Integrated Deconvolution of Oxidative, Colloidal, and Rheological Failure Modes Governing Microvascular Oxygen Delivery in Hemoglobin-Based Oxygen Carriers Under Field-Mimicking Thermal Cycling

Sathees, Adithiyan (School: Centennial High School)
Vora, Nilay (School: Centennial High School)

In trauma and mass casualty events, hemorrhage remains a leading cause of preventable death as definitive car is often delayed by limited access to safe, compatible donor blood. Deployment of Hemoglobin-based oxygen carriers, or HBOCs, is constrained by hemoglobin autoxidation to methemoglobin, colloidal instability via aggregation, and rheological drift, yet has the power to expand emergency oxygen delivery. Most existing HBOC functional evaluations rely on static chemical endpoints that do not quantify medically relevant oxygen transfer under real flow conditions. The Oxygen Flux Preservation Index, or OFPI, a functional metric was defined as normalized inlet to outlet oxygen transfer and a capillary-scale microvascular flow phantom was constructed to address this gap. Six 10 g/dL HBOC formulations (pH 7.4) were tested: Hb in PBS (F0), trehalose (F1), sodium ascorbate (F2), EDTA (F3), trehalose plus ascorbate (F4), and trehalose plus ascorbate plus EDTA (F5). For 20 days with a parallel constant 4 degrees C as a control, samples underwent field-mimicking thermal cycling from 4 degrees C to 25 degrees C to 37 degrees C. OFPI, MetHb%, oxidation index (A630/A576), aggregation (A700 and dynamic light scattering), pH, and viscosity were measured at 7 timepoints. Constant refrigeration held greater functional stability compared to thermal cycling. Oxygen flux was preserved most effectively by multi-mechanistic stabilization. Regression analysis showed OFPI loss was not explained by MetHb% alone; aggregation and viscosity contributed independent predictive power. These findings prove the OFPI to be a relevant endpoint that provides a mechanistic structure for designing HBOCs and stabilizer strategies that preserve delivery under real-world stress scenarios.

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