

Physicochemical Profiling

Log D_{7.4} Shake Flask

Background Information



'A compound with moderate lipophilicity (Log D 0-3) has a good balance between solubility and permeability and is optimal for oral absorption, cell membrane permeation in cell-based assays, is generally good for BBB penetration (optimal Log D ~2) and has low metabolic liability.'

¹Di L and Kerns EH (2003) *Current Opinion in Chemical Biology* **7**; 402-408.

- Lipophilicity is a key determinant of the pharmacokinetic behaviour of drugs. It can influence distribution into tissues, absorption and the binding characteristics of a drug, as well as being an important factor in determining the solubility of a compound.
- Log D (distribution co-efficient) is used as a measure of lipophilicity. Determining the partition of a compound between an organic solvent (typically octanol) and aqueous buffer is one of the most common methods for determining this parameter.
- Cyprotex's Log D_{7.4} assay uses the octanol / buffer shake flask method for determining lipophilicity. LC-MS/MS is used to quantify the samples.

Protocol

Method

Octanol:buffer shake flask method

Partition Solvent

n-Octanol

Ratio of Buffer: Octanol

2:1 (v:v); other ratios available on request

Control Compounds

Tolbutamide, ketoconazole

Analysis Method

LC-MS/MS quantification of both phases

Data Delivery

Log D_{7.4}

Increasing lipophilicity of a compound series generally increases permeability, protein binding and volume of distribution, and decreases solubility and renal extraction².

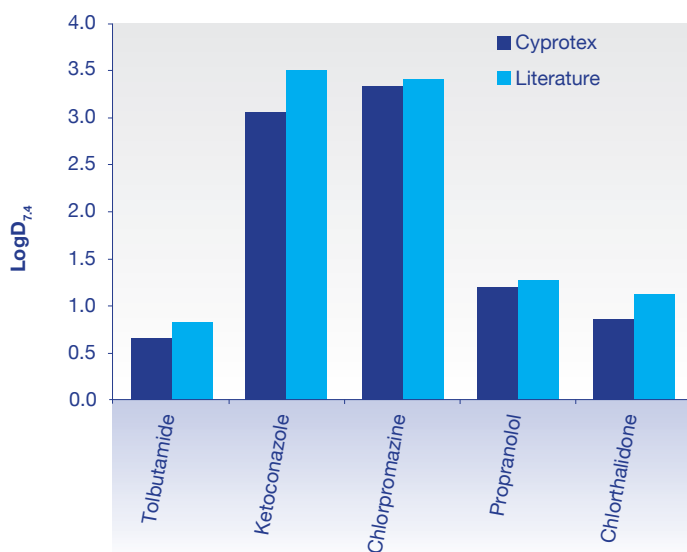


Log D_{7.4} Shake Flask

Compounds with a range of lipophilicity values were screened in Cyprotex's Log D_{7.4} shake flask method. Log D_{7.4} values were compared with data reported in the literature.

Figure 1

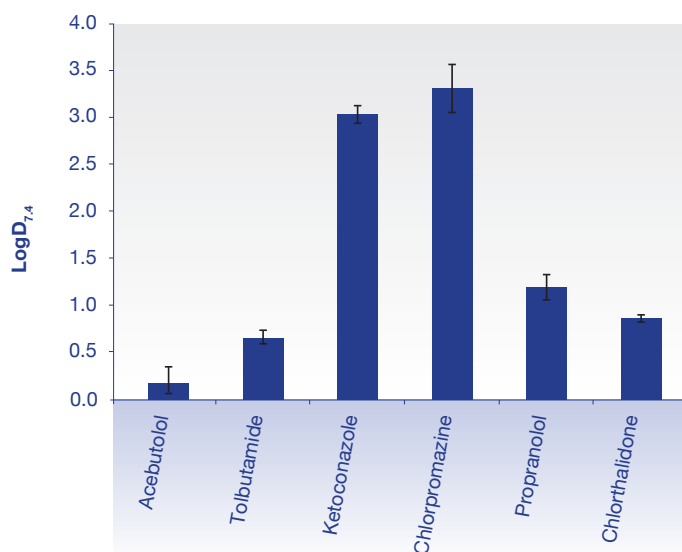
Comparison of Log D_{7.4} values generated in Cyprotex's Log D_{7.4} shake flask assay with Log D_{7.4} values reported in the literature³.



The graph illustrates good correlation of Cyprotex's Log D_{7.4} shake flask data with literature data³.

Figure 2

Inter-assay reproducibility for a range of compounds in Cyprotex's Log D_{7.4} shake flask assay.



Cyprotex's Log D_{7.4} shake flask assay exhibits good reproducibility for compounds over a range of lipophilicity.

References

- ¹ Di L. and Kerns EH. (2003) Profiling drug-like properties in discovery research. *Current Opinion in Chemical Biology* **7**; 402-408.
- ² Kerns EH and Di L. (2003) Pharmaceutical profiling in drug discovery. *Drug Discovery Today* **8(7)**; 316-323.
- ³ Wenlock MC, et al., (2011) A method for measuring the lipophilicity of compounds in mixtures of 10. *Journal of Molecular Screening* **16(3)**; 348-355