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# Prediction protein binding of drugs using Abraham ionic parameters

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**Background and Aims:** Protein binding (PB) is one of the important parameters affecting the pharmacokinetic parameters of drugs. It is useful to predict PB of a drug like molecules in early stages of drug discovery. Abraham parameters of drugs that composed of excess molar refraction, polarizability, hydrogen bond acidity and basicity and molar volume, were used to predict some ADMET properties of drugs. But in these cases, the ionization of drugs in blood pH (7.4) was ignored. Recently, Abraham parameters of drugs were proposed for ionic form of drugs. In addition, Henderson Hasselbalch equation can be used to calculate the percent of ionized form of drugs. On the other hand, classification of drugs to acidic and basic forms is useful method for predicting ADMET properties. In this study, drugs were classified to the acidic or basic form and then Abraham solute parameters according to the ionized fraction of drugs were calculated and PB of drugs were predicted using these parameters.
**Methods:** Eighty PB data points were collected from the literatures and data was classified to acidic and basic classes. Abraham solute parameters were calculated by the Pharma-Algorithms software and then these parameters convert to ionic parameters according to the fraction of ionization in blood pH (using Henderson-Hasselbalch equation). The models were build up based on multiple linear regressions (MLR) analysis and absolute average error (AAE) was computed as an accuracy criteria.
**Results:** There is a linear relation between PB and Abraham solvation parameters ($R>0.84$) and AAE is less than 0.3 in log unit. The validity of each model was confirmed using internal and external validation methods.
**Conclusions:** Ionization of drugs in blood pH is an important parameter in predicting of PB and Abraham ionic parameters of drugs can be used to predict PB of drugs with good accuracy.

**Keywords:** Protein binding; Abraham ionic parameters; Drug discovery