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Immobilized artificial membrane chromatography as a tool in medicinal chemistry and in environmental sciences

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Pidgeon and his coworkers described for the first time in 1989, the immobilization of phosphatidylcholine to propylamino-silica skeleton and up to now immobilized artificial membrane (IAM) chromatography have been employed for simulation of the environment of cell membranes. In particular, IAM chromatography constitutes a valuable tool for medicinal chemists for prioritization of drug candidates in the early drug development stages. The retention outcome on IAM stationary phases encodes lipophilicity, electrostatic and other secondary interactions in contrary to traditional octanol-water partitioning. An increasing number of publications in recent years suggest that IAM indices, including isocratic $logk_{(IAM)}$ or extrapolated $logk_{w(IAM)}$ retention factors, hydrophobicity index $CHI_{(IAM)}$ which corresponds to the percentage of acetonitrile required for equal partitioning of the solute between mobile and stationary phase (i.e. logk=0) or the polarity parameter $\Delta logkw_{(IAM)}$ can successfully model the passage of xenobiotics through biological membranes and barriers and predict pharmacokinetic properties, often in combination with additional descriptors. More recently, IAM chromatography is applied to estimate toxicological endpoints in regard to drug safety, such as the phospholipidosis potential, or in regard to chemicals risk hazard including the bio-concentration factor and aquatic organisms' toxicity. The presentation will be devoted to applications of IAM chromatography to medicinal chemistry and environmental sciences. Examples referring to modeling of human oral absorption, blood-brain penetration, skin partition as well as bioconcentration factor and median toxicity (LC_{50}) in aquatic organisms will be discussed. The combination of promising results in both medicinal chemistry and in environmental science with the speed, reproducibility and low analyte consumption suggest that a broader application of IAM chromatography in early drug discovery process and in ecotoxicity is expected in initial drug candidate selection and contribute to reduced risk hazard of chemicals.

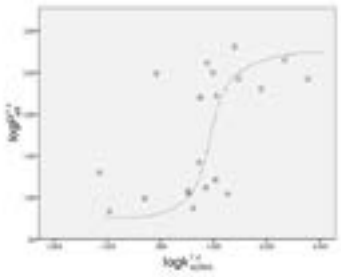

Figure 1: Plot of log(Papp (apical to basolateral Caco-2 permeability expressed in nm/s) as a function of logkw(IAM) at pH= 7.4.

Recent Publications

1. Tsopelas F, Malaki N, Vallianatou T, Chrysanthakopoulos M, Vrakas D, Ochsenkühn-Petropoulou M and Tsantili-Kakoulidou A (2015) Insight into the retention mechanism on immobilized artificial membrane chromatography using two stationary phases. Journal of Chromatography A 1396:25-33.
2. Tsopelas F, Vallianatou T and Tsantili-Kakoulidou A (2016) The potential of immobilized artificial membrane chromatography to predict human oral absorption. European Journal of Pharmaceutical Sciences 81:82-93.
3. Tsopelas F, Vallianatou T and Tsantili-Kakoulidou A (2016) Advances in immobilized artificial membrane (IAM) chromatography for novel drug discovery. Expert Opinion on Drug Discovery 11:473-488.
4. Tsopelas F, Giaginis C and Tsantili- Kakoulidou A (2017) Lipophilicity and biomimetic properties to support drug discovery. Expert Opinion on Drug Discovery 12:885-896.

5. Tsopelas F, Tsagkrasouli M, Poursanidis P, Pitsaki M, Vasios G, Danias P, Panderi I, Tsantili- Kakoulidou A and Giaginis C (2018) Retention behavior of flavonoids on immobilized artificial membrane chromatography and correlation with cell- based permeability. Biomedical Chromatography 32:1-11.

Biography

Fotios Tsopelas is a Lecturer in the School of Chemical Engineering at National Technical University (NTUA), Greece. He studied Chemical Engineering in the NTUA (1999) and Pharmacy (2004) in the National and Kapodistrian University of Athens. He completed his PhD in 2007 in Environmental Analytical Chemistry at NTUA (scholarship from Onassis Foundation) and his Postdoctoral research was focused on biomimetic chromatography for novel drug design. He has more than 25 publications in peer-reviewed scientific journals and more than 40 contributions in international conferences. He has acted as a Referee in more than 20 international journals. He has participated as a member of scientific committee in two international conferences. He has coordinated five national and international funded research projects. His research interest is mainly focused on the development of biomimetic chromatographic approaches for the evaluation of pharmacokinetic properties of candidate drugs and ecotoxicity of emerging pollutants.

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