

Solid Lipid Nanoparticles: a strategy to overcome the blood-brain barrier

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Diagnosis and therapy of brain diseases are often compromised by the difficulty to cross the blood brain barrier (BBB). Recently, the emerging field of nanotechnology has generated new promises to solve this problem. Nanoparticles (NPs) have several advantages in terms of biocompatibility, non-immunogenicity, non-toxicity and they can be functionalized to carry imaging agents and/or drugs, and to enhance the blood circulation residence time. Finally, the NPs surface can be modified with specific ligands in order to achieve site-specific delivery and successful penetration of the BBB. The objective of present investigation was to study the effect of surface characteristics of solid lipid nanoparticles (SLN) covalently coupled with the monomer of ApoE-residues (141-150) on cellular uptake in brain capillary endothelial cells. Radiolabelled and fluorescent (fluoroprobe strictly associated to SLN) have been used to evaluate the transcellular transport in in vitro BBB model based on human cerebral microvascular endothelial cells (hCMEC/D3). SLN loaded with different fluorescent dyes and functionalized with phosphatidic acid (A β ligands) and DSPE-PEG(2000)-Maleimide have been investigated. SLN uptake was monitored by confocal-laser-scanning microscopy and quantified by radiochemical techniques. The peptide mediated an efficient cellular uptake of SLN. SLN without surface-located peptide displayed less membrane accumulation and cellular uptake. These results indicate that the formulations herein analyzed are suitable tools for brain targeted drug and contrast agent delivery.

Keywords: solid lipid nanoparticles, ApoE peptide, microvascular brain capillary endothelial cells.