The fantastic voyage of solid lipid nanoparticles from the lung to the brain: non-invasive tomographic imaging as a feasible refinement process

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Solid Lipid Nanoparticles (SLN) are colloidal drug delivery systems characterized by higher entrapment efficiency, good scalability of the preparation process and increased sustained release of the payload. Surface functionalization of SLN with ligands to achieve a site specific targeting makes them attractive to overcome the limited Blood-Brain Barrier (BBB) penetration of therapeutic compounds. SLN are prepared for brain targeting by exploiting the adaptability of warm microemulsion process for the covalent surface modification with an Apolipoprotein E-derived peptide (SLN-mApoE). Furthermore, the influence of the administration route on SLN-mApoE brain bioavailability is here evaluated by means of Fluorescence Molecular Tomography, an advanced optical imaging technology that uses the Near-Infrared Spectrum (NIR) (600-900 nm) for non-invasive *in vivo* imaging and 3D quantification of the fluorescent probes. Fluorescent labelled SLN-mApoE are able to cross intact a BBB *in vitro* model. The pulmonary administration of SLN-mApoE is related to a higher confinement in the brain of Balb/c mice compared to the intravenous and intraperitoneal administration routes, without inducing any acute inflammatory reaction in the lungs. These results promote the pulmonary administration of brain-targeted SLN as a feasible strategy for improving brain delivery of therapeutics as well as the FMT's ability of quantitative assessment *in vivo*-bio-distribution studies.

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