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Retention behavior of structurally-diverse drugs on biopartitioning micellar chromatography and its potential to estimate cell permeability

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Biopartitioning micellar chromatography (BMC) utilizes micelles formed by a surfactant, such as polyoxyethylene (23) lauryl ether (Brij35), in a concentration higher than its critical micelle concentration and a reversed-phase stationary phase in order to gain insight into drug-membrane interactions, by rapid, friendly and reproducible measurements. The chromatographic column, modified by the surfactant, resembles the ordered array of the membranous hydrocarbon chains in regards to hydrophilic/hydrophobic character and the interactions of xenobiotics with the H-bonding groups of the adsorbed surfactant similar to the membrane ones. Therefore, the characteristics of the BMC are similar to biological barriers. Up to now, the reported studies of BMC to model toxicity (LD50), blood-brain barrier penetration, plasma clearance, volume of distribution as well as oral absorption are based on limited datasets and therefore, further investigations are needed. The aim of the present study was the evaluation of the potential of biopartitioning micellar chromatography to estimate cell permeability. For this purpose, retention indices (logkw) of an extended set of structurally-diverse drugs were measured on a discovery RP-18 column using as eluent phosphate buffer in the presence of Brij at a concentration of 0.04 M. The effect of the addition of NaCl in a concentration of 9.2 g/L was studied as well as the effect of increase of temperature from ambient to 37°C. Retention factors were compared with octanol-water partitioning and retention factors obtained in immobilized artificial membrane (IAM) chromatography. Retention factors were subsequently compared with Madin Darby Canine Kidney (MDCK) cell lines permeability data taken from literature and they were used to model % Human Oral Absorption (% HOA) data, compiled from literature sources. For reasons of comparison, the constructed models were compared with those derived by octanol-water partitioning.

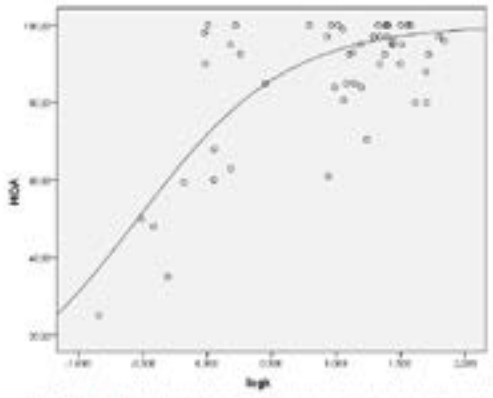

Figure 1: Relationship between Human Oral Absorption (%) and retention factor on BMC for 50 structurally diverse drugs

Recent Publications

1. Vucicevic J, Popovic M, Nikolic K, Filipic S, Obradovic D and Agbaba D (2017) Use of biopartitioning micellar chromatography and RP-HPLC for the determination of blood-brain barrier penetration of a- adrenergic/ imidazoline receptor ligands and QSPR analysis. SAR and QSAR in Environmental Research 28:235-252.
2. Stepnik KE, Malinowska I and Roj E (2014) *In vitro* and in silico determination of oral, jejunum and Caco-2 human absorption of fatty acids and polyphenols. Micellar liquid chromatography. Talanta 130:265-273.
3. Hadjmohammadi M and Salary M (2013) Biopartitioning micellar chromatography with sodium dodecyl sulfate as a pseudo α1-acid glycoprotein to the prediction of protein- drug binding. Journal of Chromatography B 912:50-55.

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. Stepnik K E and Malinowska I (2013) The use of biopartitioning micellar chromatography and immobilized artificial membrane column for in silico and *in vitro* determination of blood- brain barrier penetration of phenols. Journal of Chromatography A 1286:127-136.

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) at 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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