2	91
333	70	54	20 x 2	117
188	>1000	30	75 x 2	>2000
215	120	35	24 x 2	120
235	130	39	27 x 2	180

The greater the PPO content of the poloxamer the smaller the equivalent amount required to produce a clear homogenous system. Initially, with small amounts of poloxamer insufficient to interact with all PAA-COOH groups, cross-linking of the large PAA molecules results in large aggregates. Larger amounts of poloxamer will saturate the PAA-COOH groups preventing cross linking and giving smaller complexes: these have been studied using photon correlation spectroscopy and the sizes are also shown in Table 1. The interaction between PAA and the ether oxygens of PEO have been shown to be due to hydrogen bonding with unionised PAA-COOH groups. Thus such interactions are diminished at higher values as PAA becomes more ionised.

At pH 5 no interaction can be detected between the poloxamers and PAA (i.e. no significant scattered light). At pH 4 only those poloxamers with large PPO segments (i.e. 407, 334, 333) form detectable complexes confirming the hypothesis that the property of the poloxamer determining its interaction with PAA is the size of the PPO segment. There appears to be no correlation with PEO segment size, total molecular weight or HLB. This information is useful in choosing the most appropriate poloxamer (or poloxamine) for interfacial complexation with PAA to stabilise simple and multiple emulsions.

Law, T.K., Whateley, T.L., Florence, A.T. (1986) J.Contr.Release 3: 279-290