Recent and prominent examples of nano- and microarchitectures as hemoglobin-based oxygen carriers - DTU Orbit (11/10/2019)

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Blood transfusions, which usually consist in the administration of isolated red blood cells (RBCs), are crucial in traumatic injuries, pre-surgical conditions and anemias. Although RBCs transfusion from donors is a safe procedure, donor RBCs can only be stored for a maximum of 42 days under refrigerated conditions and, therefore, stockpiles of RBCs for use in acute disasters do not exist. With a worldwide shortage of donor blood that is expected to increase over time, the creation of oxygen-carriers with long storage life and compatibility without typing and cross-matching, persists as one of the foremost important challenges in biomedicine.

However, research has so far failed to produce FDA approved RBCs substitutes (RBCSs) for human usage. As such, due to unacceptable toxicities, the first generation of oxygen-carriers has been withdrawn from the market. Being hemoglobin (Hb) the main component of RBCs, a lot of effort is being devoted in assembling semi-synthetic RBCS utilizing Hb as the oxygen-carrier component, the so-called Hb-based oxygen carriers (HBOCs). However, a native RBC also contains a multi-enzyme system to prevent the conversion of Hb into non-functional methemoglobin (metHb). Thus, the challenge for the fabrication of next-generation HBOCs relies in creating a system that takes advantage of the excellent oxygen-carrying capabilities of Hb, while preserving the redox environment of native RBCs that prevents or reverts the conversion of Hb into metHb. In this review, we feature the most recent advances in the assembly of the new generation of HBOCs with emphasis in two main approaches: the chemical modification of Hb either by cross-linking strategies or by conjugation to other polymers, and the Hb encapsulation strategies, usually in the form of lipidic or polymeric capsules. The applications of the aforementioned HBOCs as blood substitutes or for oxygen-delivery in tissue engineering are highlighted, followed by a discussion of successes, challenges and future trends in this field.

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Corresponding author: Hosta-Rigau, L.
Contributors: Jansman, M. M., Hosta-Rigau, L.
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