Nanovesicles for drug delivery across blood-brain barrier: a cell culture study

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Efficient drug delivery across biological barriers is a central problem in pharmaceutical treatment of diseases. Most pharmaceutical drug candidates including hydrophilic molecules, biopharmaceuticals, and efflux transporter ligands have a low permeability across barriers. To solve this unmet therapeutical need colloidal drug delivery systems targeting physiological transporters of barriers hold a great promise. Nanosized, biocompatible and biodegradable vesicles containing Evans blue-albumin as a model molecule were prepared and characterized by our partners at the University of Szeged.

The aim of our study was to test the cellular toxicity and penetration across barriers of nanovesicles loaded with albumin and containing ligands for solute carrier proteins. Primary rat and human hCMEC/D3 brain endothelial and Caco-2 human intestinal epithelial cells were used as in vitro model sytems of the blood-brain and intestinal barriers, respectively. The cellular toxicity of the nanoparticles was measured by real-time cell microelectric sensing (RTCA-SP, ACEA Biosciences) and MTT assay.

The results of the MTT assay and impedance measurement for vesicles without targeting molecule correlated well. The uptake of targeted and loaded nanovesicles interfered with the colorimetric MTT assay in brain endothelial cells because of Evans blue, therefore kinetical data from impedance measurements were more informative on the cellular toxicity of these nanoparticles. The non-toxic doses determined by the cell viability tests proved to be optimal for further studies. The presence of glucose analogue in nanovesicles increased the uptake of the model molecule to cultured brain endothelial cells indicating that ligands for solute carrier proteins can be used for targeting brain endothelial cells.

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