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Glyceryl Trioleate-Water Partition Coefficients for Three Simple Organic Compounds

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Quite apart from the fact that lipid-water partitioning is only one of several factors contributing to the biomagnification of undesirable chemicals, there is the further question of whether the commonly used, and rather arbitrarily chosen, octanol-water partition coefficient is a good measure of the lipid-water partition coefficient (LEO et al. 1971, METCALF et al. 1975). While there are extensive compilations of the partitioning of organic compounds between octanol and water (LEO et al. 1971), there is little information available on partitioning between real lipids and water (MACY 1948). The isopiestic vapor pressure method used in this study is well suited for the study of partitioning of volatile organic solutes; the measurements reported here have been combined with literature data to obtain a comparison between the two types of partition coefficients for three representative organic compounds.

EXPERIMENTAL

Purity of the chemicals was verified by cryoscopy or by gas chromatography. Technical grade glyceryl trioleate (triolein) had a melting range of -7° to -5°C and a density at 37°C of 0.903. A few measurements were made with the more easily purified tripalmitin and tristearin but these two compounds were not soluble enough in any of the three solvents used here to yield partition coefficients. To the extent that they were soluble, however, they gave activity coefficients which agreed with those for triolein solutions, and any conclusions regarding triolein are probably also applicable to the other two lipids.

The determination of partition coefficients from solvent activities has been described elsewhere (PLATFORD 1976, 1977). If a solute is distributed between two immiscible solvents (water and triolein in this case) it must, at equilibrium, have the same activity in each, provided it has been assigned the same standard state in each solvent. Because the activity of any component is, by definition, the product of an

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activity coefficient and a concentration, it follows that the partition coefficient of the solute, which is a ratio of concentrations, is the inverse ratio of these activity coefficients. The solute, in this case, refers to the most volatile component in the system; it is experimentally one of the three volatile solvents, but is treated as a solute for purposes of calculating the partition coefficient.

The experiment is simple: The triolein, in solution in one of the three solvents, is equilibrated through the vapor phase with a reference solution, the solvent activity of which is known as a function of concentration. At isothermal equilibrium, the solvent activity of both solutions is the same and the solvent activity over the triolein solution can be determined by a series of experiments as a function of its concentration (the concentrations are conveniently determined by weighing, although volatility of the solute must be compensated for). The activity coefficient of the solvent, f_s^o, at zero concentration of solvent can then be obtained by extrapolation. If the activity coefficient of the same solvent in water, f_s^w, is known (and it can be estimated from its solubility in water (MACKAY et al. 1975)), then the partition coefficient of the solvent between the triolein and water on the mole fraction scale is given by f_s^w / f_s^o (PLATFORD 1976).

Most of the measurements were made on triplicate samples of both the reference solution and triolein solution and are reported in Table 1. For each run, the first column gives the mole fraction of the solvent dissolved in the reference solute. The second column gives the activity of the solvent calculated from the product $x_s f_s$. The mole fraction activity coefficient, f_s, has been determined for n-hexane in squalane (ASHWORTH 1973), for benzene in diphenylmethane (EVERETT and SWINTON 1963) and for carbon tetrachloride in both n-hexadecane (JAIN and LARK 1973) and benzophenone (RODDY and COLEMAN 1973). In the first set of results (for n-hexane), the temperature of the experiment was different from the temperature for which the activity coefficient was quoted, but this appeared to introduce no significant error. The third column gives the mole fraction of the solvent containing triolein and the fifth column gives the square of the triolein mole fraction, *i.e.*, the square of (one minus the quantity in the third column), for reasons which will be given later. Because f_s (triolein) $\cdot$ x (solvent) = a (Ref), the quantity in the fourth column can be obtained from those in the second and third columns. The sixth column gives the water activity in the constant temperature enclosure; this was controlled by the inclusion of desiccant or of a saturated aqueous solution of some appropriate salt in

Table 1 Rational activity coefficients of three solvents in glyceryl triolate

n-hexane

x(Ref)[1]	a(Ref)	x(C_6H_{14})	ln f (C_6H_{14})	x^2_{TO}	a_w	T
0.645	0.565	0.668	-0.17 ± 0.01	0.110	0	37
0.460	0.370	0.493	-0.29	0.257	0.98	37
0.368	0.283	0.405	-0.36	0.354	0.98	37
0.187	0.131	0.220	-0.52 ± 0.03	0.608	0	37
0.129	0.088	0.155	-0.57	0.714	0.1	37
0.111	0.075	0.133	-0.57	0.752	0.1	37
0.101	0.068	0.123	-0.59 ± 0.05	0.769	0.1	25
extrapolated			-0.70 ± 0.05	1.0		

benzene

x(Ref)[2]	a(Ref)	x(C_6H_6)	ln f (C_6H_6)	x^2_{TO}	a_w	T
0.520	0.516	0.767	-0.40 ± 0.05	0.054	0.98	37
0.497	0.492	0.736	-0.40	0.070	0.98	20
0.551	0.546	0.720	-0.28	0.078	0.10	20
0.310	0.303	0.588	-0.66	0.170	0.98	37
0.363	0.356	0.586	-0.50	0.171	0	37
0.071	0.068	0.324	-1.6 ± 0.1	0.457	0.10	20
0.101	0.096	0.322	-1.2	0.460	0.98	20
0.050	0.048	0.205	-1.5	0.63	0.98	20
0.033	0.031	0.169	-1.7	0.69	0.98	37
0.032	0.030	0.170	-1.7	0.69	0.98	37
0.049	0.047	0.180	-1.3 ± 0.5	0.67	0	37
extrapolated			-2.0 ± 0.5	1.0		

carbon tetrachloride

x(Ref)[3]	a(Ref)	x(CCl_4)	ln f (CCl_4)	x^2_{TO}	a_w	T
0.574 *	0.680	0.858	-0.23	0.020	0.10	25
0.476 *	0.594	0.817	-0.32	0.033	0.98	25
0.342	0.310	0.606	-0.67	0.155	0	37
0.296	0.264	0.568	-0.77 ± 0.1	0.187	0	37
0.201	0.176	0.500	-1.05	0.250	0.98	25
0.124	0.104	0.329	-1.15	0.450	0.98	37
0.031	0.025	0.118	-1.5	0.78	0.98	37
0.029	0.023	0.125	-1.7 ± 0.5	0.76	0	37
extrapolated			-2.0 ± 0.5	1.0		

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[1] Reference solute for hexane was squalane (ASHWORTH 1973).

[2] Reference solute for benzene was diphenylmethane (EVERETT and SWINTON 1963).

[3]* Reference solute for carbon tetrachloride was benzophenone for first two points (RODDY and COLEMAN 1973) and n-hexadecane for all other points (JAIN and LARK 1973).

the enclosure (ROBINSON and STOKES 1965). The last column gives the temperature at which the run was made.

The results for all three sets of data are plotted in Fig. 1. The quantities in the last two

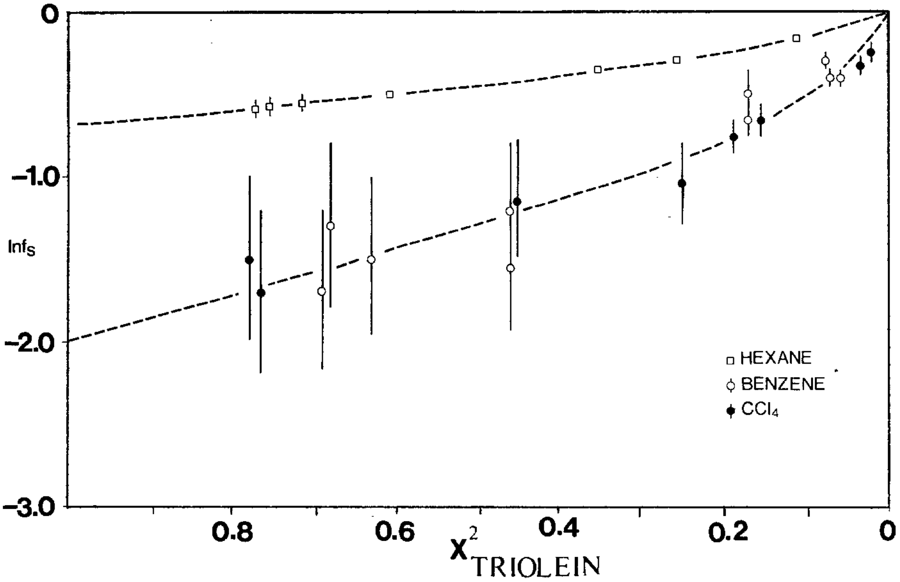

Fig. 1 Mole fraction activity coefficient of three solvents in glyceryl trioleate at 20-37°C.

columns of Table 1 indicate that $\ln f_s$ is independent of temperature and of the presence or absence of water in the system (water is soluble to the extent of 10 mole per cent in triolein at 37°; this necessitated a correction in the calculation of concentrations by weights). The reason for plotting $\ln f_s$ against x^2_{TO} in Fig. 1 is that for many systems this produces a linear plot (HILDEBRAND and SCOTT 1964) which facilitates extrapolation to $x^2_{TO} = 1$. This value of f_s for each solvent is divided into the limiting value for f^w_s in water (PLATFORD 1976, 1977; MACKAY et al, 1975) to give the partition coefficients for the three solvents. These are compared with the previously determined n-octanol-water partition coefficient in Table 2. To simplify comparison with literature values, my values have been converted to the molar scale by dividing by 54.4 for the triolein and 8.8 for the octanol. The partition coefficients for the three solvents vary over a range of about 50, but the ratios of the values in the fourth and fifth columns of Table 2 vary by a factor of less than 3.5. This good correlation probably

TABLE 2

Molarity partition coefficient for three organic solvents (20 - 37°C) (a)

	f_s^w	f_s^o	P_w^{TO}	P_w^{OCT}
n-hexane	3×10^5	0.50	11×10^3	8×10^3 (b)
benzene	2.5×10^3	0.14	330	135
CCl_4	1.1×10^3	0.14	1500	435

(a) Probable error in P is about ±20% for hexane and ±50% for benzene and carbon tetrachloride.

(b) Obtained using method described by PLATFORD (1976) and solubility data of MACKAY et al. (1975).

justifies the practice of using octanol-water partitioning as an analogue to lipid-water partitioning in animals.

CONCLUSIONS

The partition coefficients of n-hexane, benzene and carbon tetrachloride between glyceryl trioleate and water have been derived from vapour pressure measurements. Within the accuracy of about ±50%, they are independent of temperature from 20°-37°C, and are all about two or three times larger than literature values for octanol and water. This lends support to the proposition that octanol-water partition coefficients, for which there are extensive literature tabulations,are a useful substitute for lipid-water partition coefficients needed in bioaccumulation studies.

It is appropriate to add here a note of caution regarding the practice of equating the partition coefficient to a ratio of solubilities. These quantities are indeed equal if both the lipid and water are saturated with the solute in question. At solute concentrations below saturation, however, they are equal only if the solute activity coefficient is independent of its concentration in each solvent. This seems to be the case for simple solutes dissolved in water, but is not true for these same solutes in octanol or in lipid (PLATFORD 1976, 1977). A distinction should therefore be made between partition coefficients for solutes present at saturation, and for those present in trace amounts.

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