# Nanosponge-cyclodextrins functionalized with oxygen protects H9C2 cells from hypoxia/reoxygenation injury: Implications from an in vitro model

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**Objective:** Nanoparticle-based imaging and nanocarriers therapies have emerged as essential tools for many fields of modern medicine, in order to track the fate of cells and optimize drug delivery. Up to now, however, there are only few reports on the effect of nanocarriers of different types on oxygen delivery, even though this would be of great interest for the design of high impact therapies in several cardiovascular diseases (CVDs). In particular, Cyclodextrin Nanosponges (C-NS) can be envisioned as innovative tools to improve the delivery of oxygen in a controlled manner in CVDs.

**Methods:** We tested oxygenated C-NS (OX-C-NS) at different concentrations (0.2, 2 and 20 μg/ml) for their capability to reduce cell mortality during hypoxia and reoxygenation (H/R) protocols. For comparative purpose, we also tested “blank materials” (C-NS filled with nitrogen gas without oxygen) and the effects of C-NS in Normoxia. To test the effectiveness of C-NS, we used H9c2, a cardiomyoblast cell line derived from rat heart, exposed to Normoxia (5% CO2 and 21% O2) or Hypoxia (5% CO2 and 95%N2) in a Hypoxic Chamber. The cellular mortality was measured with MTT assay.

**Results:** In Normoxia, regardless of OX-C-NS formulation, the H9c2 cells displayed a tendency to an increased proliferation, which seemed somewhat correlated to the concentration of OX-C-NS used. The different concentration of OX-C-NS, applied before Hypoxia, induced a significant reduction of cell mortality compared to C-NS without oxygen. Also, the application of OX-C-NS at the beginning of reoxygenation induced a marked reduction of cell death.

**Conclusions:** OX-C-NS may induce H9c2 cell proliferation in Normoxia and may protect H9c2 from H/R injury in vitro. The administration of oxygen in a controlled manner during or after an ischemic event may be an innovative approach for reduction of Ischemia/Reperfusion injury, with consequent reduction of chronic CVDs. Our preliminary results, and in particular the observation of a remarkable efficacy in reoxygenation, suggest an interesting potentiality for medical application of C-NS during the treatment of myocardial infarction. Further studies are required to ascertain the protective potential of C-NS on cardiac I/R injury under in vivo conditions.

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