Engineered CeO_2-Based Nanozymes for Multifunctional Oxidative Stress Regulation and Therapeutic Applications

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Nanozymes are engineered nanomaterials with enzyme-like catalytic properties that offer greater stability, lower production costs, and broader environmental adaptability than natural enzymes, enabling diverse biomedical, environmental, and industrial applications.[1] The global nanozyme market is expected to grow from $5.13 billion in 2024 to $57.95 billion by 2034.[2] Among them, cerium oxide (CeO_2) nanozymes are particularly notable for their unique redox-switching ability between Ce^{3+} and Ce^{4+}, which imparts strong pro- and anti-oxidant activities. However, their practical application faces significant challenges, including the need for protective systems to maintain catalytic activity, prevent degradation or aggregation during circulation, and enable efficient targeted delivery.[3] Here, we developed two platforms using FDA-approved materials - one inorganic (silica) and one organic poly(lactic-co-glycolic acid) (PLGA)[4-5] - to encapsulate CeO_2-based nanozymes, providing enhanced stability, protection, and targeted functionality.

Firstly, we established a scalable platform for the synthesis of mesoporous nanosilica (69 ± 9 nm) encapsulating CeO_2-based nanozymes under room-temperature and ambient conditions. This strategy is readily adaptable for the incorporation of diverse nanoparticles.[6] The mesoporous silica coating significantly enhances the stability and catalytic activity of CeO_2 nanozymes in various simulated body fluids while preserving their intrinsic enzyme-like reactive oxygen species (ROS)-scavenging properties.[7] When applied to a liver fibrosis model, mesoporous silica–coated CeO_2 nanozymes exhibited combined lipid-lowering and antioxidant activities, producing sustained metabolic improvements in obese Zucker rats.[8] Moreover, co-loading with the natural compound quercetin achieved synergistic ROS modulation and downregulation of inflammatory cytokines, further expanding the therapeutic potential of this versatile nanoplatform.[9]

To gain a comprehensive understanding, we introduced PLGA as an organic matrix (in contrast to the inorganic silica) and successfully employed a double-emulsion method to synthesize two types of PLGA nanoparticles (270 ± 15 nm) incorporating a CeO_2 system. This modular strategy enables the development of multifunctional nanomaterials with synergistic catalytic, imaging, and therapeutic properties. To further enhance ROS–scavenging capacity, zirconium (Zr) was doped into the CeO_2 lattice to form $CeZrO_2$ nanoparticles with optimized Ce/Zr ratios.[10] Preliminary results reveal that a Ce:Zr ratio of approximately 7:3 nearly doubles the ROS-reducing activity compared with undoped CeO_2, providing an additional way for fine-tuning catalytic performance. These engineered materials are being explored for potential application in the diagnosis and treatment of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), a condition affecting over 25% of people worldwide that can progress to severe liver damage and hepatocellular carcinoma (HCC) in some cases.

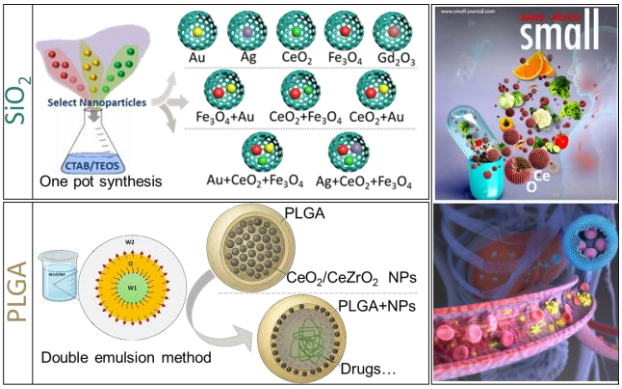

Figure 1. Two proposed platforms - one inorganic (silica, top) and one organic (poly(lactic-co-glycolic acid), PLGA, bottom) - to encapsulate CeO_2-based nanozymes.

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