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Prediction of BBB permeability using PAMPA assay

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One of the successes for CNS drugs is to penetrate the Blood-Brain Barrier (BBB) and achieve the therapeutic targets. Therefore, the rapid screening for potential BBB-penetration of drug candidates provides important information in early drug discovery research. The Parallel Artificial Membrane Permeability Assay (PAMPA) is a high-throughput screening tool applied to predict the passive transport of potential drugs across BBB. It is the non-cell-based *in vitro* assay often used in pharmaceutical industry which is carried out in a coated 96-well membrane filter. An artificial lipid membrane represented by the polar brain lipid is applied on a hydrophobic filter and the compounds are screened according to their pass from a Donor (D) compartment through the filter to an Acceptor (A) part. Subsequently, A and D wells are analyzed by LC/MS or in UV-Vis spectrophotometer. The assessed concentrations are then used for calculation of the permeability coefficient (Pe). Compounds with Pe lower than 2.0×10-6 $cm.s^{-1}$ were classified as potentially non-BBB permeable (CNS-) and compounds with Pe higher than 4.0×10^{-6} cm.s-1 were recognized as potentially BBB permeable (CNS+). Of course, the assay can predict the CNS bioavailability based on the passive diffusion and active transport as well as efflux mechanisms are not considered. In the study, we correlated PAMPA-obtained permeability of some drugs (e.g. donepezil, rivastigmine, tacrine, testosterone, furosemide, sulfasalazine) and the results were compared with the real values mentioned in the literature.

Biography

Jana Janockova has pursued her PhD in 2015 from the Department of Biochemistry, P J Safarik University in Kosice (Slovakia). Currently, as a Postdoctoral Fellow at the Biomedical Research Center (BRC), University Hospital Hradec Kralove (Czech Republic) is responsible for *in vitro* testing and identification of biochemical and pharmacological properties and cytotoxicity evaluation of newly synthetized potential therapeutics for Alzheimer´s disease, Narcolepsy or as antidotes in organophosphate intoxication.

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