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Study of the Behavior of "Uptake and Release" of Oxygen into Perfluorocarbon-Water Emulsions

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Stable O/W type emulsions of perfluorocarbon such as perfluorodecalin (FDC) and perfluorotributylamine (FTBA) were prepared by using poly(oxyethylene)-poly(oxypropylene) block copolymer (Pluronic F-68) and sorbitan monolaurate (SL-10) as emulsifiers. The relationships between the behavior of "uptake and release" of oxygen into the emulsions and the factors responsible for a stable emulsion were studied. The initial rates of "uptake and release" of oxygen into the emulsions decreased with increasing the mean particle size, the concentration of emulsifiers, and the viscosities of the emulsions. On the other hand, the saturated amount of oxygen in the emulsions was independent on the mean particle size, but depended on the total amount of the perfluorocarbons in the emulsion.

Perfluorocarbon compounds have a characteristic property of dissolving a relatively large amounts of gases such as oxygen and carbon dioxide.[1,2] This property can be applied to the preparation of an artificial blood. Indeed, many researches on the use of perfluorochemical emulsions in artificial blood have been proceeding.[3–12] To use perfluorochemicals effectively for this purpose, it is necessary to prepare them as stable O/W type emulsion. Such emulsions should exhibit suitable behavior of "uptake and release" of oxygen, but there have been few reports about fundamental studies of these emulsions from the view point of colloid science.

In this work, the relationship between "uptake and release" of oxygen into perfluorocarbon emulsions and the factors associated with stable emulsions will be discussed.

Experimental

Materials. Perfluorocarbon compounds used for preparing an artificial blood substitute must be nontoxic and have the ability to dissolve oxygen. From this standpoint, perfluorodecalin (FDC) and perfluorobutylamine (FTBA) were employed. They were supplied by Dainippon Ink Chemical Co., Ltd.

For the preparation of O/W type emulsion of these compounds, poly(oxyethylene)-poly(oxypropylene) block copolymer (Pluronic F-68) and sorbitan monolaurate (SL-10) were used as emulsifiers. They were supplied by Nikko Chemical Co.

Emulsification. For the preparation of the emulsion in a small scale, a homogenizer was used. While in a large scale, FDC and FTBA were preemulsified by use of the homogenizer for several minutes, followed by passing through a Manton Gaulin Homogenizer under about 500 kg/cm^2.

Measurements. The particle size distribution of the emulsion was determined by using a centrifugal particle size analyzer (Shimadzu Seisakusho Ltd.). The viscosity of the emulsion was measured by using a corn plate type rotation viscometer (Tokyo Keiki Co., Ltd.). The amount of oxygen dissolved in the emulsion was measured by an oxygen meter (Central Kagaku Co., Ltd.) at 25±0.1 °C. The procedure was as follows; after setting 100 ml of the emulsion into a beaker, nitrogen gas was blown into it to displace the oxygen initially dissolved in the emulsion. Oxygen was then blown into this emulsion until saturation was achieved. This process is named "uptake" of oxygen. Next, the oxygen was replaced with nitrogen, which process is called "release" of oxygen. These processes are shown in Fig. 1. Here, the concentration of oxygen in the emulsion is estimated by subtracting the concentration of oxygen in water phase from that in the total system.

Results and Discussion

For the application of a perfluorochemical emulsion to an artificial blood, the emulsion must have fine particles and exhibit a high stability for a long period. Thus, it is necessary to prepare a stable emulsion of perfluorocarbon compound. Since it is important to select suitable emulsifiers for the preparation of stable emulsions of FDC and FTBA, the emulsification tests were carried out by using several different emulsifiers. As a result, it was found that the combination of Pluronic F-68 and SL-10 provided relatively stable emulsions for both FDC and FTBA. Accordingly, these two emulsifiers were used for preparing the emulsions in this experiment.

In order to estimate optimum conditions for emulsifying FDC and FTBA, the emulsification stability tests were conducted using various ratios of Pluronic F-68 and SL-10. Figure 2 shows the photographs of emulsions of FDC with different HLB values. From Fig. 2, it can be seen that the required HLB value of FDC is located at 9.5. Also, Figure 3 illustrates the photographs of emulsions prepared with different concentra-

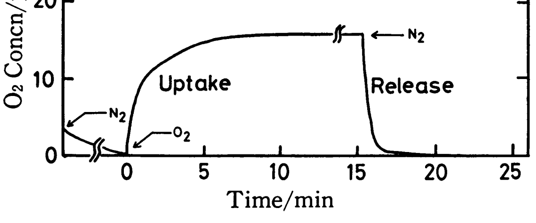

Fig. 1. The processes of "uptake and release" of oxygen into emulsion.

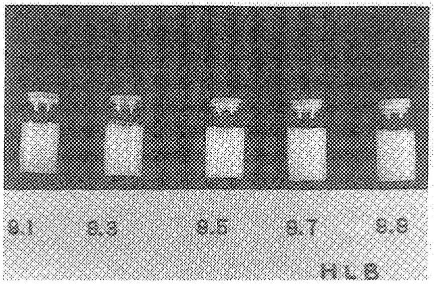

Fig. 2. Photographs of FDC emulsions with different HLB values.

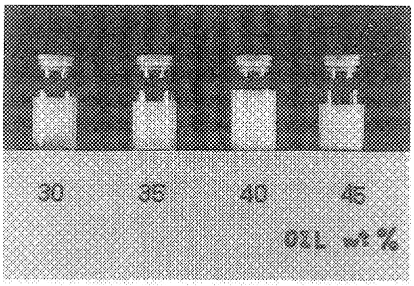

Fig. 3. Photographs of FDC emulsions with different concentration of FDC.

Table 1. The initial rates of "uptake and release" of oxygen into the fluorocarbon emulsions

Sample	Initial rate of uptake/ppm min^{-1}	Initial rate of release/ppm min^{-1}
FDC–A	12.4	6.8
FDC–B	4.4	1.8
FDC–C	2.4	0.9
FTBA–A	8.0	6.9
FTBA–B	4.4	4.9
FTBA–C	—	—
FDC-10%	10.8	8.9
FDC-20%	3.0	4.9
FDC-30%	0.4	1.7
FDC-0 d	18.4	8.9
FDC-30 d	1.0	4.9

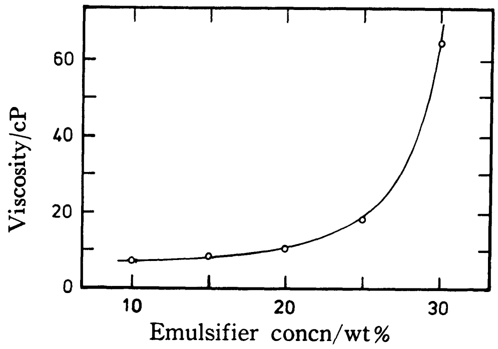

Fig. 4. The changes of the viscosity of FDC emulsion against the concentration of emulsifier.

tion of FDC. The emulsion became stable when the concentration of FDC was above 40 wt%. Further, it was found that the stable emulsion was obtained when the concentration of the emulsifiers was above 30 wt% of FDC concentration. In the case of FTBA, similar results were obtained. That is, the required HLB value of FTBA was found to be 10.3 and the stable FTBA emulsion was prepared at the conditions which the concentration of FTBA was above 40 wt% and the concentration of the emulsifiers was above 30 wt% of FTBA concentration. The mean particle size of FDC and FTBA emulsions prepared in the above conditions was below 0.2 μm and further the separation of FDC and FTBA from the continuous phase was not observed for period exceeding 60 d, respectively.

The relationships between the rates of "uptake and release" of oxygen into the emulsion and the factors which affect the emulsion stability of FDC and FTBA were examined. At first, in order to study the effect of particle size distributions of the emulsions, three kinds of FDC and FTBA emulsions with different particle size distributions were prepared. The rates of "uptake and release" of oxygen into these emulsions were measured. The proportions in weight of the emulsion particles below 0.2 μm were 96.5% in A, 58.7% in B, and 17.5% in C, respectively. The results are shown in Table 1. In the process of "uptake and release" of oxygen, the concentration of oxygen in the emulsion was changed most rapidly in A, but most slowly in C for FDC and ETBA. These results can be correlated with the interfacial area between the emulsion particles and the continuous phase. That is, the initial rates of "uptake and release" of oxygen decreased with decreasing interfacial area. Furthermore, it is noteworty that the saturated amounts of oxygen in the emulsions were constant for three samples in spite of different mean particle sizes. This indicates that the amount of oxygen dissolved in the emulsion is dependent on the total amount of perfluorocarbon, but is independent on the interfacial properties between perfluorocarbon and the continuous phase.

Figure 4 depicts how the concentrations of the emulsifiers affect the viscosity of FDC emulsions. The viscosity of the emulsion increased with increasing concentration of the emulsifiers, rapidly at above 30 wt% of them. As a next step, the effect of the viscosity of the emulsions on the rates of "uptake and release" of oxygen into them was studied. This result is given in Table 1. The concentrations of the emulsifier against FDC were 10, 20, and 30 wt%, respectively. In this case, from the measurement of particle size distribution, it was confirmed that the mean particle sizes of the three emulsions were almost the same. When the concentration of the emulsifier was 10 wt%, the concentration of oxygen dissolved in the emulsion was changed most rapidly, while at 30 wt%, it was changed most slowly. Thus, the initial rates of "uptake and release" of oxygen decreased with increasing the concentration of the emulsifier from 10 to 30 wt%. This suggests that the interfacial film of the emulsion particles would become thicker on increasing the concentration of the emulsifier.

Further, the relationship between the aging of the emulsions and the rates of "uptake and release" of oxygen into them was studied. In this study, two FDC emulsions were used. One was the emulsion freshly prepared, and the other was that aged for 30 d. The initial rates of the two emulsion are given in Table 1. The increases of the mean particle size and the viscosity were observed for the emulsion aged for 30 d compared with that freshly prepared. In addition, the initial rate of "uptake and release" of oxygen for the emulsion aged for 30 d was slower than that freshly prepared.

The results obtained in this study are summarized as follows:

(1) The initial rate of "uptake and release" of oxygen into the emulsion decreased with increasing the mean particle size of the emulsion.

(2) The saturated amount of oxygen in the emusion was independent of the mean particle size of the emulsion, but was dependent on the total amount of fluorocarbon in the emulsion.

(3) The initial rate of "uptake and release" of oxygen into the emulsion decreased with increasing the concentration of the emulsifiers and the viscosity of the emulsion.

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