Illuminating the structure of iron carbohydrates in complex biological environments

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Intravenous iron carbohydrate nanoparticles are widely used nanomedicines to treat iron deficiency anaemia, which is associated with illnesses such as chronic kidney disease and inflammatory bowel disease (1,2). A variety of clinical and biological studies on these products (ferric carboxymaltose and iron sucrose) are available (3); however, their undergoing structural changes during the early stages of entering the human bloodstream are not fully understood. Using a combination of small-angle x-ray and neutron scattering (SAXS/SANS), we investigated how size, shape and agglomeration state of iron carbohydrates was influenced by interaction with proteins in the plasma. Hereby, SAXS was used to study the iron core, and was complemented by SANS to investigate the much weaker scattering signature of the carbohydrate shell. Our SAXS experiments indicated formation of agglomerates from single iron cores, which have a different shape and size depending on the iron carbohydrate. SANS measurements also enabled calculation of the thickness and shape of the carbohydrate shell. Experiments on interactions of iron sucrose with human serum albumin suggested adsorption of the protein to the NP surface after only 1h of incubation time, while for ferric carboxymaltose no adsorption was seen. With this approach, we shine light on the correlation of physicochemical parameters of iron carbohydrates with their behavior in biological environments for better prediction of clinical outcomes.

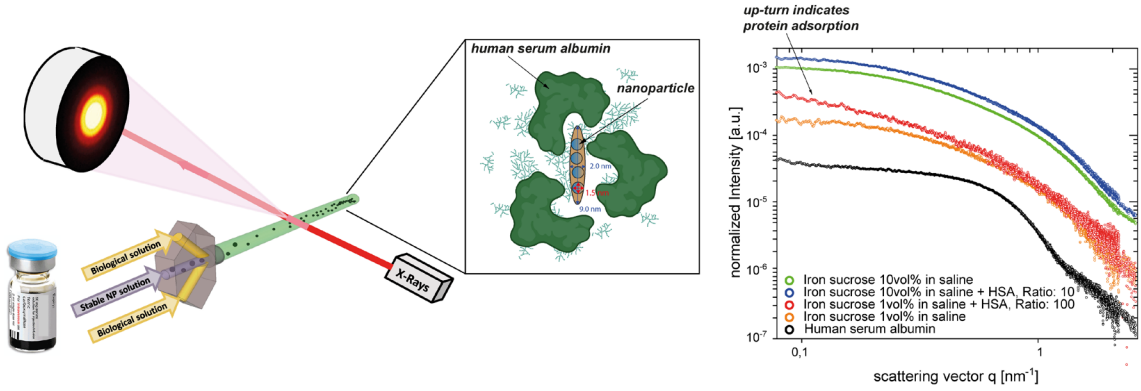

Figure 1 - Modelling the interaction between human serum albumin and iron sucrose through SAXS. Adapted from Anaraki et al. [4,5].

[1] M. Praschberger, et al., *Biometals*, **2015**, *28*(1), 35-50.
[2] J. Rottembourg, et al., *Nephrology Dialysis Transplantation*, **2011**, *26*(10), 3262-3267.
[3] N. Nikravesh, et al., *Nanomedicine: Nanotechnology, Biology and Medicine*, **2020**, *26*, 102178.
[4] N. Iranpour Anaraki, et al., *Nano Research*, **2020**, *13.10,* 2847-2856.
[5] N. Iranpour Anaraki, et al., *ACS Applied Nano Materials*, **2022**.