

PHYSICOCHEMICAL ASSESSMENT OF NOVEL FORMULATIONS OF EMULSIFIED
PERFLUOROCARBONS

S.K. Sharma, S.S. Davis, O.L. Johnson, K.C. Lowe*, Departments of Pharmacy and
*Zoology, University of Nottingham, University Park, Nottingham NG7 2RD.

Emulsified perfluorocarbons (PFC) can dissolve oxygen and this property makes them attractive as potential oxygen-transport fluids (Riess and Le Blanc, 1982). Some of the physiological effects of emulsified PFC have been examined in several species, including humans (Lowe and Bolland, 1985). The most widely tested preparation is the commercial emulsion, Fluosol-DA 20% (F-DA; Green Cross, Japan) which contains perfluorodecalin (FDC) and perfluorotripropylamine, emulsified with Pluronic F-68 surfactant (Naito and Yokoyama, 1978). A specific problem inherent with available commercial emulsions is their poor storage stability, resulting in increased particle size (Riess and Le Blanc, 1982). The major cause of droplet growth in emulsions is coalescence, but this can normally be retarded using emulsifying agents which form electrostatic and mechanical barriers at the oil/water interface. However, a more subtle means of instability can occur by a process of molecular diffusion known as Ostwald Ripening (Davis et al, 1981) and this can occur even if particles have excellent barriers to coalescence. We report here some of the physicochemical properties of novel formulations of PFC emulsions stabilised against Ostwald Ripening.

FDC (ISC Chemicals Ltd, Avonmouth) was emulsified by sonication for 30 mins with 4% Pluronic F-68 in an aqueous phase, to give a final 20% (w/v) preparation containing 1.0% of the following high b.p. oils to enhance stability: perfluoro-perhydroacenaphthylene (C-12), perfluoroperhydrofluorene (C-13), perfluoroperhydrophenanthrene (C-14) or perfluoroperhydrofluoranthrene (C-16); control emulsions contained no oil additives. Emulsion stability was assessed by particle size analysis using Photon Correlation Spectroscopy (PCS) after storage at either 4°C or 37°C for up to 63 days. Changes in mean stability index after 44 days at 4°C are given in the table:

Oil additive	B.p. of added oil (°C)	Mean size (nm)	Stability parameter
Control (no additive)	-	551	0.86
C-12	173-175	531	0.55
C-13	192-194	434	0.40
C-14	215-216	325	0.36
C-16	242-245	293	0.17

* Stability parameter = P.D. x Dt/Do where P.D. = polydispersity of emulsion, Do = initial mean particle size and Dt = particle size after time t days.

These results show that FDC emulsions can be stabilised by addition of perfluorinated high b.p. oils. The degree of stability achieved either at 4°C or 37°C appears to be directly related to the b.p. and hence, molecular weight of added oil. We therefore conclude that FDC emulsions stabilised against Ostwald Ripening with high b.p. oils may have potential value for in vivo use as components of oxygen-transport fluids.

This project was supported by ISC Chemicals Ltd, Avonmouth, Bristol. Emulsions described in this paper are covered by Patent No 85,04916.

Davis, S.S. et al (1981) J. Coll. Interface Sci. 80: 508-511.
Lowe, K.C., Bolland, A.D. (1985) Med. Lab. Sci. 42: 367-375.
Naito, R., Yokoyama, K. (1978) Green Cross Corp. Tech. Inform. Ser. 5.
Riess, J.G., Le Blanc, M. (1982) Pure Appl. Chem. 54: 2383-2406.