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EPSA: a novel supercritical fluid chromatography technique enabling the design of permeable cyclic peptides

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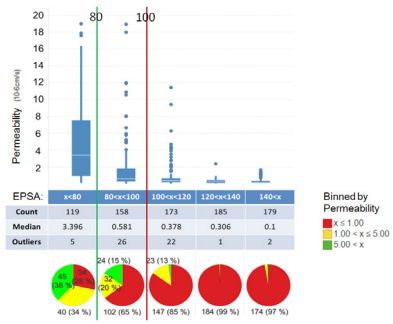
Applications of a new chromatographic method using SFC technology developed recently at Pfizer are described here. The EPSA method, as readout of polarity, correlates retention on a specific stationary phase with the exposed polarity of a molecule. Changes in retention can be interpreted by changes in polarity induced by the presence of intra-molecular hydrogen bonding (IMHB): indeed, IMHBs tend to impact molecular conformation, inducing hidden polarity that results in a decrease in analyte retention on the EPSA support. We demonstrate here the impact of this method on multiple beyond rule of five projects (NS5A, Oxytocin Receptor, CXCR7 Modulator, others). Given that conformational changes (induced and/or stabilized by the formation of IMHB) increases potential for membrane permeability, we show here that EPSA, and the EPSA prediction model, have significant impact in peptide drug design.



Biography

Gilles Goetz is a Principal Scientist at Pfizer in Groton, Connecticut, USA. He received his BSc (1991) and PhD (1995) at the University of Strasbourg in France. After his Post-doctoral studies at the University of Hawaii (1996-97) and of Neuchatel (CH) (1998-99) studying marine and fungal natural products, he joined Monsanto in 2000. There, he worked through mergers and acquisitions for Pharmacia and Pfizer successively in the natural product group, the HTS group (analytical support), and the purification group. In 2010, he transferred to the expert purification group at Pfizer Groton and in 2011 to the molecular properties group. He is a part of the team influencing medicinal chemistry design through insights into molecular properties such as polarity, lipophilicity, shape, and conformation that will impact molecular behaviors like solubility, permeability, and efflux. They develop and use mainly chromatographic techniques (EPSA) to assess those properties, and work towards predicting molecular behaviors.

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