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Membrane-Coated Haemoglobin-Based Oxygen Carriers with Antioxidant Properties as Novel Red Blood Cell Substitutes

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To counteract the shortage and limitations of donor blood, research efforts have been put into creating red blood cell (RBC) substitutes. Specifically, haemoglobin (Hb)-based oxygen carriers (HBOCs) have been thoroughly investigated since, as stated in the name, they make use of Hb, which is the main component of native RBCs and, as such, it has evolved to have optimal oxygen transport ability.
Herein, we have fabricated a HBOC system consisting of a ~310 nm-sized Hb-loaded nanoparticle that was subsequently coated with nanozymes (NZs, cerium oxide nanoparticles) and RBC-derived membranes (RBC-M) (**Figure 1**).[1] NZs were added to scavenge reactive oxygen species (ROS), thereby protecting the loaded Hb against oxidation. The NZ's long-term storage stability was furthermore compared to native enzymes. Next, RBC-M coating was investigated as an alternative to PEGylation, since RBCs have circulation times up to 120 days. Three RBC-M coating approaches were optimized and assessed by fluorescence, electron microscopy, and protein adsorption studies. It was furthermore shown that all the RBC-M coatings preserved the oxygen delivery and ROS scavenging properties of the underlaying components. Finally, their biocompatibility in terms of hemocompatibility, endothelial cell viability and cell uptake was demonstrated. Thus, to summarize, we have presented a multifaceted HBOC system with potential to become an RBC substitute in the future.

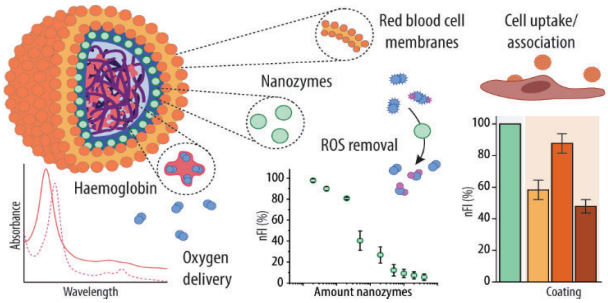

Figure 1: Illustration of the HBOCs' assembly and its different functionalities.

1. M. M. T. Jansman, C. Coll-Satue, X. Liu, P. J. Kempen, T. L. Andresen, P. W. Thulstrup and L. Hosta-Rigau, *Hemoglobin-based oxygen carriers camouflaged with membranes extracted from red blood cells: Optimization and assessment of functionality*, **Biomaterials Advances**, 2022, In Press.

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