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Frontal Analysis Continuous Capillary Electrophoresis: An Approach to Predict Plasma Proteins and Polymeric Nanoparticles Interactions

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Summary

Polymeric-based nanoparticles (PNPs) have gained attention over the past decades for their use either as nanocarriers to vehicle drugs or as therapeutic agents [1]. However, once administered into the bloodstream, a dynamic interplay occurs between their surface and plasma proteins. Consequently, studying NP-protein interactions is of great interest to predict their in vivo fate and biodistribution, especially towards abundant plasma proteins, such as human serum albumin (HSA). A few capillary electrophoresis (CE)-based methods have been reported to estimate NP-plasma protein binding parameters [2]. Among them, frontal analysis continuous capillary electrophoresis (FACCE) is a methodology of choice, providing plateau heights proportional to the free ligand concentration. Based on the size and surface charge of our PNPs, their electrophoretic mobility did not allow for efficient electrokinetic injection during the FACCE process, so measurement of HSA was rather required. Although FACCE has been used once to measure dendrimer-HSA interactions [3], this was done on highly charged dendrimers able to be electrokinetically introduced. To date, no FACCE quantitating the protein counterpart has been reported. Therefore, our work aims at evaluating the affinity between PDMAC-based NPs [4] and HSA, by selectively injecting HSA into the capillary. Since the FACCE principle relies on mobility differences between the free and the bound ligand, our PNPs were fully characterized. Considering that HSA is a protein prone to adsorb to the silica capillary, extensive optimization of the method was needed under physiological conditions, including silica modification. High intermediate precision was obtained (RSD ~ 1.5%) as well as a linear calibration ($R^2 > 0.99$) between plateau heights and HSA concentrations. Moreover, after HSA-PNPs mixture incubation, free HSA was detected with high repeatability (RSD < 2%). This fast technique allows henceforth the construction of adsorption isotherms in less than 30 min, giving access to the intrinsic binding constant and stoichiometry of the HSA-PNPs interactions.

Acknowledgement

This work is part of the ANR project (ANR-21-CE06-0017).

References

[1] F. Farjadian, A. Ghasemi, O. Gohari, A. Roointan, M. Karimi, M.R. Hamblin, Nanopharmaceuticals and nanomedicines currently on the market: challenges and opportunities, Nanomed. 14 (2019) 93–126.
[2] M. Zarei, J. Aalaie, Profiling of nanoparticle–protein interactions by electrophoresis techniques, Anal. Bioanal. Chem. 411 (2019) 79–96.
[3] N. Sisavath, L. Leclercq, T. Le Saux, F. Oukacine, H. Cottet, Study of interactions between oppositely charged dendrigraft poly-l-lysine and human serum albumin by continuous frontal analysis capillary electrophoresis and fluorescence spectroscopy, J. Chromatogr. A 1289 (2013) 127–132.
[4] S. Han, S. Pensec, D. Yilmaz, C. Lorthioir, J. Jestin, J.-M. Guigner, F. Niepceron, J. Rieger, F. Stoffelbach, E.

Nicol, O. Colombani, L. Bouteiller, Straightforward preparation of supramolecular Janus nanorods by hydrogen bonding of end-functionalized polymers, Nat. Commun. 11 (2020) 4760.