

Evaluating the Capacity of NO-releasing Nanoparticles to Be Used in Conjunction with Earthworm Erythrocrucorin and Maintain NO Bioactivity: A Potential Blood Substitute Candidate

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Discovering an alternative oxygen therapeutic for use in transfusions instead of human based blood products has been an ongoing objective of biomedical research. The giant extracellular hemoglobin or erythrocrucorin, LtHb, from earthworms (*Lumbricus terrestris*), is one candidate that holds promise as an effective hemoglobin based oxygen carrier (HBOC) due to its large number of oxygen transport sites and its stability. LtHb, however, is known to scavenge intravascular NO readily and subsequently cause excessive vasoconstriction. The inability of LtHb to minimize this transfusion-associated toxicity arising from nitric oxide (NO) depletion remains as an issue preventing its clinical usage. This study evaluates the potential of NO releasing nanoparticles to be used in conjunction with LtHb to form an optimal HBOC. Results showed that NO is released from newly synthesized nanoparticles: 78% through nitrous acid dissociation, and 22% through a nitrite reduction. Furthermore, the particles were able to nitrosate thiol containing molecules to form bioactive NO – a species of NO that does not get scavenged by acellular hemoglobins and that can therefore prevent vasoconstriction. Lastly, the particles accelerated the reaction of LtHb that is responsible for compensating for NO scavenging. Indeed, the combination of LtHb alongside NO releasing nanoparticles seems to be an optimal blood substitute candidate.