

## Calculation of the Octanol/Water Partition Coefficient (Log P<sub>oct</sub>) from Gradient RP-HPLC Retention

### Purpose

Lipophilicity of drug molecules plays an important role in their absorption, permeation and disposition. The common lipophilicity scale of molecules is defined by the octanol/water partition coefficient (log P<sub>oct</sub>). However, the method of measurement of partition coefficients is time consuming and the determination of log P<sub>oct</sub> for poorly water soluble substances is difficult. Because of these disadvantages, we use a rapid method for the calculation of log P<sub>oct</sub> values by using HPLC retention time data.

### Assay protocol

Reference and test compounds are solved in an acetonitril/ buffer mixture. An aliquot is injected onto the HPLC system and the retention times (RT) are measured with three different mobile phases.

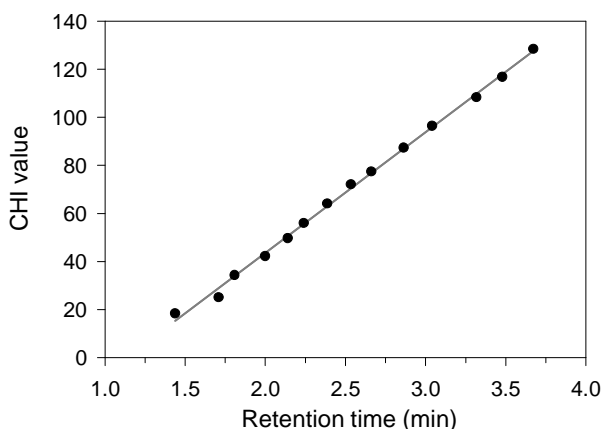
- Reference compounds: A calibration curve is performed by plotting the highest RT of each compound against its known Chromatographic Hydrophobicity Index (CHI) value.
- Test compounds: The RT measured for each test compound is converted to CHI value by using the calibration curve established with reference compounds.

With the number of hydrogen bound counts (HBC) of the test compounds and their CHI values, the log P is calculated according to the equation:

$$\text{Log } P_{\text{oct}} = 0.054 \text{ CHI} + 0.36 \text{ HBC} - 1.10$$

### Calibration curve

The figure shows the calibration curve performed with 14 reference compounds.



### Model validation

Seven commercially available drugs with known log P<sub>oct</sub> values were tested to validate our method. The log P<sub>oct</sub> of the test compounds was calculated using the method described previously.

Test compound	Retention time (min)	CHI value	HBC	Log P calculated	Log P literature
Aniline	1.908	39.03	1	0.90	1.09
Phenol	2.026	44.95	1	1.50	1.37
Hydrocortisone	2.254	56.38	3	1.55	2.63
Cortisone	2.266	56.98	1	1.42	1.94
4-Nitroaniline	2.129	50.11	1	1.39	1.62
Progesterone	3.110	99.32	0	3.70	3.57
Anthracene	3.372	112.5	0	4.45	4.19

The CHI and the log P<sub>oct</sub> values determined for the 7 test compounds with our HPLC system are presented in the table. The calculated Log P is in good accordance with values from the literature.

### Benefits of the method

- The short cycle time of the HPLC allows the determination of the log P value of large numbers of compounds in a short time.
- Log P values ranged between 0 to 5 can be calculated.
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*Please don't hesitate to contact us for a customized quotation*

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