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Calculation of lipophilicity for Pt(II) complexes: experimental comparison of several methods

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Platinum containing compounds are promising antitumor agents, but must enter cells before reaching their main biological target, namely DNA. Their distribution within the body, and hence their activity is to a large extent determined by their lipophilicity, thus there is a strong interest to develop computational methods to predict this important property. This study analyses accuracy of five methods, namely ALOGPS [1], KOWWIN [2], CLOGP [3] and two quantum chemical approaches [4,5], to predict octanol/water partition coefficients (logP) for sets of 43 and 12 Pt(II) complexes, collected from the literature and measured by the authors, respectively. Fragment-based methods for logP estimation give generally poor results due to lack of suitable values for metal-containing fragments. However, the ALOGPS program can be extended with data from the first set in LIBRARY mode [6,7], and in this way resulted in the highest prediction ability for the measured molecules. The program was also able to correctly predict errors in calculated logP values for new molecules using the algorithm described in [8].

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