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# **Magnetic Oxygen-Loaded Nanodroplets: Role of Perfluorocarbon Core and Polymeric Coating in Magnetic Droplet Vaporization for Oxygen Release**

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## **Extended Abstract**

Oxygen-loaded nanodroplets (OLNDs) have garnered considerable interest in the field of nanomedicine as new therapeutic systems for treatment of hypoxic tissues diseases due to their high biocompatibility and efficiency in delivering oxygen [1,2]. They consist of liquid emulsions with dimensions of approximately 500 nm based on a polymeric shell and a perfluorocarbon (PFC) core inside which oxygen is dissolved. When exposed to an ultrasound (US) field, OLNDs undergo first acoustic droplet vaporization (ADV), passing from liquid nanodroplets to gaseous microbubbles, and then acoustic cavitation phenomena enabling the oxygen release [3,4].

To further enhance their potential, OLNDs can be functionalized with magnetic nanoparticles (NPs) making them responsive also to a magnetic field. The interaction between an AC magnetic field with NPs on the droplets surface, indeed, generates a local temperature rise, that triggers magnetic droplet vaporization (MDV) and the delivery of oxygen in the solution [5,6]. One of the main advantages of magnetic NP-promoted vaporization is the magnetic field ability to penetrate tissues, reaching deeper regions of human body compared to conventional acoustic techniques [7].

The present study aims to optimize the preparation process of magnetic OLNDs by using two different PFCs for the core (perfluoropentane and decafluoropentane) and three types of coating (dextran, chitosan and polyvinyl alcohol) and to compare the oxygen release induced by magnetic and the US fields.

After a physicochemical characterization, the magnetic response of the samples was tested in order to assess their functionalization with Fe<sub>3</sub>O<sub>4</sub> NPs. Additionally, their acoustic behaviour was investigated to evaluate possible variations due to the presence of NPs in the droplets structure. Finally, the evaluation of vaporization induced by the magnetic field was performed, along with the measurement of released oxygen. To this aim, each sample was heated up to fixed temperatures around the specific PFC boiling point, and the oxygen concentration was measured before and after each heating process to determine its increment due to MDV.

The characterization analysis showed that the presence of NPs on the droplets surface resulted in a slight increase in their size, as expected, without significantly affecting their acoustic response. A difference in the functionalization efficiency was found depending on the type of coating used, due to differences in electrostatic interaction with NPs. Additionally, the oxygen study demonstrated that the release profile varies depending on both the PFC core and coating of the nanodroplets. In particular, the core determines the temperature at which vaporization occurs and the subsequent oxygen release starting point, while the coating choice affects the rigidity of the droplets shell and, combined with the functionalization rate, determines the release trend. In conclusion, the final analysis of the US-induced oxygen release, carried out on the respective non-magnetic OLNDs, confirmed the critical role of both the PFC core and coating in determining the release performance of these systems. This comparison reinforces the previous findings and highlights the great potential, versatility and efficiency of that magnetic nanodroplets hold for oxygen delivery in nanomedicine.

