3D printed hierarchical hydrogel–nanogel scaffolds for controlled delivery of nonsteroidal anti-inflammatory drugs

Leonardo Caserio, Emanuele Mauri, Davide Moscatelli

Dept. Chemistry, Materials and Chemical Engineering, Politecnico di Milano, Milan (Italy)

Introduction

3D bioprinting offers promising opportunities for developing advanced drug delivery systems with tailored architectures. Hydrogels are widely used due to their high biocompatibility, porosity, and tunable swelling behavior. However, due to the 3D printing process, they often show limited mechanical properties and poor modulation of drug release when drugs are simply embedded within their mesh.

To address these limitations, nanogels (NGs) can be incorporated into the hydrogel matrix to create a hierarchical structure with improved control over diffusion and release. In this work, we developed a formulation based on methacrylated NGs embedded within a gelatin methacrylate (GelMA) matrix. Using extrusion-based 3D printing followed by UV crosslinking, we produced composite scaffolds in which the NGs remain covalently bound within the matrix, preventing uncontrolled release and enabling localized, sustained drug delivery.

Methods

NGs were synthesized from hyaluronic acid and polyethylene glycol, functionalized with methacrylate groups, and dispersed into a GelMA-based ink. Porous scaffolds were fabricated via extrusion printing and UV crosslinked. Physicochemical and mechanical characterizations were performed via NMR, FTIR, rheology, swelling/degradation tests, and printability. Diclofenac was used as model drug to assess release via HPLC. Biocompatibility of the 3D printed constructs was confirmed in accordance with ISO standards.

Results

NGs showed ~30% methacrylation and integrated well into the GelMA network without compromising printability. Rheological data indicated a moderate decrease in G' and G'' but enhanced critical strain. Optimal printing parameters were identified via printability maps. The hierarchical scaffold exhibited sustained drug release (~37% in 7 days), while hydrogel systems alone released ~62%. Structural integrity was maintained over time, highlighting the composite's potential for applications such as patches or implantable drug depots.

Conclusion

The developed 3D printed hierarchical scaffolds offer a stable, biocompatible, and reproducible platform for controlled drug delivery, with strong potential for personalized therapeutic applications