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Engineered silica nanocarriers as a high-payload delivery vehicle for antioxidant enzymes

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ABSTRACT

Antioxidant enzymes for the treatment of oxidative stress-related diseases remain a highly promising therapeutic approach. As poor localization and stability have been the greatest challenges to their clinical translation, a variety of nanocarrier systems have been developed to directly address these limitations. In most cases, there has been a trade-off between the delivered mass of enzyme loaded and the carrier's ability to protect the enzyme from proteolytic degradation. One potential method of overcoming this limitation is the use of ordered mesoporous silica materials as potential antioxidant enzyme nanocarriers. The present study compared the loading, activity and retention activity of an anti-oxidant enzyme, catalase, on four engineered mesoporous silica types: non-porous silica particles, spherical silica particles with radially oriented pores and hollow spherical silica particles with pores oriented either parallel to the hollow core or expanded, interconnected bimodal pores. All these silica types, except non-porous silica, displayed potential for effective catalase loading and protection against the proteolytic enzyme, pronase. Hollow particles with interconnected pores exhibit protein loading of up to 50 wt.% carrier mass, while still maintaining significant protection against proteolysis.

1. Introduction

While vascular oxidative stress remains a well-characterized disease state found in multiple pathologies (e.g. acute lung injury, septic shock, radiotoxicity), treatment strategies that directly address this mechanism remain elusive [1–5]. Arguably, delivery of antioxidant enzymes (e.g. catalase and superoxide dismutase) remains one of the more promising therapeutic approaches. Yet, the inability to deliver sufficient quantities of enzyme for prolonged durations remains a considerable technological challenge [6,7]. To overcome this limitation, nanocarrier systems, which can protect the loaded enzyme from proteolytic degradation while permitting active targeting, have been developed [8–14]. To date, despite the exciting advances made by multiple groups, there have been trade-offs between the degree of enzyme protection and the degree of loading. As this protection is based upon internally loading the enzyme into protease-inaccessible pockets, it is hypothesized that a material with a high internal surface area could permit high internal protein loading while simultaneously limiting the accessibility of subsequently exposed proteases. One such candidate material that would meet this requirement is mesoporous silica.

Biomedical research on mesoporous silica [15–17] has gained unbridled momentum since they were first reported as prospective drug delivery systems in 2001 [18]. Their exceptional properties, i.e. well-ordered structure, high surface area and easy pore size control, have made mesoporous silica promising biomaterials for tissue engineering [19–21], enzyme loading [22] and drug delivery [23–26]. Serving as effective orthopedic materials, mesoporous silicas have the potential for enhanced osteogenic bioactivity compared with traditional silica bioglass, owing to their large pore size and pore volume, which accelerates apatite formation [27,28]. These materials can also be customized to have pores similar to the molecular size of most drugs, including proteins, and can therefore serve as potential carriers for oral as well as parenteral (intramuscular or intravenous) drug delivery and can be incorporated into scaffolds for tissue regeneration or reconstruction. Vallet-Regi et al. [29,30] recently reviewed the growing biomedical applications of nanostructured mesoporous silica matrices. Indeed, the literature in this area encompasses several in vitro studies that have demonstrated controlled retention and release of proteins, enzymes and pharmaceuticals from silica systems [23,31–47].

The present study investigated catalase loading into and onto selected mesoporous silica types ranging from non-porous to silica designed with pores hypothesized to be large enough to freely accommodate catalase. Itoh et al. recently reported the loading of catalase into silica particles with sheet-like mesopores and

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