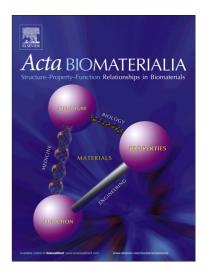
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ACCEPTED MANUSCRIPT

Nitric oxide-releasing injectable hydrogels with high

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peroxynitrite

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Abstract

Nitric oxide (NO) is an endogenous molecule with many critical biological functions that depend on its concentration. At high levels, NO provides broad-spectrum antibacterial effects through both its pathogen inhibition and killing abilities. However, its short half-life has been a great challenge to its clinical application in pharmaceutical forms. In this study, we incorporated the NO donor S-nitrosothiolated gelatin (GelSNO) into injectable gelatin-based hydrogels (GHs) to controllably release NO. Under catalysis by horseradish peroxidase, H₂O₂ oxidizes phenol moieties functionalized on gelatin to quickly form phenol-phenol crosslinks that encapsulate GelSNO. Through thermal, visible light, and oxidizing agent-driven mechanisms, NO is released from the GH/GelSNO hydrogels. By varying the GelSNO concentration, the release of

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