Resonance enhanced PTIR imaging for the investigation of nES GEMMA size-selected liposomal drug delivery systems at the nanoscale

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Liposomes have gained great importance in the medical field for applications such as vaccine adjuvants or drug delivery systems due to their exceptional structural and functional versatility. Especially in clinical applications where liposomes are used for designing drug delivery systems for e. g. target-oriented cancer treatment, their encapsulation efficiency is of crucial importance to avoid overmedication. Common techniques to determine encapsulation efficiency usually need some kind of marker system such as radioactive carbohydrates or fluorescent dyes if the encapsulated drug does not exhibit autofluorescence. However, marker-based techniques are expensive, require very careful handling due to carcinogenicity that a prevailing majority of those marker substances have and they need careful adaptation to the investigated system. Additionally, they suffer from leakage, insufficient specificity and they also affect the biological system. Alternatively, encapsulation efficiencies can be averaged for vesicles during bulk measurements.

Photothermal induced resonance (PTIR) spectroscopy combines Infrared (IR) spectroscopy with Atomic Force Microscopy (AFM) and thus permits access to label-free, molecule-specific information at the nanoscale. Resonance enhanced PTIR provides an increased signal sensitivity using a pulsed tunable laser source emitting short laser pulses at the frequency of the contact resonance of the AFM cantilever.

We propose a novel combination of nES GEMMA and resonance enhanced PTIR for the investigation of drug encapsulation at the single liposome level. nES GEMMA (nano-Electrospray Gas-phase Electrophoretic Mobility Molecular Analysis) enables separation of nanoparticles according to their size and collection of these size-selected nanoparticles on flat surfaces for subsequent PTIR analysis. Here, we present our latest results investigating liposomes (85 nm in diameter) filled with Cytarabine - a chemotherapeutic drug e. g. used for leukemia treatment - through resonance enhanced PTIR imaging in contact mode. PLL (Phase locked loop) images were recorded at specific wavelengths characteristic for liposomes and the encapsulated drug, respectively, revealing the spatial distribution of both on a single liposome level (Figure 1). These preliminary results pave the way for the analysis of encapsulation efficiency of single nanocarriers with well-defined particle size.

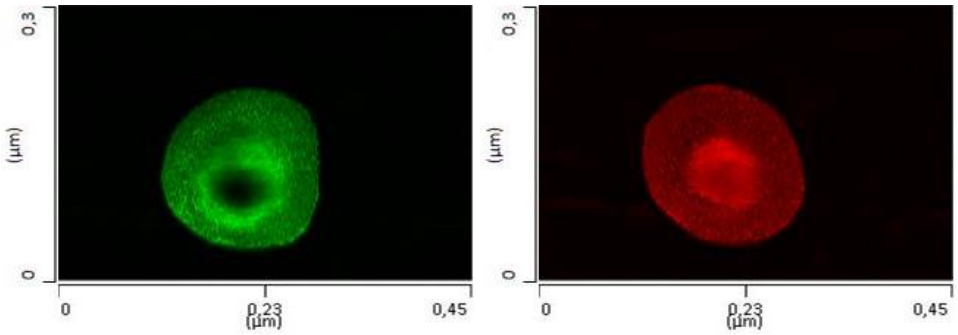

Figure 1. Lateral distribution of lipids (green, left image) and encapsulated drug (red, right image) within the same size-selected nanocarrier