Injectable Hybrid Hydrogen-releasing Hydrogel for Osteosarcoma Treatment and Bone Regeneration

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Introduction

Osteosarcoma, the most common primary bone malignancy, often recurs after resection plus chemo/radiotherapy due to residual cells and the lack of conformal, osteogenic fillers. To address these challenges, we designed a multifunctional injectable hydrogen and heat-releasing hybrid hydrogel. This hydrogel designed by mussel-inspired catechol chemistry by assembly of oxidized silk fibroin (SFO), oxidized lignin (O-LN), polydopamine modified mesoporous magnesium silicate nanoparticles loaded with ammonia borane (AB) ($MgSiO_3$-PDA@AB) as a hydrogen (H_2) ion releasing sources for therapy and osteogenesis. The designed hydrogel combines mild photothermal (~45°C) and H_2 therapy for selective eradication of osteosarcoma while safeguarding the healthy tissues from overheating followed by bone healing.

Methods and Materials

SF from B. mori was extracted, tyrosinase-oxidized, and coordinated with Fe^{3+} to form catechol-Fe nodes. Alkaline lignin was demethylated and oxidized to yield O-LN. $MgSiO_3$ mesoporous nanoparticles were prepared via Stöber-derived SiO_2 followed by hydrothermal Mg incorporation and coating with PDA, then loaded with AB. Self-assembly of SFO/Fe^{3+}, OLN, and $MgSiO_3$-PDA@AB afforded syringe-cast hydrogels. Formulations were optimized regarding Fe^{3+}, O-LN, nanoparticle content to achieve robust, multifunctional hydrogel networks with controlled gelation, injectability, adhesiveness, photothermal response, and on-demand H_2 release for selective osteosarcoma eradication and bone regeneration.

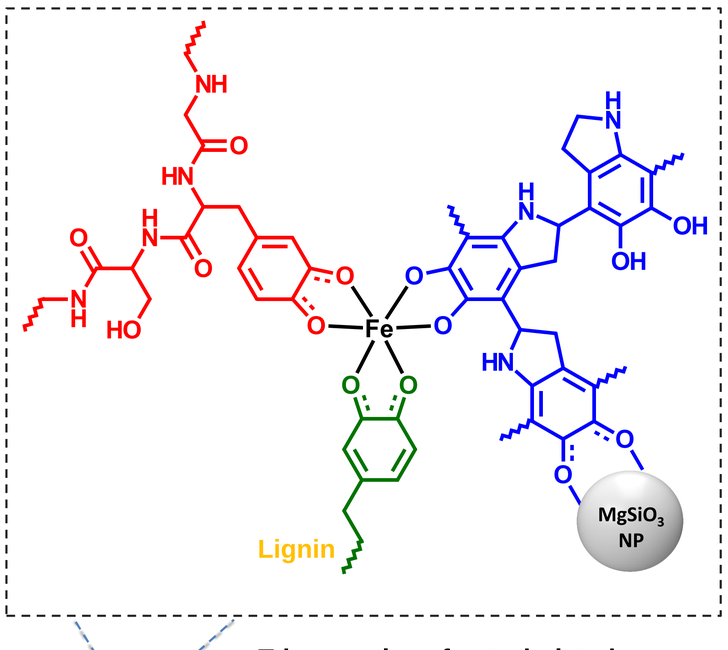
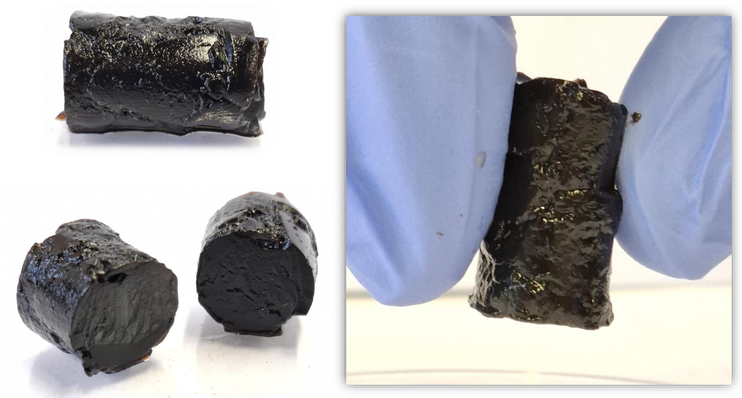


Figure 1. Synthesis of the hydrogel building blocks.

Results

Chemical analyses (^{1}H-NMR, FT-IR, UV-Vis, XRD, SEM-EDX) verified successful oxidation/modification and nanoparticle integration. Gelation was tunable via Fe^{3+} content and pH (optimal 8-9.5), yielding injectable, water-stable constructs that adhered to bone-mimetic and metallic surfaces. Under 808-nm irradiation, formulations reproducibly reached mild photothermal ranges with rapid on/off cycling. Complementarily, the $MgSiO_3$-PDA@AB component provided sustained hydrogen release in tumor-relevant conditions, supporting combined hydrogen-thermal action. Overall, the platform offers controllable properties including injectability, adhesion, photothermal performance, and therapeutic H_2 delivery for localized osteosarcoma ablation and defect reconstruction.



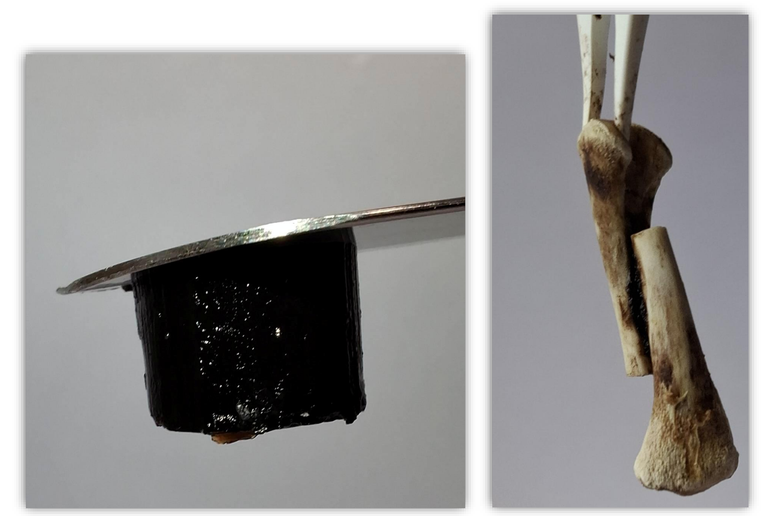
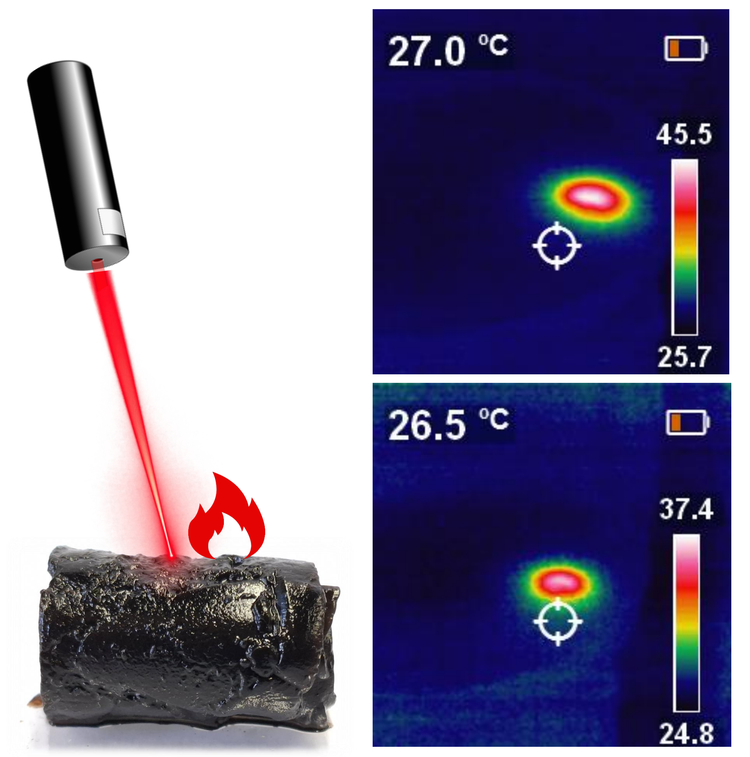


Figure 2. Injectability, self-healing, printability and adhesion properties



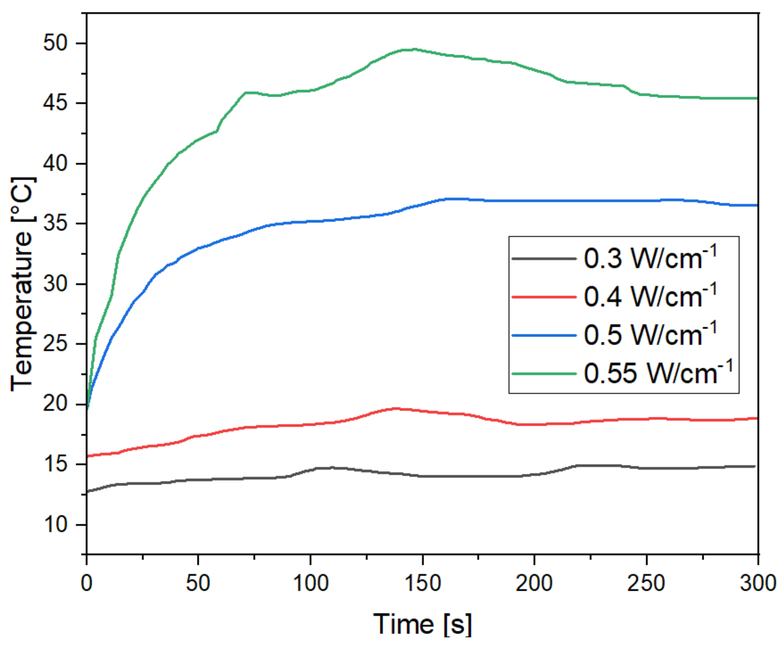


Figure 3. NIR Laser Triggered Photothermal Conversion

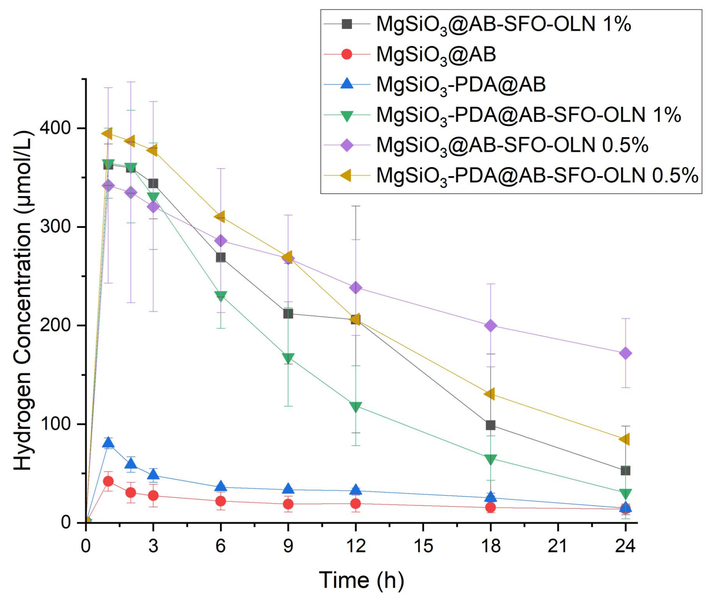


Figure 4. Hydrogen release profile

Discussion and Conclusions

We introduced hydrogen-thermal therapy as a novel, localized approach for osteosarcoma via a multifunctional, stimuli-responsive hydrogel. Formulated from FDA-approved, bioactive components, materials integrate photothermal conversion with H_2 delivery, for an efficient tumor eradication. Next, we will assess cytocompatibility and in vitro and in vivo performance toward minimally invasive tumor control with concurrent bone repair.

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