IAM chromatography: information provided and relevance in the prediction of permeability

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**In silico method: BR Analysis [2, 3]**

Experimental method: IAM chromatography

The interest for IAM (Immobilized Artificial Membranes) chromatography in the prediction of drug permeability is increasing [1]. Here we firstly collected IAM,PC,DD2 log \( K_{\text{w,IAM}} \) data for a dataset of 253 molecules. Then we applied block relevance (BR) analysis [2, 3] to extract the relative contribution of intermolecular forces governing log \( K_{\text{w,IAM}} \) and \( \Delta \log K_{\text{w,IAM}} \) (a new combined descriptor [4] calculated from log \( K_{\text{w,IAM}} \)). Finally, the relationship between log \( K_{\text{w,IAM}} \), \( \Delta \log K_{\text{w,IAM}} \) and passive permeability determined in both PAMPA [5] and MDCK-LE [6] systems was looked for.

**Experimental method: IAM chromatography**

The analyses were performed at 30°C with 20 mM ammonium/acetate at pH 7.0 (when mixtures with acetonitrile at various percentages were used then extrapolation at 100% buffer was performed to obtain log \( K_{\text{w,IAM}} \)). The stationary phase was IAM,PC,DD2. (Regis, 10cmx4.6cm 10um packing 300Å pore size). The flow rate was 1.0 ml/min.

**Results**

BR analysis showed that log \( K_{\text{w,IAM}} \) is mainly a descriptor of the molecular dimensions and shape whereas \( \Delta \log K_{\text{w,IAM}} \) mostly describes polarity of neutral compounds.

Models provided the basis for a rational application of IAM chromatography in permeability prediction.

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**References**