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Chromatography platform to highlight compounds behavior in a membrane: A journey of interactions

Laurence Philippe-Venec

PIC Analytics

Understanding compound behavior in solution and in the proximity of a membrane is key for properties optimization towards permeability.

Chromatography is a reliable tool to study the chameleonic behavior of compounds by understanding evolving interactions with different chromatographic supports that mimic membranes.

A platform of diverse chromatographic methods that include Capillary Electrophoresis to measure pKa, Reversed-phase HPLC on C₁₆-amid support and on a Polystyrene Divinyl Benzene support to measure lipophilicity in protic and aprotic solvents will be described. The association of these reversed-phase chromatographic techniques will lead to the notion of DeltaLogP and will provide precious information on change of conformation of the molecule under the formation of Intramolecular Hydrogen Bonds. Similar IMHB can be described through the shielding of the polarity of a molecule by highlighting the absence of interactions of H-Bond donors with a polar support: the applied Supercritical Fluid Chromatography (SFC) technique will lead to the measurement of a polarity index, called EPSA.

I will show how these experimental chromatographic descriptors support in-vitro ADME properties optimization for the design of permeable compounds in Drug Discovery.