

High-accuracy water solubility determination using $\log K_{OW}$ from different methods

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Introduction

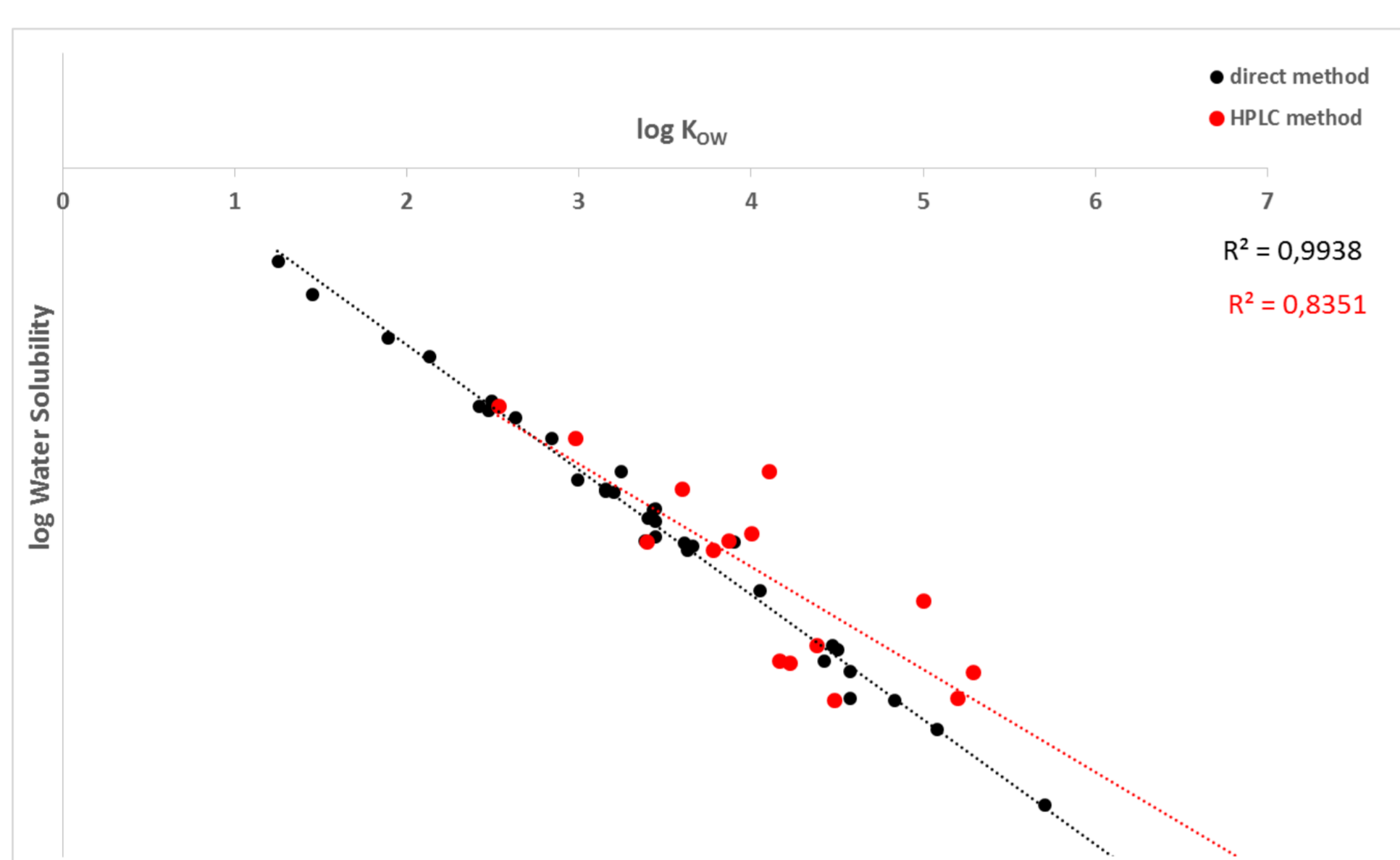
Octanol-Water partitioning coefficient (K_{OW}) is one of the most critical parameters for environmental risk assessment and ecotoxicology. Since it describes hydrophobicity of a substance and indicates potential for bioaccumulation and is used in many models, for instance, bioconcentration and bioaccumulation Arnot-Gobas equations (Arnot and Gobas, 2006).

Three different OECD guidelines are provided in order to measure the K_{OW} of chemicals. The OECD guideline 107 (Shake-Flask Method) is the classical method to measure equilibrium between octanol and water phases. Another guideline may be followed for very hydrophobic substances (OECD guideline 123 using the Slow-Stirring Method). However a large part of the data found in literature come from the HPLC method, an indirect method, described in OECD guideline 117. This poster aims to assess the relevance of $\log K_{OW}$ values derived from the HPLC method.

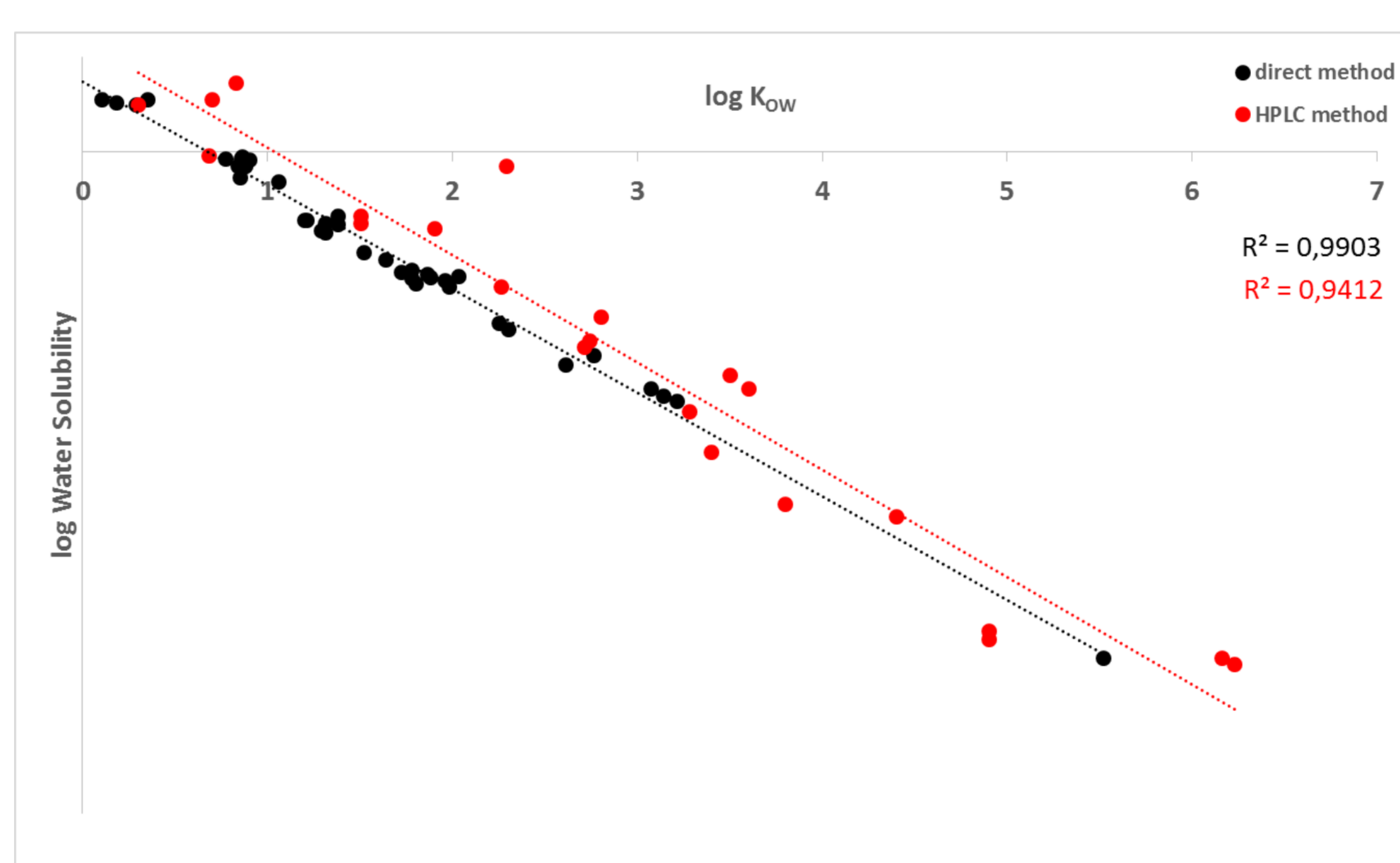
Methodology

Following the works of Yalkowsky and Valvani (1980), reviewed by Ran *et al.* (2001), there is a direct and linear relationship (GSE for General Solubility Equation) between the $\log K_{OW}$ and the log of subcooled water solubility (S_w^L) for non-polar organic chemicals. Data of these two parameters were plotted for 3 groups of compounds: non-oxygenated, oxygenated but non-hydroxylated and oxygenated and hydroxylated substances. Also $\log K_{OW}$ data have been distinguished following the experimental method used: direct (if Shake-Flask or Slow-Stirring methods) or indirect (if HPLC).

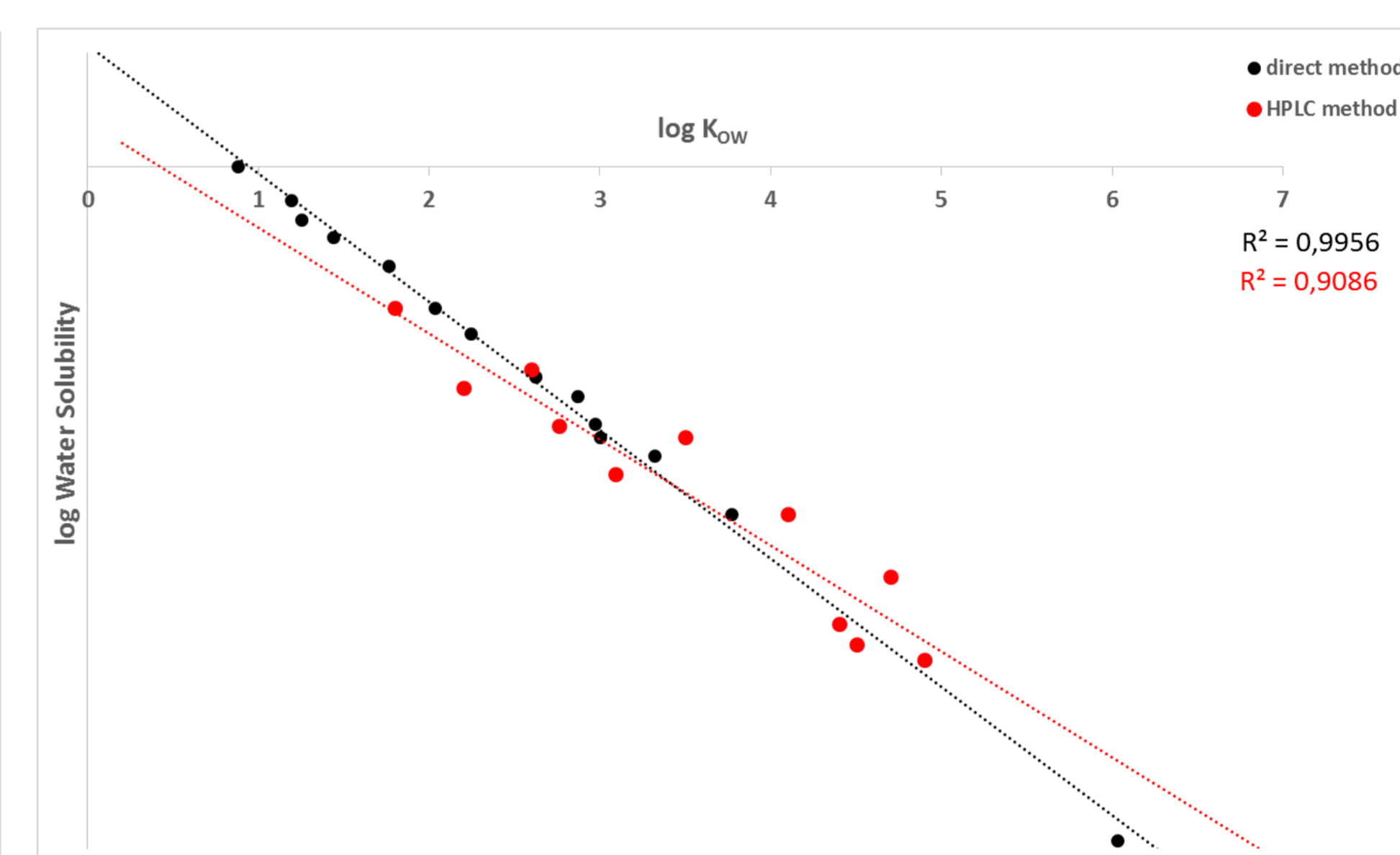
Results



Graph 1: Correlation of $\log K_{OW}$ and water solubility for non-polar compounds.



Graph 2: Correlation of $\log K_{OW}$ and water solubility for oxygenated compounds, except alcohols,



Graph 3: Correlation of $\log K_{OW}$ and water solubility for alcohols.

For the three groups of compounds studied (non-polar, non-hydroxylated oxygenated or hydroxylated), the R^2 with HPLC data points are always lower. Therefore the relationship between the $\log K_{OW}$ based on HPLC data and the water solubility is relatively poor compared to shake-flask and slow stir data. Moreover, we observed the equation driven by HPLC data points often leads to an overestimation of $\log K_{OW}$ value, sometimes up to one order of magnitude. We estimated an average overestimation of 0.3 for non-polar and oxygenated compounds. The value of $\log K_{OW}$ for Alcohols compounds were predicted with an average absolute error of 0.3 log. On the contrary data from direct methods strongly fit with the regression line with a R^2 superior at 0.99.

Discussion

The results show that HPLC data are not accurate enough to be used for $\log K_{OW}$ when high accuracy is required:

- KREATIS excluded HPLC data from High-Accuracy QSAR/QSPR model development
- Overestimations of $\log K_{OW}$ can have important consequences for regulatory purposes (C&L).
- The choice of standard reference may explain the poor accuracy of $\log K_{OW}$ for HPLC studies. Samsara *et al.* (2013) and Begnaud *et al.* (2015) showed inaccurate $\log K_{OW}$ occurs when suitable standards are lacking as retention time strongly depends on the chemical class and is improved by calibration to the test item. Nevertheless SF or SS methods still provide the most reliable $\log K_{OW}$ results.

Summary

Because of the high dependence of HPLC method on the reference compounds, data provided by this method should be excluded for the development of High-Accuracy QSAR/QSPR models.

Water Solubility or other $\log K_{OW}$ dependant parameters should use direct methods to determine $\log K_{OW}$ for the sake of accuracy.

References

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