Equations for water-triolein partition coefficients for neutral species; comparison with other water-solvent partitions, and environmental and toxicological processes

Michael H. Abraham [a,*], William E. Acree Jr. [b]

[a] Department of Chemistry, University College London, 20 Gordon St, London WC1H 0AJ, UK
[b] Department of Chemistry, 1155 Union Circle Drive #305070, University of North Texas, Denton, TX 76203-5017, USA

HIGHLIGHTS

- Water-triolein partition coefficients are collected for 200 compounds.
- These partition coefficients are analysed using Abraham descriptors.
- Separate equations are needed for wet and dry triolein.
- Water-triolein is not a good model for 16 environmental systems.
- Water-triolein is not a good model for 17 aqueous toxicological systems.

GRAPHICAL ABSTRACT
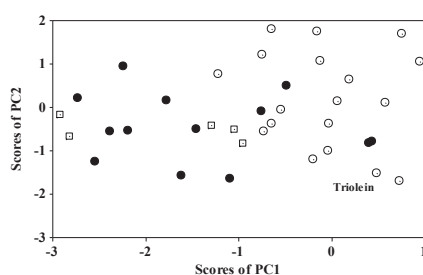
ABSTRACT

Linear free energy relationships, LFERs, have been constructed for water-triolein partition coefficients for neutral species. It is shown that separate equations are required for wet and dry triolein. From a comparison of the equation coefficients for water-wet triolein with those for 52 other water-solvent systems it is shown that there is little correspondence between triolein and any of the 52 other solvents - only the water-isopropyl myristate system is close to the water-wet triolen system. A comparison of equation coefficients for the water-wet triolein system with LFER coefficients of 16 environmentally important processes shows that wet triolein is not a suitable model for any of the processes, although a number of other water-solvent systems are possible models for some of the environmental processes. A comparison of LFER coefficients with those of 17 aqueous toxicological processes reveals that most of the water-solvent systems, including water-wet triolein, will be poor models for any of the toxicological systems, but the water-lower alcohol systems show promise as models for a number of the toxicological systems. Our method of comparison of coefficients for LFERs that have exactly the same independent variables can be extended to various other types of system.

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1. Introduction

The water-octanol partitioning system has commonly been used as a model for environmental and biological processes (Leo and Hansch, 1971; Dearden, 1985). There is no particular reason why this system was chosen. Indeed, other water-solvent systems have

* Corresponding author.
E-mail addresses: m.h.abraham@ucl.ac.uk (M.H. Abraham), bill.acree@unt.edu (W.E. Acree).

been used quantitatively, notably oleyl alcohol (Meyer and Hemmi, 1935), although this important work went almost unnoticed for 60 years (Abraham, 1996). There have been a number of studies on comparisons of various water-solvent partitioning systems (Collander, 1950, 1951; Niimi, 1991; Kishino and Kobayashi, 1994) including the water-triolein system (Niimi, 1991). In addition, water-solvent systems have been examined as surrogate systems for various environmental and other processes (Chiou, 1985; Jabusch and Swackhamer, 2005; Quinn et al., 2014; Hung et al., 2014). One difficulty over these 1:1 comparisons is that the number of comparisons becomes very large as the number of systems increases. Thus for five systems, nine 1:1 comparisons are needed, but for ten systems no less than 44 1:1 comparisons are required. Another difficulty is that 1:1 comparisons are restricted because of the limited number of overlapping compounds in the two series. Chiou (Chiou, 1985) compared water-octanol partition coefficients, *Poct*, with water-triolein partition coefficients, *Ptrio*, and showed that there was not quite a linear relationship between log *Poct* and log *Ptrio*. However, a plot of log *Ptrio* against log *Poct* (Quinn et al., 2014) is a reasonable straight line. These results are not incompatible because different data sets were used; 38 assorted compounds (Chiou, 1985) and 18 polychlorobiphenyls, PCBs (Quinn et al., 2014). Clearly, some other method needs to be employed in order to obtain some general comparison of systems.

A recent development has been the use of multiple linear regression analysis, MLRA, in which a number of independent variables are used to correlate some dependent variable. The linear free energy equations, LFER, thus generated are also known as polyparameter linear free energy equations, PP-LFER, and have been used extensively (Endo and Goss, 2014) to analyze environmental processes. We have applied the LFER method to numerous water-solvent partitioning systems (Abraham and Acree, 2010; Hart et al., 2015) and have then used the coefficients in the LFERS in order to compare systems. The water-triolein system is one of the partitioning systems that we have not studied, and the purpose of this work is to set out an LFER for the water-triolein system and then to use the various LFERs that have been constructed to compare water-solvent systems both with each other and with environmental and biological/toxicological processes.

2. Methods

2.1. Data analysis

Our method relies on two LFERs, one for transfer processes occurring within condensed phases, Eq. (1), and one for processes involving gas-to-condensed phase transfer, Eq. (2) (Abraham, 1993; Abraham et al., 2004, 2010; Hart et al., 2015).

$$SP = c + e\,E + s\,S + a\,A + b\,B + \nu\,V \tag{1}$$

$$SP = c + e\,E + s\,\mathbf{S} + a\,A + b\,B + l\,L \tag{2}$$

The dependent variable, SP, is some property of a series of solutes in a fixed phase. In the case of Eq. (1) this will include the logarithm of a water-solvent partition coefficient, *P*. We shall not use Eq. (2) to compare systems, but it is a useful equation to have and so we will apply Eq. (2) just to the water-triolein system. The independent variables, or descriptors, are solute properties as follows: E and S refer to the excess molar refraction and dipolarity/polarizability descriptors of the solute, respectively, A and B are measures of the solute hydrogen-bond acidity and basicity, V is the McGowan volume of the solute and L is the logarithm of the solute gas phase dimensionless gas to hexadecane partition coefficient at 298 K. There have been a number of reviews of our method

(Abraham et al., 2004; Poole et al., 2009, 2013), that of Clarke and Mallon (Clarke and Mallon, 2012) is particularly thorough.

In order to apply Eq. (1) to the water-triolein system we need values of the water-triolein partition coefficient, *Ptrio*. These can be obtained by direct partition, that is partition into wet triolein, or indirectly from solubilities in water, *Sw*, and in triolein, *Strio* through Eq. (3), that is partition into dry triolein; solubilities are expressed as mol dm^{-3}.

$$Ptrio = Strio/Sw \text{ or } \log Ptrio = \log Strio - \log Sw \tag{3}$$

The data base of log *Ptrio* values can be increased by the incorporation of values derived from gas-triolein partition coefficients, *Ktrio*, through Eq. (4) where *Kw* is the gas-water partition coefficient. In this work we use dimensionless values of *Ktrio* and *Kw*. We make a distinction between values for dry and wet triolein, and we list all the log *Ktrio*, log *Ptrio*, and log K_w values that we use as Supplementary material, Table S1 (Lindenberg, 1951; Patton et al., 1984; Chiou, 1985; Chiou and Manes, 1986; Niimi, 1991; Alessi et al., 1995; Philippe et al., 2003; Jabusch and Swackhamer, 2005; Hung et al., 2012, 2014; Quinn et al., 2014).

$$\text{Log } Ktriol = \log Ptriol + \log K_w \tag{4}$$

A preliminary analysis of the log *Ptrio* values showed that those for carboxylic acids (Patton et al., 1984) were quite out of line. The dielectric constant of triolein is very small, $\varepsilon = 3.02$ (Litchfield, 1971) and by comparison with dimerization constants for propanoic acid in various solvents (Kojima et al., 1970) the dimerization constants for the carboxylic acids in triolein will be about 500 mol^{-1} dm^3. Then at the total concentration in triolein as given (Patton et al., 1984), most of the acid will be present as the dimer. We therefore did not consider these compounds further. Although the solubility of water in triolen is very small, it is possible that it has an influence on partition. We had enough data to divide the data set into partition into dry triolein and wet triolein and obtained LFERs for partition into dry and wet triolein separately, and also combined into a 'total' data set, Eqs. (5)–(7). In these equations, N is the number of data points (not the number of compounds because there are some multiple entries), SD is the regression standard deviation, R is the correlation coefficient, F is the F-statistic and *PRESS* and Q^2 are the leave-one-out statistics. *PSD* is the predictive standard deviation (Abraham et al., 2009).

$$\text{Log } Ptrio(\text{Total}) = 0.406 + 0.876\,E - 1.712\,S - 2.946\,A$$
$$- 3.820\,B + 4.000\,V \tag{5}$$

$$N = 231,\ SD = 0.345,\ R^2 = 0.980,\ F = 2207.1,\ PRESS$$
$$= 28.884,\ Q^2 = 0.979,\ PSD = 0.358$$

$$\text{Log } Ptrio(\text{Wet}) = 0.531 + 0.856\,E - 1.191\,S - 3.110\,A$$
$$- 3.913\,B + 3.522\,V \tag{6}$$

$$N = 141,\ SD = 0.294,\ R^2 = 0.985,\ F = 1730.0,\ PRESS$$
$$= 12.963,\ Q^2 = 0.983,\ PSD = 0.310$$

$$\text{Log } Ptrio(\text{Dry}) = 0.489 + 0.945\,E - 1.892\,S - 2.784\,A - 3.627\,B$$
$$+ 4.012\,V \tag{7}$$