

DETERMINATION OF THE TRANSPORT ACROSS CACO-2 CELL MONOLAYERS OF COMPOUNDS VARYING IN LIPOPHILICITY USING LC-MS

Allan Wong,¹ Ben Ross,¹ Alun Jones,¹ Per Artursson,² Lucia Lazorova,² and Istvan Toth¹

1 School of Pharmacy, The University of Queensland, St Lucia, 4072 Australia.

2 Department of Pharmacy-Pharmaceutics, Uppsala University, Box 580, S-751 23 Uppsala, Sweden.

Caco-2 cell monolayers cultured onto Transwell polycarbonate filters provide a useful in vitro tool for studying the transepithelial transport of potential drug candidates (Artursson, 1990). Thus, these monolayers mimic the human intestinal monolayer through which drugs must pass to enter the blood stream. The Caco-2 assay involves adding a drug of interest to the apical side of the cell monolayer and measuring the rate of transport of the drug to the basolateral side. Concentration of drug in the basolateral layer is often determined by using expensive and hazardous radiolabelled drugs. An LC-MS method for determining Caco-2 permeability values for a range of compounds with differing lipophilicities was developed. Permeability of cephalexin, an antibiotic drug and modified Leu-enkephalin peptides was determined via this assay. Treatment of the collected solutions and choice of column were extremely important to the success of this method. Attachment of sugars or sugar/lipoamino acid (Toth, 1994) to the Leu-enkephalin peptide sequence was also shown to stabilize the peptide against degradation.

References

Artursson, P., *J. Pharm. Sci.*, 79 (1990) 476-482.

Toth, I., *J. Drug Targeting*, 2 (1994) 217-239.
