Are Log P Calculators Accurate? Benchmarking on 96 000 Compounds

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Introduction

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In recent years, the importance of compound similarity assessment and virtual screening has increased significantly. In this context, one of the key properties of pre-screening compounds is the lipophilicity, which is usually represented by the Log P (octanol/water partition coefficient) value. The most accurately Log P is predicted using artificial intelligence methods such as neural networks, decision trees, or support vector machines. However, these methods often require a large amount of training data, which is not always available. Therefore, Log P calculators, such as e.g., MLOGP or MiLogP, are often used instead of accurate methods for predicting Log P values. These calculators use correlation equations or semi-empirical methods to estimate Log P values and are usually faster than accurate methods. Log P values predicted by these calculators can then be used for screening compounds. However, it is not clear whether these calculators are accurate enough for generating data sets to be used for virtual screening.

In this study, we have benchmarked 96,000 compounds on eight benchmark sets, six of which were provided by the ALODGPS project and two sets of compounds were derived from the AUCS-Mago collection.

Methods

The test set was compiled of 80% of a collection of 96,000 molecules, provided by the NYCOMED collection and the AUCS-Mago collection.

The following methods were used to calculate Log P:
- The FreeWaters Log P program was used to calculate Log P values for N-alkyl dissecting the same set of molecules.
- The MLOGP and MiLogP programs were used to calculate Log P values for N-alkyl and naphthyl analogs of the molecules provided by the AUCS-Mago collection.

Results

The benchmarking was performed by comparing the performance of the various Log P calculators, including the FreeWaters Log P program, with the reference Log P values, which were calculated using the MLOGP and MiLogP programs.

Conclusions

The FreeWaters Log P program was the most accurate among the methods tested. The results confirmed that the FreeWaters Log P program is a suitable tool for predicting Log P values for a large set of compounds, which can be used for virtual screening.

References


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