

Analysis of exosomes and liposomes in biological media by Electrical Asymmetrical Flow Field-Flow Fractionation coupled to Nanoparticle Tracking Analysis

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The quest for innovative and groundbreaking drug candidates is continuing at high pace, especially in the field of bio- and nanomedicine. A lot of effort is currently being put into the rational design of such candidates in order to improve their quality and efficacy. However, the increasing complexity of bio- and nanomedical drug candidates also demands for more sophisticated analytical tools that enable a better understanding of their physico-chemical properties, especially in complex human and biological media, thereby allowing a deeper insight into their behavior in more realistic real-world application scenarios. Key parameters that need to be addressed here are e.g. the concentration and surface charge as well as the particle size and number concentration. Both Field-Flow Fractionation (FFF) [1] and Nanoparticle Tracking Analysis (NTA) [2] are well-established and powerful analytical techniques that provide this crucial information thus being valuable tools to enhance the quality and efficacy of innovative bio- and nanomedical drugs. We here present Electrical Asymmetrical Flow FFF (EAF4) coupled to Multi-Angle Light Scattering (MALS) and NTA for the analysis of liposomes and exosomes in complex, biological media. Coupling of both systems was realized using a static flow splitter to deliver the sample at an appropriate flow speed for the NTA measurement. The combined setup was successfully applied to analyze liposomes and exosomes spiked into cell culture medium and rabbit serum, respectively. Obtained results highlight the benefits of the EAF4-MALS-NTA platform to study the behavior of these promising drug delivery vesicles under in vivo like conditions.

[1] C. Contado, Analytical and Bioanalytical Chemistry, 2017, 409(10), 2501-2518.

[2] V. Filipe, A. Hawe, W. Jiskoot, Pharmaceutical Research, 2010, 27, 796-810.

1. Successful online coupling of EAF4-MALS and NTA
2. EAF4 as online sample purification step prior to analysis by MALS and NTA
3. Direct access to size distribution (MALS, NTA), number concentration (NTA) and Zeta potential (EAF4) in complex biological media

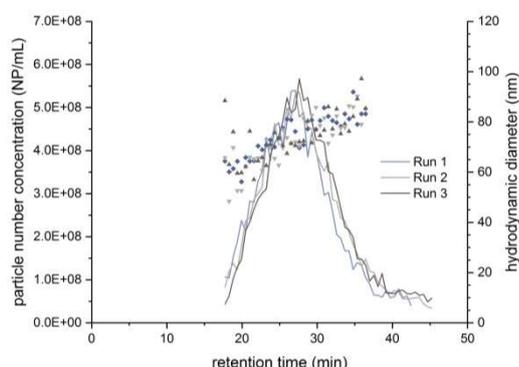


Figure: Particle number distribution overlaid with the hydrodynamic diameter of liposomal Doxorubicin HCl in DMEM cell culture medium obtained from three consecutive EAF4-MALS-NTA measurements.

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