J. Chem. Tech. Biotechnol. 1985, **35A**, 73–82

Fluorocarbon Microemulsions

C. Ceschin, J. Roques, M. C. Malet-Martino and A. Lattes

Laboratoire des IMRCP, UA CNRS 04-470, Université Paul Sabatier, 118 Route de Narbonne, 31062 Toulouse Cédex, France

(Manuscript received 15 February 1984 and accepted 13 October 1984)

The microemulsification of various perfluorinated (or almost completely fluorinated) oils with different perfluorinated (or almost completely fluorinated) surfactants with or without cosurfactant is described. Ternary or pseudoternary phase diagrams are discussed. The sizes of the monophasic areas are related to surfactant and cosurfactant nature, weight ratio surfactant/cosurfactant and oil.

Keywords: Fluorocarbon microemulsions; fluorinated oils; fluorinated surfactants.

1. Introduction

Perfluorocarbons combine high gas-dissolving capacities with extreme chemical and biological inertness. These properties have suggested their use as oxygen carriers in artificial blood and in liquid breathing.[1–7] However, fluorocarbons are highly hydrophobic molecules. To solve the problem of simultaneous transport of mineral salts, metabolites and other compounds of biological importance, it is necessary to use the perfluorocarbons as an oil in water (O/W) emulsion.[4,8] The formation of such emulsions requires large quantities of energy, generally provided either by sonication[9,10] or by high-pressure homogenisation based on shearing.[4,11] To avoid such harsh treatment which can lead to the undesirable release of fluoride ions[9] thereby altering the composition of the resulting preparations, it would appear desirable to seek self-emulsifying systems. In this respect, microemulsions seem particularly attractive since they are fluid, transparent, thermodynamically stable microheterogeneous systems which are formed spontaneously by adding suitable surfactants (or a surfactant+a cosurfactant) to a non-miscible mixture of water and oil.[12–15] A biocompatible O/W microemulsion would therefore be useful as a blood substitute.

Fluorocarbon microemulsions were obtained for the first time by admixing a fluorinated compound (e.g. $(CF_3)_2CFO(CF_2)_8OCF(CF_3)_2$) with a low-boiling chlorofluorocarbon (CF_2Cl-CCl_2F). This mixture was then added to an aqueous system containing three surfactants [nonylphenol polyethylene glycol ether, $(CF_3)_2CFO(CF_2)_3CONH(CH_2)_3NO(CH_3)_2$, $(CF_3)_2CFO(CF_2)_2(CH_2)_2(OCH_2CH_2)_{10}OH$) and stirred until a microemulsion formed. The halofluorocarbon was then removed by evaporation.[16]

Chabert *et al.* prepared aqueous microemulsions of fluorocarbons ($C_6F_{13}CH{=}CHC_6F_{13}$, C_8F_{18} . . .) by mixing the compound with water or aqueous saline solution in the presence of two non-ionic polyfluorinated emulsifiers ($C_mF_{2m+1}(C_2H_4O)_nH$), one predominantly lipophilic (n=16–40) and the other predominantly hydrophilic (n=1–15).[17] The disadvantage with these methods is that they use a manufacture artifice, or a mixture of various surfactants with non well-defined compositions.

In 1981, Mathis and Delpuech described aqueous microemulsions of fluorocarbons (F-decalin, $C_8F_{17}CH{=}CH_2$) with a single non-ionic fluorinated amphiphile of general formula $R_FCH_2(OC_2H_4)_nOH$ where n=5,6.[18–20]

One example of 'four-component practically perfluorinated microemulsions' was reported

recently using for the first time an ionic surfactant, sodium perfluoro-octanoate, with 2,2,3,3,4,4,4-heptafluorobutan-l-ol as a cosurfactant.[21]

Unlike the hydrogenated systems, where, due particularly to their use in enhanced oil recovery, the conditions to produce microemulsions and their physicochemical behaviour are beginning to be well-known, no systematic study of the formulation of fluorinated microemulsions has, to the authors' knowledge, been reported. This study of the microemulsification of various perfluorinated oils (or almost completely fluorinated oils) has been undertaken with different perfluorinated surfactants (or almost completely fluorinated surfactants) with or without cosurfactant.

For this preliminary study, the biocompatibility of the surfactants and cosurfactants was not considered. The main purpose was to obtain microemulsions and to establish guide lines for the microemulsification of fluorinated compounds.

2. Materials and methods

2.1. Materials

Butan-l-ol (Prolabo) was used as supplied. Tetradecafluorohexane (C_6F_{14}), hexadecafluoroheptane (C_7F_{16}), octadecafluorooctane (C_8F_{18}) and octadecafluorodecahydronaphthalene (F-decalin) were purchased from Fluka and were used as supplied. All other materials used in this study, undecafluorohexanoic acid ($C_5F_{11}COOH$), pentadecafluorooctanoic acid ($C_7F_{15}COOH$), lithium heptadecafluorooctanesulphonate ($C_8F_{17}SO_3Li$), 3,3,4,4,5,5,6,6,7,7,8,8,-9,9,10,10,10-heptadecafluorodecanesulphonic acid ($C_8F_{17}C_2H_4SO_3H$), 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctanesulphonic acid ($C_6F_{13}C_2H_4SO_3H$), 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecane ($C_8F_{17}C_2H_5$), 1,1,1,2,2,3,3,4,4,7,7,8,8,9,9,10,10,10-octadecafluoro-5-decene-($C_4F_9CH{=}CHC_4F_9$), 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-decene ($C_8F_{17}CH{=}CH_2$), 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octene ($C_6F_{13}CH{=}CH_2$) and 3,3,4,4,5,5,6,6,6-nonafluoro-1-hexanol ($C_4F_9C_2H_4OH$) were generously provided by ATOCHEM (PCUK) and were used as supplied. There was no indication in ^{19}F n.m.r. spectra of the presence of appreciable amounts of branched isomers.

Sodium pentadecafluorooctanoate ($C_7F_{15}COONa$) was prepared from the corresponding carboxylic acid (pentadecafluorooctanoic acid, PCUK).[22]

The ternary or quaternary mixtures were prepared with doubly distilled water, at 25±0.1°C.

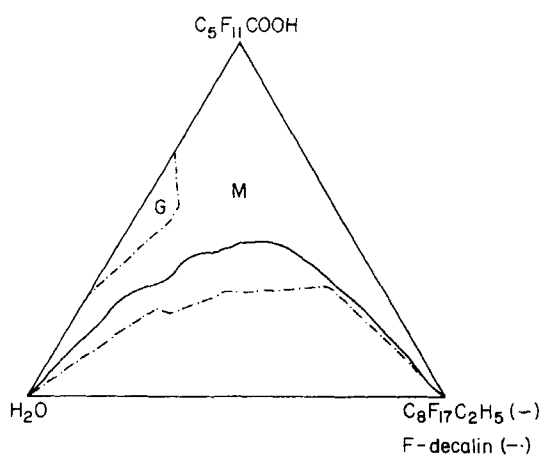

Figure 1. Ternary phase diagram of the system $C_5F_{11}COOH/C_8F_{17}C_2H_5$ or F-decalin/H_2O in wt% at 25°C. M is the region of microemulsions. The other area of the diagram consists of heterogeneous non-miscible mixtures. G is a transparent gel.