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LOGKOW
A Databank of Evaluated Octanol-Water Partition Coefficients

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ABSTRACT

The octanol-water partition coefficient is a laboratory-measured property of a substance. Partition coefficients are used extensively in medicinal chemistry, drug design, ecotoxicology and environmental chemistry. A very large compilation of partition coefficients is described, which contains also details of experimental measurement, CAS Registry Numbers, Recommended Values and literature references in Chemical Abstracts form.

Introduction

If a third substance be added to two immiscible solvents in contact, it will distribute itself between the two solvents. At equilibrium, the ratio of solute concentrations in the two solvents will attain a definite value. This was noticed at an early date (1).

The value of this partition coefficient will in general depend upon temperature, pressure, concentration and the nature of solvents and solute. As used in the present context, the partition coefficient usually refers to very dilute solutions, in which the solute has the same molecular form in both solvents. (Thus organic acids – which dimerize – and salts – which ionize – are usually excluded from this strict definition).

The octanol-water partition coefficient, K_{ow}, is a thermodynamic measure of the tendency of a solute to prefer a non-aqueous milieu to water. The octanol-water pair has been of particular interest for at least 30 years (2). It was known, from about 1900, that the narcotic action of many organic compounds could be correlated with their oil-water partition coefficients. In modern times, the “oil” of preference has become octanol (3).

Currently, K_{ow} has wide use in two principal areas, viz., medicinal chemistry/drug design and environmental chemistry. In medicinal chemistry, its usefulness resides in its participation in *quantitative structure-activity relationships* (often abbreviated as QSAR). A QSAR may take the form

$$BR = a + b \log K_{ow} \qquad (1)$$

where BR is biological response (protein-ligand binding, metabolism, CNS agent and microbial action, etc.)(4). In environmental chemistry, the general relation (1) has been useful in correlating such properties of organic pollutants as bioaccumulation and soil-water partition coefficients (5,6).

Data Evaluation in the Databank

Like any physico-chemical property, K_{ow} may be measured in a number of ways. The methods differ enormously in ease of execution, inherent precision, apparatus required, etc. (7). For example, the reported K_{ow} data for DDT cover a range of 1000 (8). The author has compiled a Databank of experimental K_{ow} data for over 20,000 compounds (8). In addition to the K_{ow} data themselves, details of experimental measurement, abstracted from original publications are also included, as well as Recommended Values (wherever possible). Data sources are fully referenced.

Search and display of data in LOGKOW

The Databank may be searched by molecular formula, by Chemical Abstracts Registry Number or in “browse” mode. A typical output data display for a compound is given in Fig. 1. In addition to the data already mentioned, the display includes IUPAC names, pK_a values and S.M.I.L.E.S. notation (Simplified Molecular Input Line Entry System: a method for representing the structure of a molecule as a string of ASCII symbols).

Availability and Updating

The Databank is available online at **www.tds-tds.com**. A version on PC diskettes may be purchased from the author It is hoped that the Databank will be available free of charge on the Internet in future.

The Databank is updated monthly.

REFERENCES

1. W. Nernst, Z. Phys. Chem. **8**, 110 (1891).
2. A Leo, C. Hansch and D. Elkins, Chem. Rev. **71**, 525 (1971).
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4. C. Hansch and A. Leo, *Exploring QSAR: fundamentals and applications in chemistry and biology*, American Chemical Society, Washington (1995).
5. D. W. Connell, *Bioaccumulation of Xenobiotic Compounds*, CRC Press, Boca Raton (1990).
6. G. G. Briggs, J. Agric., Food Chem. **29**, 1050 (1981).
7. J. Sangster, J. Phys. Chem. Ref. Data **18**, 1111 (1989).
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Figure 1

FORMULA: $C_7H_6O_3$ **CAS#:** 99-06-9 **pK_a:** 4.05

NAME: Benzoic acid, 3-hydroxy-

SMILES: c1c(O)cc(C(=O)O)cc1

Log Kow	Footnote	Ref	Temp	Equil Method	Anal Method	Aq Phase	Phases Anal	Meth Ref
1.37		82Han	----------------- HPLC retention time correlation ------------					
1.47	59	89Wan	25	SF	AS	pH2-8	AQ	
1.48		75Kor	20	SF		pH2		
1.48		90Kora		SF	AS	pH1.2	AQ	
1.50		64Fuj	25	SF	AS	W	AQ	
1.50		81But	------------------ HPLC retention time correlation ------------					
1.55		92Da	25	SF	AS	pH2	AQ	
1.56	53	81Dea		SF	AS	pH1	ORG	79Can

Footnote: 53: filter-probe rapid-mix apparatus
59: ion-corrected to neutral form

RECOMMENDED VALUE: 1.50

References:

64Fuj: T. Fujita, J. Iwasa and C. Hansch, "A new substituent derived from partition coefficients", J. Am. Chem. Soc. **86**(23), 5175-5180 (1964).

75Kor: Ya. I. Korenman, "Extraction of hydroxybenzene acids and some of their derivatives from aqueous solution", J. Appl. Chem. USSR (Engl. Transl.) **48**(6), 1472-1474 (1975).

79Can: F. F. Cantwell and H. Y. Mohammed, "Photometric acid-base titrations in the presence of an immiscible solvent", Anal. Chem. **51**(2), 218-223 (1979).

81But: W. Butte, C. Fooken, R. Klussmann and D. Schuller, "Evaluation of lipophilic properties for a series of phenols, using reversed-phase high-performance liquid chromatography and high-performance thin-layer chromatography", J. Chromatogr. **214**(1), 59-67 (1981).

81 Dea: J. C. Dearden and G. M. Bresnen, "Thermodynamics of partitioning – some considerations of intramolecular hydrogen bonding and steric effects", J. Pharm. Pharmacol. **33**(Suppl.) 107P (1981).

Etc.