

# Using Quantitative Structure Activity Relationships in an Undergraduate Lab Setting

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A system for introducing the principles of QSAR to undergraduates, which relies on the simultaneous analysis of many biologically active molecules, has been implemented in Freshman Chem. laboratory. Computational modeling of molecular structures and calculation of physical properties allows for the generation of sufficient information to define statistically relevant relationships between physical properties and biological activities. Application of this approach to a series of 12 Phenylalkylamine hallucinogens with geometries optimized using semi-empirical AM1 methodology results in a strong nonlinear correlation between activity and the calculated octanol/water partition coefficient (Log P). The correlation equation [ $\text{Log (Activity)} = -0.863799 \text{ Log P}^2 + 5.14208 \text{ Log P} - 5.74332$  ( $R=0.789$ )] compared very favorably with that for experimentally determined LogP values [ $\text{Log(Activite)} = -0.5 \text{ Log P}^2 + 3.15 \text{ Log P} - 3.17$   $R=.79$ ]. A comparison of molecular electrostatic potential (EP) calculated at the same level of theory to Hammett constants (F) for a series of substituted benzoic acids yields a similarly strong relationship were [ $F = 7.8511 \text{ EP} + 31.592$   $R= 0.812$ ]. EP, which can be easily calculated, can therefore be used as an acceptable replacement for Hammett constant values in the evaluation of QSAR relationships where electronic substituent effects are important.

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