

An electrochemical approach for the detection of modified hemoglobins as novel oxygen carriers

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Hemoglobin-based oxygen carriers (HBOCs) have been in demand as therapeutic agents and alternatives to red cells in blood transfusions (1). Limitations of previously tested HBOCs include their issue of safety and efficacy as well as complications leading from their vasoactivity. This is due to the constriction of blood vessels arising from the rapid and irreversible binding of hemoglobin's heme-iron to the vasodilator, nitric oxide (2, 3). Novel potential HBOCs have been developed by modifying hemoglobin with the non-toxic and bio-compatible polyethylene glycol (PEG) (1, 4, 5). A significant increase in the rate of nitrite reduction to NO was demonstrated in PEG conjugated hemoglobin (Hb-PEG) compared to human hemoglobin A (HbA). Moreover, conjugating PEG with cross-linked hemoglobin bis-tetramers (BT-PEG5K₄) showed even greater nitrite reductase activity and enhanced oxygen binding and transport abilities compared to cross-linked hemoglobin bis-tetramers (BT-Hb) and Hb-PEG (1, 5).

In this study, we detected the redox potential of the heme-iron and reported the electron affinity of HbA and the potential HBOCs: $\alpha\alpha$ -Hb, $\alpha\alpha$ -Hb-PEG5K₂, Hb-PEG5K₂, Hb-PEG5K₆, BT-Hb, and BT-PEG5K₄, using linear sweep voltammetry (LSV) in different pH conditions on hanging drop mercury electrode (HMDE). All the modified hemoglobin structures demonstrated electrochemical reduction signal corresponding to the conversion of Fe³⁺ to Fe²⁺ in their heme centre. The rapid electrochemical detection of the heme-iron showed promising results considering the requirement of heme-iron in HBOCs to remain in the reduced state for the reversible binding and release of molecular oxygen.

References:

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