COMPUTER AIDED PROPERTY BASED DRUG DESIGN

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Poor oral bioavailability, high clearance, low solubility and formulation difficulties often are responsible for the failure of active compounds in a modern drug design process. All these pitfalls are closely related to physicochemical properties. A key property is the most basic and most acidic pKa value, respectively.

The most reasonable approach to calculate pKa values is based on Hammet/Traft equations, which characterize the influence of substituents on the pKa value of a known scaffold. These equations are therefore an ideal starting point for property based drug design.

An example is given, how to modify an active scaffold, to receive a series of structures with more desirable physico-chemical properties, such as solubility or LogD. Substituents are chosen from a database and connected to a specified position. The results are analyzed graphically by PSA and Lipinski's "rule of five" properties, to select the most promising candidates for synthesis.

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