Bioadhesive hydrogels based on collagen and combined with gallium-bioglass nanoparticles for bone regeneration

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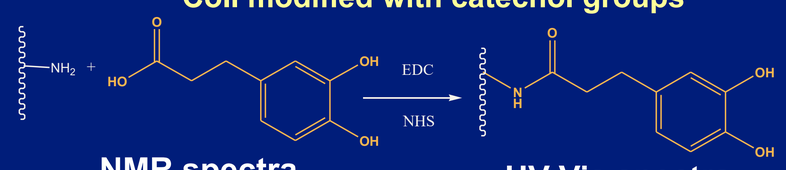
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INTRODUCTION

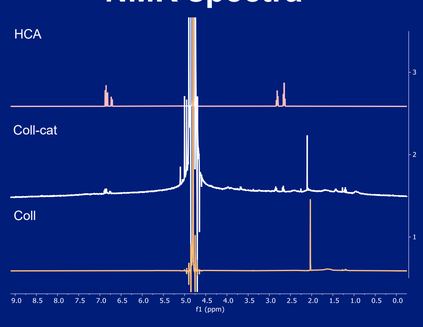
Bone can self-regenerate after fractures; however, when fractures are extensive, bone grafts may be necessary. Conventional orthopaedic implants lack antibacterial activity, are non-biodegradable, and exhibit limited biocompatibility, thereby increasing the risk of inflammation and infection. Since this option presents several limitations and risks for the patient, hydrogels represent a promising alternative for bone regeneration, as they possess a structure similar to the extracellular matrix, are biocompatible, and can incorporate molecules that stimulate osteogenesis. Collagen (Coll) is a primary component of bone, making it an ideal material for developing new scaffolds for bone applications. Here, we develop hydrogels based on Coll modified with catechol groups. This biomimetic approach is inspired by the exceptional adhesion ability of marine mussels to wet, irregular surfaces. These hydrogels were combined with gallium-doped bioglass nanoparticles (GaBGNPs) to improve osteoblast cell viability and proliferation, thus promoting osteoconductivity and biomineralization.

MATERIALS AND METHODS

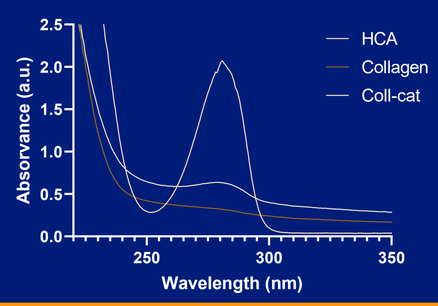
Coll modified with catechol groups



NMR spectra



UV-Vis spectra



Synthesis of GaBGNPs by sol-gel method

Solution A pH 2.0
- Tetraethyl orthosilicate
- EtOH
- H_2O

+

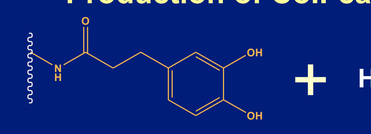
Solution B pH 11.5
- Calcium nitrate
- di-Ammonium hydrogen phosphate
- Gallium nitrate
- H_2O

↓ Final solution

↓ Wash the precipitation

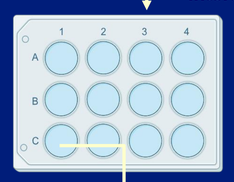
↓ Drying and calcination → **GaBGNPs**

Production of Coll-cat Hydrogels

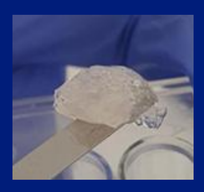


+ H_2O

↓ Intramolecular interactions



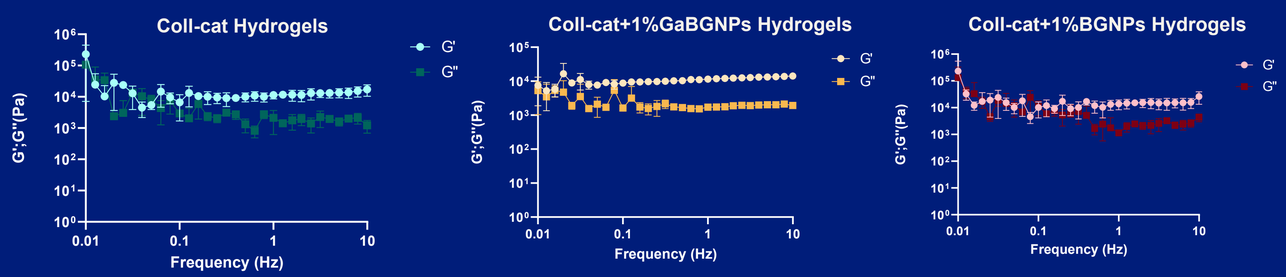
Hydrogels formed at 5ºC or/and 37ºC



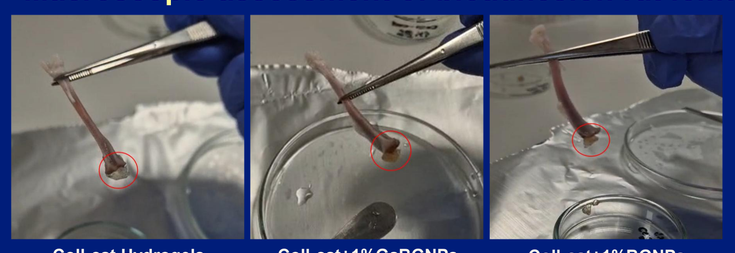
RESULTS AND DISCUSSION

Coll-cat hydrogels characterization

Rheological properties

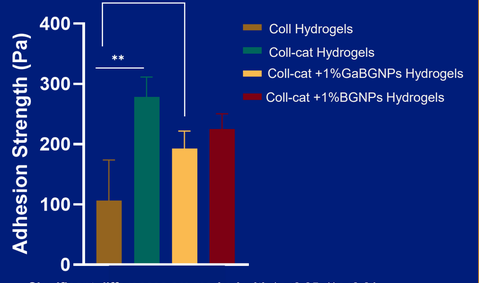


Macroscopic assessment of bioadhesion rat femur



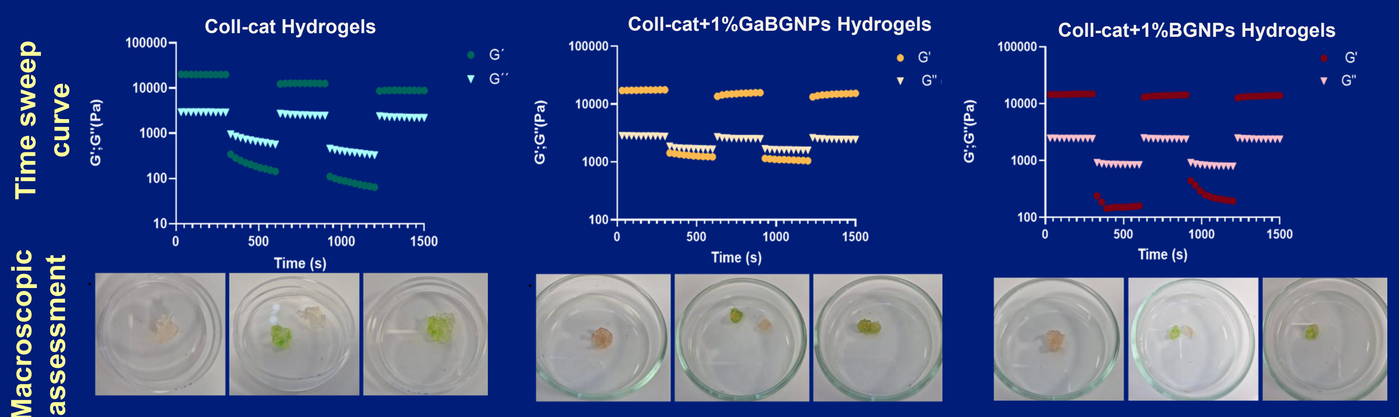
Coll-cat Hydrogels | Coll-cat+1%GaBGNPs Hydrogels | Coll-cat+1%BGNPs Hydrogels

Lap-shear test

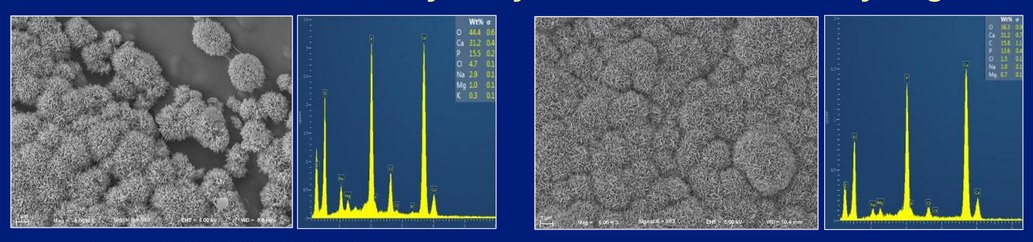


Significant differences are marked with *p<0.05; **p<0.01

Self-healing properties



Biomineralization analysis by SEM/EDS of Coll-cat Hydrogels

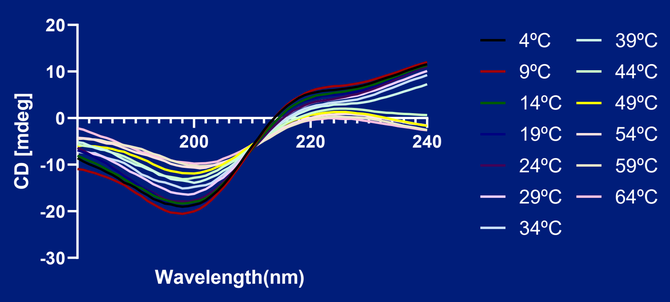


Coll-cat+1%GaBGNPs Hydrogels | Coll-cat+1%BGNPs Hydrogels

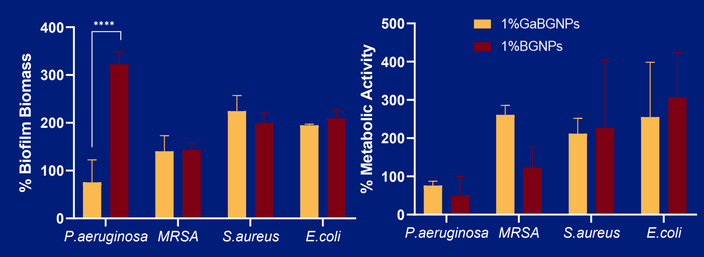
After incubation in SBF for 21 days at 37ºC

Antibacterial activity

Circular dichroism spectra of Coll-cat Hydrogels

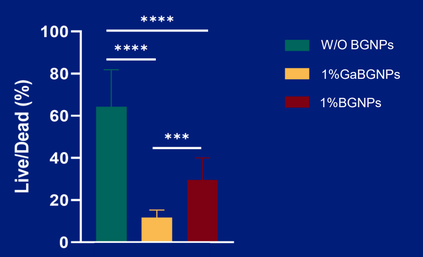


Biofilm eradication assay: BGNPs



Statistical differences are marked with ****p<0.0001

Bacterial viability: Coll-cat Hydrogels



Live/Dead of *P.aeruginosa*

Statistical differences are marked with ***p< 0.001, and ****p<0.0001

CONCLUSIONS

The modification of collagen with catechol groups significantly enhanced the hydrogel's adhesive properties, as demonstrated in adhesion tests on rat femur and porcine skin. The incorporated Ga-BGNPs exhibited antibacterial activity against clinically relevant microorganisms, including *E. coli*, *S. aureus*, *MRSA*, and *P. aeruginosa*. The hydrogel+GaBGNPs system showed higher effectiveness against *P. aeruginosa*, a pathogen known for its antibiotic resistance and clinical challenges in bone infections. Overall, the produced hydrogels represent a promising system for bone regeneration, combining enhanced adhesive capacity, bioactivity and antibacterial properties.

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