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Chromatography platform to highlight compound behavior in a membrane-like environment : a journey of interactions

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Understanding compounds behavior in solution and in the proximity of a membrane is key for properties optimization towards oral bioavailability.

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

A platform of diverse chromatographic methods that include Reversed-phase HPLC on C18 and C16-amid support to measure lipophilicity in a water/lipidic system will be described, as well as Reversed-phase HPLC on a Polystyrene Divinyl Benzene, or PLRPS, that provides lipophilicity in an aprotic solvent, mimicking the lipidic layer of the membrane. The comparison of lipophilicity between aprotic and protic solvents, or DeltaLogP between the two systems, will provide previous information on change of conformation of the molecule under the formation of IntraMolecular Hydrogen Bond. Similar IMHB can be described by studying the hidden polarity of a molecule or the presence of interactions of Hydrogen Bond Donors with a selected polar support in a Supercritical Fluid Chromatography (SFC) system.

We show how these experimental descriptors support ADME properties optimization for the design of oral bioavailable Compounds in Drug Discovery phase.

Biography

Laurence Philippe-Venec is the founder and owner of PIC Analytics, an independent consulting company with recognized expertise in Separation Sciences and Physicochemical Properties providing support for the characterization and development of druggable compounds. Since obtaining a PhD in 1991 by developing and implementing an efficient axial compression packing methodology for large scale purification, Laurence has built a history of excellence in developing methods to transfer compound isolation and purification from the analytical stage to large scale production. Proactively supporting medicinal chemistry research has provided opportunities to advance her knowledge of separation techniques for chiral and achiral molecules, delivering and characterizing high purity isomers to help meet FDA regulations. Working at the frontier between discovery and pre-clinical development, Laurence has integrated a broad range of disciplines implementing efficient methods for characterization of compounds for early toxicology studies prior to formulation developed for varying paths in drug administration.

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4