In vitro evaluation and optimization of drug delivery from glutathione-conjugated PEG coated liposomes

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G-Technology®
- to-BBB’s core platform and stands for liposomes coated with glutathione-conjugated polyethylene glycol (GSH-PEG) to mediate safe targeting and enhanced delivery of drugs to the brain.
- GSH, a natural anti-oxidant, is found at high levels in the brain and its active (sodium-dependent) receptor is abundantly expressed at the blood-brain barrier (BBB).

Aims
- In vitro testing of the G-Technology® to evaluate and improve the liposome formulation for brain delivery.
- To determine the uptake mechanism of the G-Technology®.

Experimental setup
Dextran-fluorescein of 4kDa (FD4) was encapsulated in liposomes (HSPC:Cholesterol:mPEG-DSPE, 1:0.75:0.09) and quantified after removal of non-encapsulated FD4. The liposomes were post-inserted with GSH-PEG-DSPE (GSH-PEG liposomes) or mPEG-DSPE (control liposomes). The size of the liposomes and the amount of GSH-PEG-DSPE was varied while the total amount of (GSH-)PEG-DSPE in the different experiments was kept constant at 5%.

Uptake of FD4 in bovine primary Brain Capillary Endothelial Cells (BCEC) or canine kidney cells (MDCK) after treatment with liposomes was determined.

Results Microscopy

In vitro experiments were performed to optimize liposomes coated with GSH-conjugated PEG for enhanced delivery of drugs to the brain. Dextran-fluorescein (FD4) containing liposomes with GSH-PEG or with PEG only were incubated with MDCK cells and BCEC. The studies have shown that uptake of FD4 from liposomes in cells is enhanced by GSH and that this uptake is an active process. Highest uptake was found using more then 3% GSH-PEG in the formulation and with a liposome size of 100 nm. The same methods will be used to further investigate the mechanism of GSH-mediated uptake and improvement of GSH-coated liposomal delivery systems.