THE EFFECT OF BATCH VARIABILITY ON MICELLAR PROPERTIES AND IN-VIVO RELEASE CHARACTERISTICS OF PLURONIC F127 GELS

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The commercial method of preparation of Pluronic F127 produces batches with a distribution of oxyethylene and oxypropylene chain lengths. The influence of the chain length distribution on the micellar and gelation properties has not been reported. These physical properties may well determine the release characteristics of these gels which have potential use as controlled release systems. In this work we have investigated relations between the molecular composition and the micellar properties and *in vivo* release characteristics of different batches of Pluronic F127.

The molecular characteristics of batches from two different suppliers were determined by gel permeation chromatography in tetrahydrofuran. All batches exhibited varying degrees of polydispersity of molecular size. Two batches representing extremes of size distribution were selected for further study; batch 1 with a main peak at 2.1×10^4 and batch 2 with twin peaks at 1.2×10^4 and 2.7×10^4 (relative to polystyrene). NMR analysis revealed a difference of only 0.5% in the oxyethylene content of these two batches.

Total intensity light scattering and viscometric measurements showed an increase of micellar aggregation number, N, and a corresponding decrease of micellar hydration, δ, over the temperature range 35-45^{o} for batch 1 whilst these changes were observed over the range 25-35^{o} for batch 2 (see Table 1). Our

Table 1. Micellar properties of two batches of Pluronic F127

	Batch 1			Batch 2	
Temp ^{o}C	N	δ gH_2O/g F127	Temp ^{o}C	N	δ gH_2O/g F127
35	2.5	7.5	25	6.9	7.0
40	8.8	6.5	30	15.3	6.5
45	13.3	4.9	35	28.7	5.9

previous studies (Attwood et al 1984) have clearly established that such changes in micellar size and hydration are responsible for the gelation of this poloxamer. Onset of gelation with increase of solution concentration at elevated temperatures may be detected by a dramatic decrease of the apparent diffusion coefficient of the micellar species. Photon correlation spectroscopy showed that gel formation in solutions of batch 1 commenced at lower solution concentration and was characterised by a more dramatic increase of intermicellar interaction than was noted with batch 2.

In vivo release rates from gels of the two batches implanted in rats were assessed by γ-scintigraphy. The release characteristics from concentrated solutions (30%) of the poloxamer containing 0.5% technetium labelled diethylene triamine penta acetic acid (DTPA) were determined by loss of activity from the gel formed at the injection site and gain of activity in the kidneys. The two batches had similar release rates with mean half lives of 31 and 38 mins for batches 1 and 2 respectively.

Our studies have shown that whilst batch variability of Pluronic F127 can result in appreciable differences of micellar properties and gelation characteristics, *in vivo* release rates from implants of this poloxamer are not significantly affected by the molecular characteristics of the batch.

Attwood, D., Collett, J.H. and Tait, C.J. (1984) J.Pharm.Pharmac., 36 : 52P.