# MULTIPLE W/O/W EMULSIONS STABILISED WITH POLOXAMER AND ACRYLAMIDE GELS

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There has been interest recently in the use of water-in-oil-in-water (w/o/w) emulsions as drug delivery systems (Davis 1976). They are, however, complex and inherently unstable systems and their potential as controlled release systems cannot be properly assessed until problems with their stability in vitro and in vivo are solved. In an attempt to improve stability and to further retard the release of drugs two different methods have now been used to prepare w/o/w emulsions by forming a polymeric gel in the internal or external (continuous) aqueous phases.

The first of these methods is based on the production in the external aqueous phase of crosslinked, hydrophilic gels by $\gamma$-irradiation of the emulsifier, a polyoxyethylene-polyoxypropylene ABA block copolymer (poloxamer) (Al-Saden et al 1980a). As these compounds are surface-active (promoting o/w emulsification) and are capable of being crosslinked, o/w emulsions may be prepared which contain the poloxamer in the continuous aqueous phase. After emulsification, the surfactant molecules can be cross-linked at the o/w interface and in the continuous phase by $\gamma$-irradation, forming a network of surfactant molecules which link the dispersed oil globules. Multiple emulsions prepared by re-emulsifying a primary w/o emulsion in water saturated with nitrous oxide and containing poloxamer (types F68, F87, F88 or a combination of these) were sealed under nitrogen and exposed to $^{60}Co$ $\gamma$-irradiation. The viscosity of the emulsions, which increased gradually up to the gel point, was monitored used a Ferranti-Shirley cone and plate viscometer. The gel-point of the emulsions depended on the type and concentration of the poloxamer. These systems which are w/o/gel systems do not cream as ungelled multiple emulsions do. On mixing with water the gel swells and w/o droplets are released from the gel matrix.

As the hydrophilic nature of the poloxamer compounds prevents their use as stabilizers of the primary w/o emulsion and as the more lipophilic members of the series which might be used degrade on irradiation (Al-Saden et al 1980a,b) an alternative approach, a modified emulsion polymerisation method, was used to gel the internal phase. A w/o emulsion, was formed using acrylamide (6% w/v) and N,N-methylenebisacrylamide (2% w/v) in water previously flushed with nitrogen as the aqueous phase. The emulsion was sealed under nitrogen and exposed to $^{60}Co$ $\gamma$-irradiation at doses of up to 0.25Mrad. The gelatinous polyacrylamide-in-oil dispersion produced was then redispersed in hydrophilic surfactact solutions (e.g. 2% w/v Triton X165 or Span 80/Tween 80 3:1) to produce a w/o/w emulsion containing a crosslinked polyacrylamide gel in the internal aqueous phase. The resultant system is an acrylamide gel/o/w emulsion with similarities to the gelatin microsphere /o/w system described by Hashida et al (1977).

One drawback of these approaches is the possible adverse effects of $\gamma$-irradiation on any entrapped drugs, particularly with the first method which requires relatively high doses of radiation. It is possible, however, that the oil may exert a protective effect on labile drugs and this has still to be investigated.

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