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Foxy5-Loaded Thermosensitive Hydrogel Incorporating Hyaluronic Acid for Bone defects Applications

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INTRODUCTION & AIM

Bone defects present a significant clinical challenge, making efficient repair crucial [1].

Hyaluronic acid (HA), a biocompatible polysaccharide, binds effectively to CD44 receptors, which are overexpressed in inflammation and cancer. This interaction is essential for bone regeneration, particularly in therapies for bone defects, addressing the increasing demand for regenerative solutions [2].

This study aims to formulate HA-based hydrogels using different molecular weights of HA, along with Poloxamer 407 (P) and tannic acid (TA), to develop thermosensitive hydrogels. Foxy5, a Wnt5a-mimicking peptide, enhances the proliferation, differentiation, and migration of type H endothelial cells, synergizing with BMP2's paracrine effects to regulate vascular-osteogenic coupling.

METHOD

The hydrogel was developed by formulating it with HA of various molecular weights (0.5%), P (22%) (HyHA), TA (1%) (HyHAT), and Foxy5-loaded hydrogels (HyHAF, HyHATF). Morphology, gelation, osmolality, viscosity, swelling, biodegradation, and total drug dispersion properties were studied. The physical stability of all hydrogel formulations and the chemical stability of Foxy5 within the hydrogel were analyzed. In vitro the release of Foxy5 was assessed via HPLC.

RESULTS & DISCUSSION

All hydrogels demonstrated good chemical and physical stability over 14 days, with gelation within 50 seconds at 27°C, a viscosity of 534.43 cP, and a pH of 7.62. The formulations could be smoothly injected at 4°C and underwent rapid gelation at 37°C, filling complex defect geometries while maintaining shape stability. Swelling and biodegradation were controlled, with only 27% mass loss after 15 days. SEM analysis revealed a 3D crosslinked network conducive to sustained drug release and cell ingrowth. The Foxy5 load was approximately 90%, and release studies demonstrated that HyHATF significantly increased Foxy5 release.

Time point (Day)	W0(g)	W1(g)	Degradation
1	0.2117	0.2081	2%
3	0.2005	0.1935	3%
5	0.1849	0.1585	14%
7	0.1980	0.1700	15%
9	0.2006	0.1673	17%
11	0.2009	0.1604	20%
13	0.2045	0.1578	23%
15	0.2021	0.1466	27%

Fig. 1. Changes in gelation time, pH , and viscosity of the HyHATF hydrogel within 14 days, as well as its biodegradation profile over 15 days.

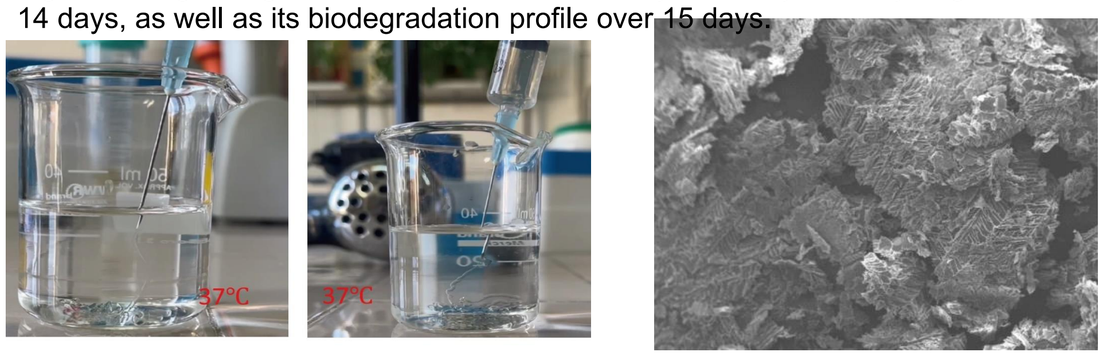

Fig.2. Thermosensitive injectability and SEM results of HyHATF hydrogel.

CONCLUSION

The thermosensitive hydrogel system provides an effective carrier for the Foxy5, enhancing type H vessel-mediated bone repair. This strategy significantly promotes efficient bone tissue regeneration and offers an innovative solution for clinical bone defect treatment.

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