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Non-vasoconstrictive Hemoglobin Nanoparticles as Oxygen Carriers

Hans Bäumler
Institute of Transfusion Medicine, Charité-Universitätsmedizin Berlin
Charitéplatz 1, 10117 Berlin, Germany
hans.baeumler@charite.de

Extended Abstract

Artificial oxygen carriers, favorably hemoglobin-based oxygen carriers (HBOCs), are being investigated intensively during the last 30 years with the aim to develop a universal blood substitute. However, serious side effects mainly caused by vasoconstriction triggered by nitric oxide (NO) scavenging due to penetration of nanosized HBOCs through the endothelial gaps of the capillary walls and/or oxygen oversupply in the precapillary arterioles due to their low oxygen affinity led to failure of clinical trials and FDA disapproval. To avoid these effects, HBOCs with a size between 100 and 1000 nm and high oxygen affinity are needed.

We present unique hemoglobin particles (HbPs) of around 700 nm with high oxygen affinity and low immunogenicity using a novel, highly effective, and simple technique (Bäumler & Georgieva 2010, Xiong et al. 2012). The fabrication procedure provides particles with a narrow size distribution and nearly uniform morphology. The content of hemoglobin (Hb) in the particles corresponded to 80% of the Hb content in native erythrocytes.

Isolated aortic rings from rats were suspended in organ bath and connected to a force transducer. HbPs (10%) was applied by complete exchange of the physiological solution in the organ bath by the test solution. The muscle tension of the aortic rings was determined 30, 60 and 180 min after the bath exchange. In parallel experiments, 10% acetate-ringer was applied as negative control. A vasoconstriction was not observed in any aortic ring preparation treated with HbPs.

Furthermore, we demonstrate a successful perfusion of isolated mouse glomeruli with concentrated HbP suspensions and albumin particle suspension as control in vitro (Xiong et al. 2013). A normal, nonvasoconstrictive behavior of the afferent arterioles is observed, suggesting no oxygen oversupply and limited NO scavenging by these particles.

It was also shown in vivo that a repeated infusion of HbPs in telemeterized rates did not show any increase of blood pressure during a periode of 28 days.

All these results are highly promising being on the right way for the design of a new oxygen carrier.

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