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# Molecular parameter prediction tools for calculating the partitioning of organic compounds between gas and particle phase indoors

Objective: For the ecotoxicological assessment of a chemical substance in indoor spaces, it is important to know its partitioning behavior between gas phase, particle phase and settled house dust. Due to the complex interaction of molecules with the different compartments, the dynamics is usually modeled. However, this requires precise knowledge of the physical and chemical properties of the compounds and the respective matrices.
Methods: The following prediction methods were applied and compared: quantitative property-property relationships (QPPR), quantitative structure-activity relationships (QSAR), quantitative structure-property relationships (QSPR), linear free-energy relationships (LFER) and quantum mechanical (QM) tools.
Results: The prediction of molecular properties of chemical pollutants is now an indispensable part of tools for assessing their fate in the environment and their toxicity. Many organizations provide extensive information on this, although the quality of the data is not necessarily guaranteed. It is therefore up to the user to evaluate whether a value used is realistic or not. Computer-based models can be used to generate data quickly and easily, but the algorithms hidden behind them are practically impossible to trace. An assessment will therefore preferably be based on practical aspects and individual experience. In general, experimentally measured values are considered to be more reliable than computed values. However, this is only the case if the experiments are carried out with much care and precision.
The number and quality of prediction models is practically unmanageable. The most popular QSAR and LFER tools are SPARC, OPERA, the OECD QSAR Toolbox and the UFZ-LSER database. These allow reasonable molecular parameters to be obtained for many compounds. However, there are exceptions. It has been shown that molecules containing heteroatoms such as silicon and/or fluorine often cannot be treated with standard algorithms. Therefore, a QSAR or LFER algorithm may only be used for the specified substance group. It must also be made clear that the quality of a QSAR and LFER result depends heavily on the training set. SPARC for example fails at the vapor pressures of semi-volatile compounds and OPERA fails at the air/water partitioning coefficient of PFAS. It is therefore advisable to validate the result using a reference compound with known properties.
Quantum mechanical prediction tools are more reliable and flexible because each molecule is calculated individually. The result does not depend on the properties of other molecules. However, it is necessary to identify the dominant conformer ensemble in each phase. The currently most powerful method for this is the density functional theory (DFT) based so-called CRENSO workflow.
The errors of predicted values are very different. For quantum chemically generated data according to CRENSO, an uncertainty of 0.5 log units was reported. Small error ranges are often specified for QSAR and LFER algorithms, but, as already mentioned, these usually only relate to the respective training set. Realistically, errors of 1 - 2 log units must be expected here. However, this does not include possible outliers. Various databases are available to the user, in some of which the selected values are also commented.
Conclusion: Despite, or perhaps because, access to algorithms and databases is so easy today, scientific expertise can and must be expected. The user should still be able to evaluate the quality of predicted or experimentally determined molecular properties of organic compounds. This also applies to the fact that sometimes calculations on the partitioning behavior of substances are only possible with limitations. A recommendation as to which calculation tool or database should be chosen for a specific substance, a specific parameter and

specific compartment cannot be given. This must be decided individually, taking into account all necessary and available information.

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