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THE SOLUBILITY OF OXYGEN IN HIGHLY FLUORINATED LIQUIDS

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SUMMARY

Solubility of gases, especially oxygen, in fluorocarbons has achieved important status because of the latter's probable utility in artificial blood and liquid breathing, but only diverse data determined by various methods is scattered throughout the literature and company technical reports. One method, gas chromatography, was used to calculate and compare the oxygen and air solubility of a large number of fluorocarbons. Correlations were made between the oxygen solubilities and some of the physical properties of the compounds. Likewise, solubilities calculated using some lower parachor values resulted in a fairly good correlation.

RESULTS AND DISCUSSION

Since the primary reason for adding perfluorinated compounds to artificial blood is to carry oxygen, the amount of oxygen that a particular fluorocarbon can dissolve is of great interest. All other things being equal, the more oxygen that a compound dissolves the more useful it will be as a blood substitute and also as a breathable liquid. Only scattered and quite diverse data on oxygen solubilities of highly fluorinated compounds have been published (Table 1). Transport of carbon dioxide is of course also of tremendous importance in these endeavors, but since fluorocarbons dissolve two to three times as much of this gas as oxygen it is not the limiting factor affecting the choice of fluorocarbon.

The oxygen solubilities of twenty-five highly fluorinated liquids along with some of their known properties are listed in Table 2. Figure 1 is a plot of most of these values in order of decreasing solubility compared with calculated oxygen solubilities using the following equations and published parachors [1].

$$\sigma = \frac{(Pd)^4}{M}$$

$$\text{Log } L = -(0.025)\,\sigma$$

where

σ = surface tension
P = parachor
d = density
M = molecular weight
L = O_2 solubility

TABLE 1

Various determinations of dissolved oxygen in FC75

	O_2 25°C	AIR					
		O_2	N_2	Total	CO_2	Method	Ref.
	ml/100ml	ml/100 ml			ml/100 ml		
Our Values	52.2	10.5	27.2	37.7	-	G.L.C.	
3M	48.8	12.6	27.9	40.5	192	G.L.C.	[2]
	(48.5)^a	(11.7)^a	(26.7)^a	(39.4)^a			
duPont	-	10.6	28.3	38.9	-	G.L.C.	[3]
Allied	9.0	-	-	-	135	Volumetric	[4]
Sloviter	63 and 50.2	9.95	-	-	-	Enzyme^b	[5]
Nose	48^a	-	-	-	160	-	[6]
Geyer	81.4^c	-	-	-	-	-	[7]
Zander	46.9^d	-	-	-	-	Manometric^e	[8]

a. Measured at 37°C.
b. Glucose oxidase in the presence of excess glucose was used to measure dissolved oxygen in an emulsion.
c. Measured at 38°C.
d. Determined from figure 3 of reference 8.
e. Van Slyke manometric apparatus.

All but three of the calculated values fall below the observed values. This is not too surprising since all the parachor values, except for fluorine, were calculated using hydrocarbon models. Because of the uniqueness of perfluorocarbons compared to hydrocarbons and the effect of the highly electronegative fluorines on other atoms such as chlorine and bromine, we took the liberty of lowering the parachors for these two atoms and also the ring structure parachors. When replotted using these new values, a closer correlation results (figure 2). The value for nitrogen might also have been lowered, but we had available only one nitrogen-containing compound (FC47). In fact, the limited number of compounds tested make all these

TABLE 2

Oxygen solubility and other fluorocarbon properties

Code	Fluorocarbon Formula	Source	Oxygen Solubility ml/100 ml 25°C	Vapor Pressure mm Hg 37.5°C	Viscosity cs 25°C	Boiling Point °C	M.W. Daltons	Density gm/ml 25°C	Surface Tension dynes/cm 25°C
PP2	C_7F_{14}[a]	ISC[b]	57.2	180	0.88	76	350	1.788	14.2
E2	$CF_3CHF[OCF_2CF(CF_3)]_2F$	duPont	55.7	56	0.60	104.4	452	1.656	12.9
PFOBr	$CF_3(CF_2)_7Br$	3M	52.7	---	1.0[c]	140.5	499	1.890	16.4
$C_7F_{15}Cl$	$(CF_3)_2CF(CF_2)_4Cl$	Penn[d]	52.7	---	0.82	108	404	1.77	---
P12F	$(CF_3)_2CFO(CF_2)_6F$	Allied	52.5	39	0.95	121	504	1.721	---
FC75	$C_8F_{16}O$[e]	3M	52.2	51	0.82	102	416	1.783	14.8
C_8F_{18}	C_8F_{18}	PCR	52.1	---	0.85[c]	100-105	438	1.738	13.9
$C_3F_6Br_2$	$CF_3CFBrCF_2Br$	PCR	51.7	---	0.52[c]	72.8	310	2.155	---
$C_7F_{15}Br$	$(CF_3)_2CF(CF_2)_4Br$	Penn[d]	51.4	---	0.76[c]	120	449	1.977	---
P1D	$[(CF_3)_2CFOCF_2CF_2]_2$	Allied	50.3	13	1.2	135	570	1.748	13.8
C_9F_{20}	C_9F_{20}	Arm[f]	49.6	---	1.2[c]	119	488	1.84	---
HFB	C_6F_6	ISC[b]	48.8	---	0.5	81.5	186	1.599	---
E3	$CF_3CHF[OCF_2CF(CF_3)]_3F$	duPont	47.3	10	1.3	152	618	1.738	14.2
$C_9F_{19}Cl$	$(CF_3)_2CF(CF_2)_6Cl$	Penn[d]	45.6	9.6	1.5	151	504	1.83	---
PFTHDCP	$C_{10}F_{16}$[g]	Sun[h]	42.6	---	2.20	139	424	1.903	---
E4	$CF_3CHF[OCF_2CF(CF_3)]_4F$	duPont	42.2	1.9	2.3	194	784	1.770	15.2
L1822	$C_{10}F_{18}$[i]	3M	41.8	---	2.14	---	---	1.91	---
P11D	$[(CF_3)_2CFO(CF_2)_4]_2$	Allied	41.8	3	3.58	199	770	1.820	18.1
PP5	$C_{10}F_{18}$[j]	ISC[b]	40.3	13.6	2.61	142	462	1.946	15
E5	$CF_3CHF[OCF_2CF(CF_3)]_5F$	duPont	39.7	0.4	3.90	224	950	1.792	15.9
PFDMA	$C_{12}F_{20}$[k]	Sun[h]	39.4	---	4.35	175-180	524	2.00	---
FC47	$N(C_4F_9)_3$	3M	38.4	2.5	2.52	174	671	1.900	16
PP9	$C_{11}F_{20}$[l]	ISC[b]	38.4	5.2	3.32	160	512	1.972	15
DMB	$C_6H_4(CF_3)_2$	Pierce	35.4	---	0.58[c]	116	214	1.379	---
E9	$CF_3CHF[OCF_2CF(CF_3)]_9F$	duPont	33.3	0.08	20.4	308-490	1614	1.848	---

a) Perfluoromethylcyclohexane. b) ISC Chemicals Ltd., Avonmouth, Bristol, England. c) Determined in our lab. d) Pennwalt Corp. e) Mainly perfluorobutyltetrahydrofuran and perfluoropropyltetrahydropyran, also called FC80 and FX80. f) Armageddon Chem. Co., Durham, N.C., purified here. Believed to be 85% perfluorononane according to IR and G.C. g) Perfluorotetrahydrodicyclopentadiene. h) Sun Ventures, a Division of The Sun Oil Company, Marcus Hook, Penn. i) Large mixture of compounds from the electrochemical fluorination of decalin. j) Perfluorodecalin. k) Perfluorodimethyladamantane. l) perfluoromethyldecalin.

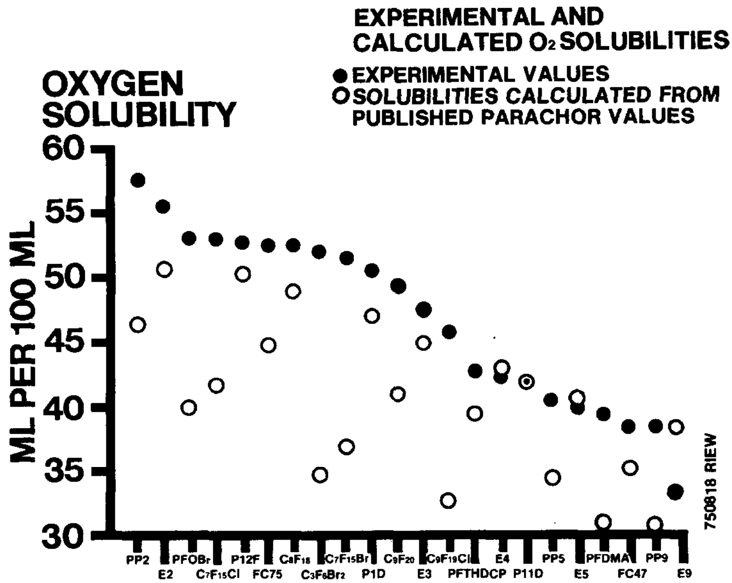

Fig. 1. The experimental oxygen solubilities of 22 fluorocarbons are compared to values calculated using published parachor [1].

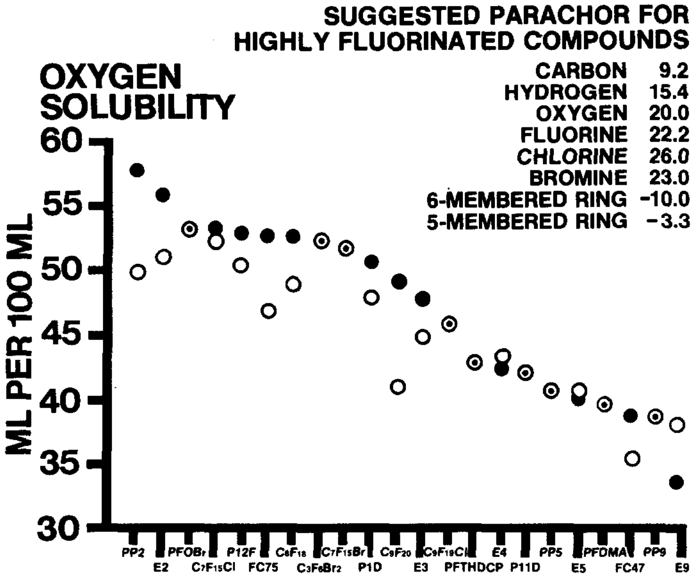

Fig. 2. Experimentally determined oxygen solubilities compared to values calculated using the parachors given.

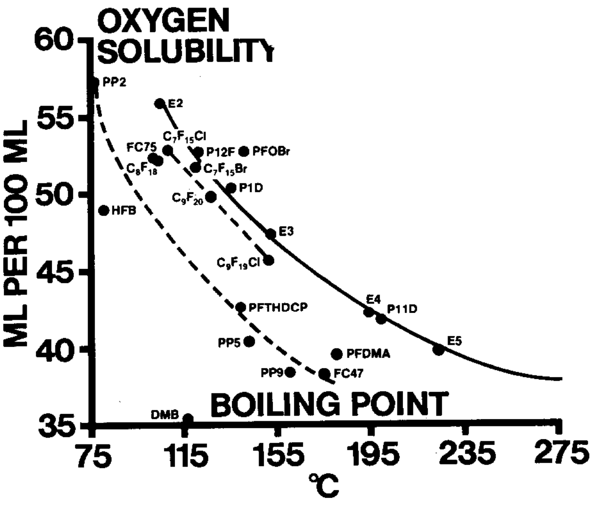

Fig. 3. Oxygen solubility of 22 fluorocarbons versus their boiling point.

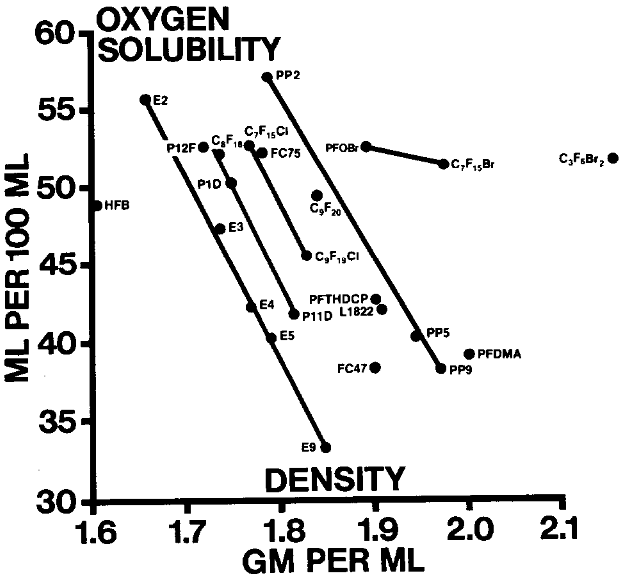

Fig. 4. Oxygen solubility of 23 fluorocarbons versus their density.

values at best tentative. Hopefully, however, they will continually be modified in the future to provide an increasingly useful means of predicting the oxygen solubilities of fluorocarbons of novel structure.

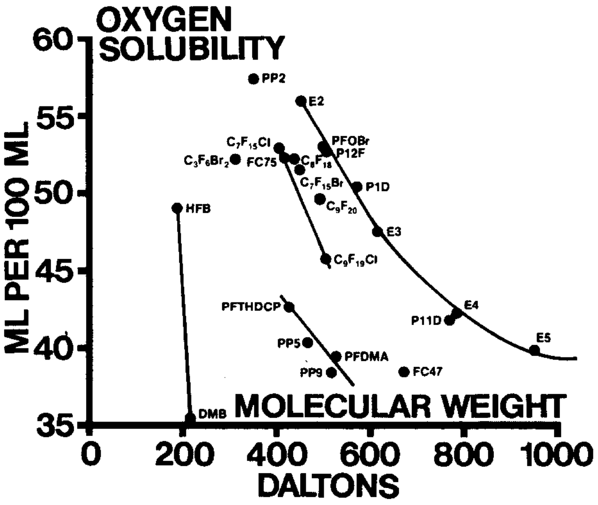

Fig. 5. Oxygen solubility of 23 fluorocarbons versus their molecular weight.

In an effort to find a simpler correlation between oxygen solubility and the physical properties of fluorocarbons, the graphs shown in figures 3-5 were plotted. These figures indicate that there are definite relationships between oxygen solubility and boiling point, density and molecular weight, within a given family of compounds. More or less parallel curves can be drawn among the fluorinated ethers (E-series, P1D, P11D, and P12F), the cyclic compounds (PP2, PP5, PFTHDCP and PFDMA), and the straight chain compounds. The latter compounds generally fall between the other two classes. Being a cyclic ether, FC75 also falls between the cyclic compounds and the ethers.

By plotting the oxygen solubility vs. viscosity (figure 6) surprisingly all the compounds (except the two aromatic compounds HFB and DMB) fall roughly along a single curve. Consequently, if the viscosity of a perfluorinated liquid is known or can be estimated, its oxygen solubility can be approximated. This correlation suggests that to maximize oxygen solubility new compounds should be designed that have the lowest viscosity within the desired boiling point range. For example, perfluorooctylbromide, with one third the viscosity, dissolves 30% more oxygen than perfluorodecalin although both compounds have approximately the same boiling points.

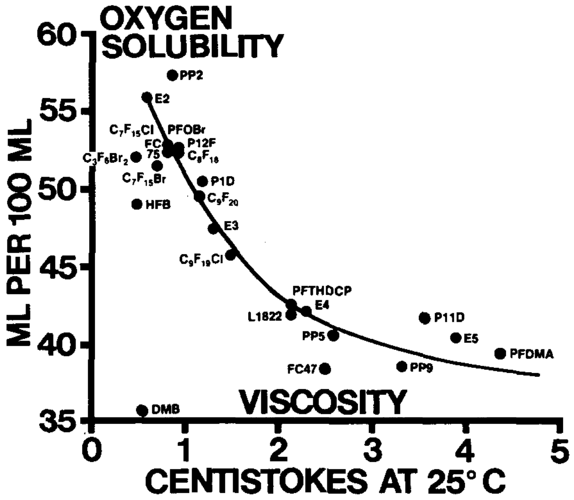

Fig. 6. Oxygen solubility of 24 fluorocarbons versus their viscosity.

Oxygen is more soluble than nitrogen in perfluorocarbons as in most other liquids. As a result, the percent oxygen dissolved in perfluorocarbons is always greater than the percent oxygen in the gas used to saturate it. The relationship is shown in figure 7 for various concentrations of oxygen and nitrogen bubbled through perfluorodecalin.

Air was bubbled through ten other fluorocarbons and in spite of the different solubilities, the percent dissolved oxygen was close to 28% in all but one case (Table 3). This phenomenon would appear to be advantageous to

TABLE 3

Air solubility in fluorocarbons

FC	AIR ml/100 ml	O_2 ml/100 ml	N_2 ml/100 ml	% O_2 in dissolved air
PP5	29.8	8.6	21.2	28.8
PFOBr	24.1	9.8	24.3	28.6
E2	42.4	11.1	31.3	26.1
PID	38.2	10.5	27.8	27.4
$C_7F_{15}Cl$	37.4	10.5	26.9	28.1
FC75	37.7	10.5	27.2	27.9
FC47	30.7	8.6	22.1	28.0
E5	31.8	8.6	23.2	27.3
L1822	32.0	9.0	23.0	28.2
C_8F_{18}	37.4	10.5	26.9	28.1
$C_7F_{15}Br$	36.0	10.2	25.8	28.4
Average	35.2	10.0	25.4	27.9

an animal infused with a perfluorochemical emulsion and breathing air. However, in reality, while an average of 48 ml/100 ml dissolved in the eleven fluorocarbons when bubbled with pure oxygen, only 10 ml/100 ml (∿ 21%) dissolved when air was used. This, of course, is the same as the percent oxygen in air so there does not seem to be any advantage from the preferential oxygen solubility at this particular concentration.

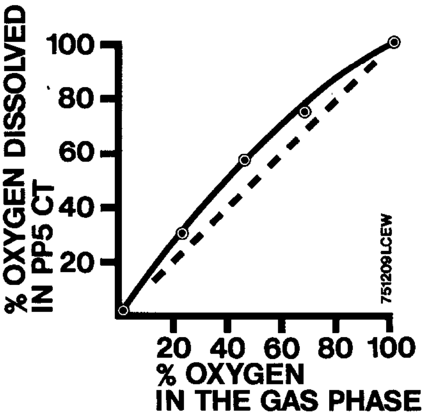

Fig. 7. Preferential solubility of oxygen (solid line compared to dashed) over nitrogen in perfluorodecalin.

MATERIALS AND METHODS

Gas chromatography was used to measure the oxygen solubility of 25 highly fluorinated liquids. The gas chromatograph used was equipped with a Carle 100 microdetector system and 12' x ¼" column packed with 45/60 13x molecular sieves. The column and injector temperatures were set at 70°C, and a helium gas flow of 60 cc/min was used. Under these conditions sharp symetrical well separated oxygen and nitrogen peaks were obtained on a Hewlett Packard Mosely 680 strip chart recorder. Consequently, measurement of peak heights was found to be a quantatively accurate method for measuring the varying amounts of oxygen. No error in linearity of height could be detected in the range used. The average reproducibility of peak heights was ± 0.95% and the average error in the precision of the method was ± 1.9%.

Fifteen ml of each fluorocarbon was magnetically stirred in a YSI model 5301 stirrer bath. The temperature of the circulating bath water was controlled by a Haake pump at 25°C $\pm$ 0.3. The fluorocarbon was bubbled with O_2 by means of a 1.5 inch 20 gauge needle inserted through a rubber stopper. A shorter needle allowed excess gas to escape. Saturation is reached within 15 minutes, but bubbling and stirring were continued during the entire sampling procedure. After several flushes, injections were made with Precision Sampling 50 μl Pressure-Lok syringe. Samples of fluorocarbon were drawn slowly and carefully into the syringe. At least 15 injections of 20 μl of the oxygenated fluorocarbon were made alternately with injections of 20 μl of pure O_2. Simple division of the average peak heights of the fluorocarbon sample by that obtained from pure O_2 yields the volume percent (cc/100 ml) of O_2 in the fluorocarbon.

The fluorocarbons are retained on the molecular sieve column which had to be periodically heated to above 300°C to drive them off. The separation between oxygen and nitrogen returns to normal with the injection of a sample of air when the column has been completely purged.

We also measured the volume of air that dissolves in eleven of the fluorocarbons. The method used was similar to that just described for pure O_2 except only five injections each of air (10 μl) and fluorocarbon (20 μl) were made. Because of differences in detector sensitivity and the tendency of the second component to have a slightly broader and consequently lower peak height, it was necessary to calculate a correction factor (1.05) for % of O_2. This was done either by the injection of air or by comparing injection of pure nitrogen and pure oxygen. Argon and oxygen are not separated on the molecular sieve column used, but argon has close to the same solubility as oxygen in fluorocarbon [2].

The solubility of two other oxygen plus nitrogen mixtures in perfluorodecalin were determined. Different quantities of oxygen and air were thoroughly mixed using two flasks before bubbling through the fluorocarbon. Alternate injections of the fluorocarbon and gas mixture were made and the percent oxygen calculated in each case as above.

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