

Cloe Screen CHI

cyprotexexperts in **ADME**

Background Information



'The method is recommended as part of a protocol for high throughput physicochemical property profiling for rational drug design.'

¹Valko K, Bevan C and Reynolds DP. (1997) *Anal Chem* 69; 2022-2029.

- Chromatographic hydrophobicity index (CHI) is a rapid gradient HPLC method for measuring lipophilicity and was first described by researchers from GlaxoSmithKline, UK¹.
- The ADME characteristics of a compound are highly dependent on its lipophilicity.
- Lipophilicity of a compound affects distribution into tissues, binding characteristics, absorption and elimination processes as well as solubility.
- CHI correlates closely with traditional octanol-buffer distribution coefficient log D.
- Rapid system which is cost effective and highly economical in terms of compound requirements.
- Widely accepted method for determining lipophilicity.

Protocol

Analysis method

Reversed phase (C18) gradient with LC-MS/MS

Calibration

Literature accepted standards with known CHI values

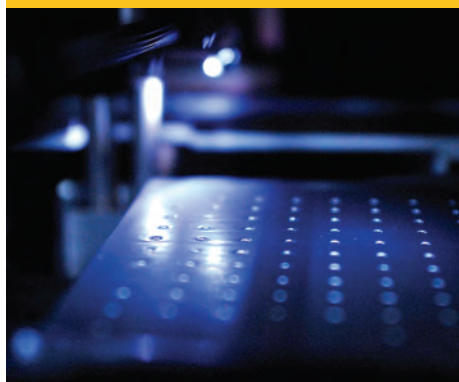
Compound Requirements

20 μ L of 10 mM solution in DMSO

Data Delivery

CHI_{7,4}

Lipophilicity is a critical determinant of the ADME properties of a drug - it can influence solubility, permeability, oral absorption, cell uptake, blood brain barrier penetration and metabolism.



Cloe Screen CHI

24 compounds were screened in Cloe Screen CHI_{7,4} in quadruplicate on 4 separate occasions. These data are highly reproducible for a range of CHI values.

Cloe Screen CHI_{7,4} also correlates well with log D_{7,4}.

Table 1

Cloe Screen CHI_{7,4} data correlate closely with log D_{7,4} data.

Compound name	Mean log D _{7,4}	Cloe Screen CHI _{7,4}
Phenylbutazone	0.55 ^(2,3)	57
Chlorpropamide	0.58 ^(2,3,4)	39
Trimethoprim	0.60 ⁽⁴⁾	39
Warfarin	0.76 ^(2,3,4,5,6,7)	46
Benzthiazide	1.12 ⁽⁴⁾	58
Chloroquine	1.28 ⁽⁴⁾	58
Carbamazepine	1.32 ^(3,4,8)	60
Dextromethorphan	1.40 ^(3,4)	60
Prednisone	1.48 ⁽³⁾	53
Midazolam	1.53 ⁽⁹⁾	76
Betamethasone	1.82 ⁽³⁾	60
Haloperidol	2.59 ^(2,3,4,10,11)	67
Ketoconazole	3.23 ^(3,4)	82
Nicardipine	3.77 ^(2,3,12)	102

Figure 1

Cloe Screen CHI_{7,4} data from 24 drugs show highly reproducible intra- and inter-assay data. (error bars represent the standard deviation of 4 CHI_{7,4} determinations).

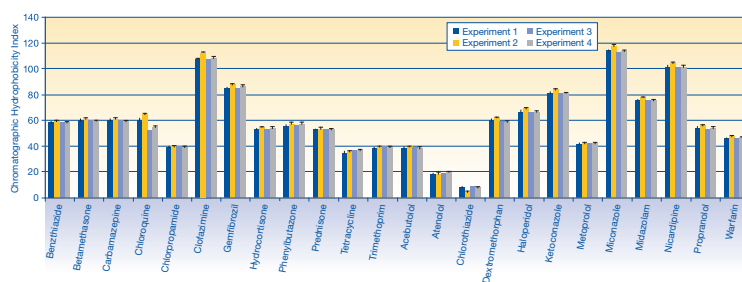
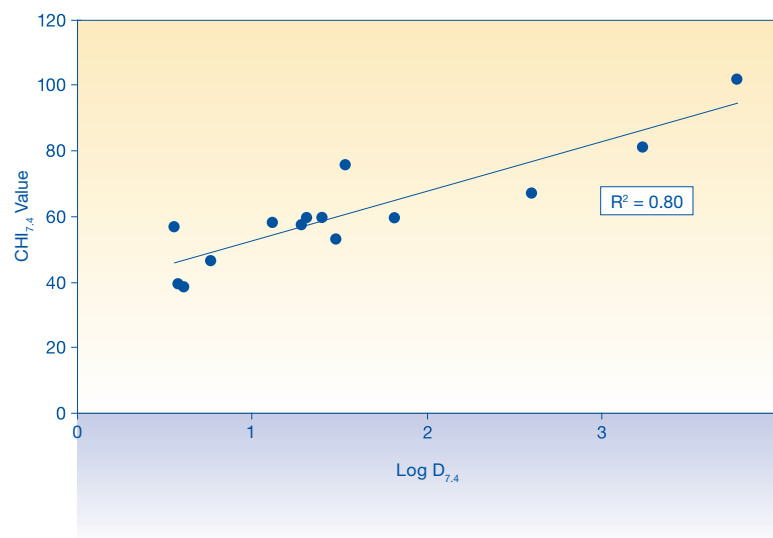


Figure 2

Cloe Screen data show close correlation between CHI_{7,4} and log D_{7,4} for 14 known drugs (see table).



References

- Valko K *et al.* (1997) *Anal Chem* **69**; 2022-9.
- Ritschel WA and Hammer GV. (1980) *Int J Clin Pharmacol Ther Toxicol* **18** (7); 298-316.
- Cloe Screen Log D Shake Flask data - for protocol details see Cloe® Screen Log D_{7,4} Shake Flask.
- Cloe Select GLpKa data - for protocol details see Cloe® Select pK_a and log P.
- Murakami H *et al.* (2000) *Am J Physiol Heart Circ Physiol* **279** (3); H1022-8.
- Camenisch G *et al.* (1998) *Eur J Pharm Sci* **6** (4); 317-24.
- Yazdaniyan M *et al.* (1998) *Pharm Res* **15** (9); 1490-4.
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