THE OCTANOL-WATER PARTITION CONSTANT: K_{ow}

The distribution of nonpolar organic compounds between water and natural solids (e.g., soils, sediments and suspended particles) or organisms, can be viewed in many cases as a partitioning process between the aqueous phase and the bulk organic matter present in natural solids or in biota (*1*). As early as 1900, investigators studying the uptake of nonpolar drugs by organisms discovered that they could use water-immiscible organic solvents like *n*-octanol as a surrogate for organisms or parts of organisms insofar as accumulation of these pharmaceutical organic molecules from the water was concerned. Although the extent of the uptake from the water was not identical to that into the organisms, it was directly proportional. That is, within a series of compounds, greater partitioning into *n*-octanol corresponded to a greater accumulation into an organism. More recently, environmental chemists have found similar correlations with soil humus and other naturally occurring organic phases. These correlations exist because the same molecular forces controlling the distribution of compounds between water-immiscible organic solvents and water also determine environmental partitioning from water into natural organic phases.

The octanol-water partition coefficient is defined simply by;

$$K_{ow} = \frac{C_{octanol}}{C_{water}}$$

where $C_{octanol}$ is the molar concentration of the organic compound in the octanol phase and C_{water} is the molar concentration of the organic compound in water when the system is at equilibrium. The units are usually dropped and K_{ow} is generally reported as a unitless ratio.

Since the solubility in each solvent can be approximated by;

$$C = \frac{1}{\overline{V}\, \gamma}$$

and

$$K_{ow} = \frac{\gamma_w^{\,sat}\, \overline{V}_{H2O}}{\gamma_{oct}^{\,sat}\, \overline{V}_{oct}}$$

If we add octanol and water to a flask, shake it vigorously and then wait for the two phases to separate, the system will eventually reach equilibrium. The two phases will be mutually saturated with one another, i.e., the octanol phase will contain 20% water and the water phase will contain $8 \times 10^{-3}\%$ octanol. Thus, in actual fact, the partition coefficient, K_{ow} is the ratio of the molar concentration of an organic compound in *octanol saturated with water* to the molar concentration in *water saturated with octanol.*

For a series of neutral nonpolar compounds partitioning between octanol and water, we find the K_{ow} value is determined largely by the magnitude of the aqueous activity coefficient (a measure of the dissimilarity between the organinc solute and the aqueous solvent). In other words, the major factor that determines the magnitude of the partition constant of a nonpolar or moderately polar organic compound between an organic solvent and water is the incompatibility of the compound with water. The nature of the organic solvent is generally of secondary importance. Consequently, we would not be surprised to find a correlation between K_{ow} and water solubility.

Methods of Estimating K_{ow} for Organic Compounds.

1) Aqueous Solubility

For similar classes of compounds, excellent linear relationships are found between aqueous solubility and K_{ow}, in the form;

$$log \ K_{ow} = a \ log \left(\frac{1}{C_w^{sat}} \right) + b$$

For a specific group of compounds, by measuring the aqueous solubility we can obtain the K_{ow} or vice versa. This relationship works for compounds of similar polarity and molecular size.

For example, an linear relationship for benzenes with nonpolar substituents is given by;

$$log K_{ow} = -0.86 \ log C_w^{sat} + 0.75$$
$$r^2 = 0.98$$

2) High Performance Liquid Chromatography

In Reverse Phase High Performance Liquid Chromatography, RP HPLC the organic solute is transported in a polar mobile phase (water or methanol-water mixtures) through a nonpolar stationary phase (C_{10} to C_{18} n-alkanes covalently bound to a porous silica support). As the organic solutes move through the system they partition between the polar mobile phase and the oily surface of the nonpolar stationary phase. It is generally considered that the solute is actually *adsorbed* at the surface of the stationary phase, rather than being *absorbed* (dissolved) into it. For a series of structurally related compounds of similar size and shape, good correlations between K_{ow} and the retention time (the time for the solute to travel through the stationary phase or column) are obtained.

Linear correlations in the form of the following are obtained;

$$log \ K_{ow} \ = \ a \ log \ t \ + \ b$$

where a = slope, t is the retention time and b = intercept.

3) Estimations based on Structural Group Contributions

Much work has gone into developing structural group contribution methods and these are amoung the mostly widely used quantitative structure activity relationships used today. The approach is similar to that used for predicting K_H values but has been refined by adding a number of correction factors to include a variety of intra and inter molecular interactions, including geometry, flexing chains, branching, electronic factors, polyhalogenation and intramolecular H-bonding.

$$log K_{ow} = \Sigma f_i + \Sigma F_j$$

where f_i values quantify contributions from each structural unit' and F_j values account for special intramolecular interactions.

K_{ow} as a Predictor of Other Partitioning Phenomena

The *n*-octanol/water partition coefficient has proved useful as a means to predict partitioning between water and sediments, soil adsorption, biological uptake, lipophilic storage, biomagnification and toxicity.

1) The Organic Matter-Water Partition Coefficient, K_{om}

Particulate natural organic matter (humins) contains both polar and nonpolar characteristics and may exist as organic chains coiled into globular units and coatings adsorbed on solid particles. Nonpolar solutes can physically penetrate between the chains and find themselves "dissolved" in the nonaqueous medium because of the porous nature of flexible macromolecules. Thus, we can imagine the natural organic matter behaving like an organic solvent, such as octanol, and the organic solutes as distributing itself between two immiscible solutions, and we may define a partition coefficient;

$$K_{om} = \frac{C_{om}}{C_w}$$

where C_w is the molar aqueous concentration of uncharged organic solute, and C_{om} is the molar concentration of the organic solute associated with the natural organic matter. Linear relationships have been established for specific classes of organic solutes between K_{ow} and K_{om}. An example being for aromatic hydrocarbons;

$$\log K_{om} = 1.01 K_{ow} - 0.72$$
$$r^2 = 0.99$$

2) Bioconcentration

It has long been recognized that nonpolar organic compounds accumulate in organisms to an extent that is directly related to the magnitude of K_{ow}. For example, the bioconcentration factor (BCF) which is defined as the concentration of the organic compound in an aquatic organism divided by the concentration in the water has been shown to correlate with octanol-water partition constants;

$$\log BCF\left(\frac{mol/g \; wet \; fish}{mol/mL \; water}\right) = 0.85 \log K_{ow} - 0.70$$
$$r^2 = 0.90$$

based on tests on fathead minnows, rainbow trouts and bluegills.

3) Acute Toxicity

In a large number of studies in which fish or daphnia were used as test organisms, it was also found for various compound classes, that the acute toxicities of the compounds correlated quite well with their K_{ow}'s. It was found that the LC_{50} (the concentration of a compound causing 50% mortality in a particular species after a certain time period) for guppies correlates with the K_{ow} for many classes of organic compounds. For example, the following relation was obtained for chlorobenzenes for a 14 day LC_{50} (μM);

$$\log\left(\frac{1}{LC_{50}}\right) = 0.977 \; \log K_{ow} + 5.00$$
$$r^2 = 0.97$$

(1) Environmental Organic Chemistry, 2 nd Ed., R.P. Schwarzenbach; P.M. Gschwend; D.M. Imoden, J. Wiley and Sons, **2004**.