Engineering a collagen–hyaluronic acid scaffold based on the articular cartilage structure for generating osteoarthritis models

Marina Frutos-Lizano[a,b], Natalia Izquierdo[a,b], Cristina Remírez de Ganuza[a,b,c], Manuel Arruebo[a,b,c], Gracia Mendoza[a]

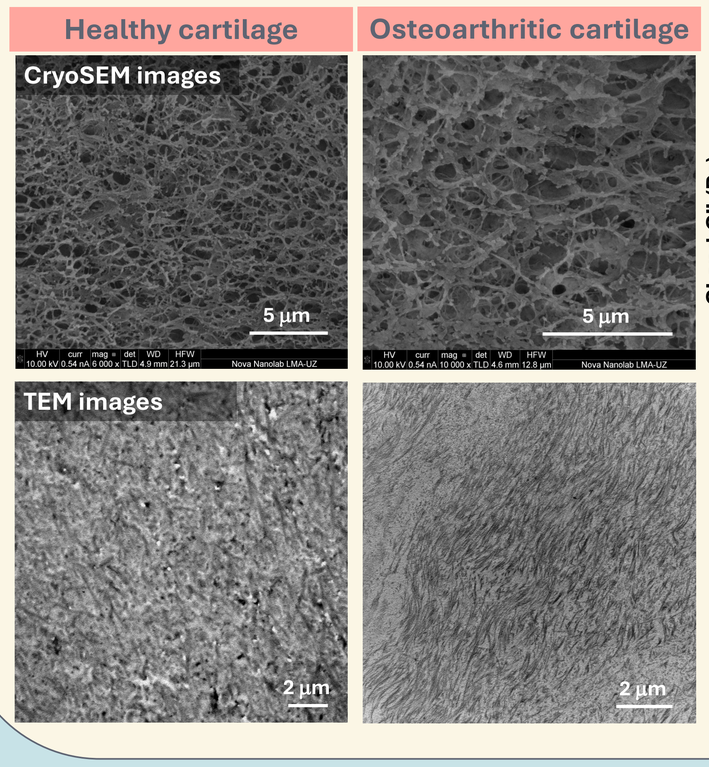
[a]*Aragon Health Research Institute (IIS Aragon), 50009 Zaragoza, Spain*
[b]*Department of Chemical and Environmental Engineering, University of Zaragoza, Campus Río Ebro-Edificio I+D, C/Poeta Mariano Esquillor S/N, 50018 Zaragoza, Spain*
[c]*Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC-Universidad de Zaragoza, 50009 Zaragoza, Spain*

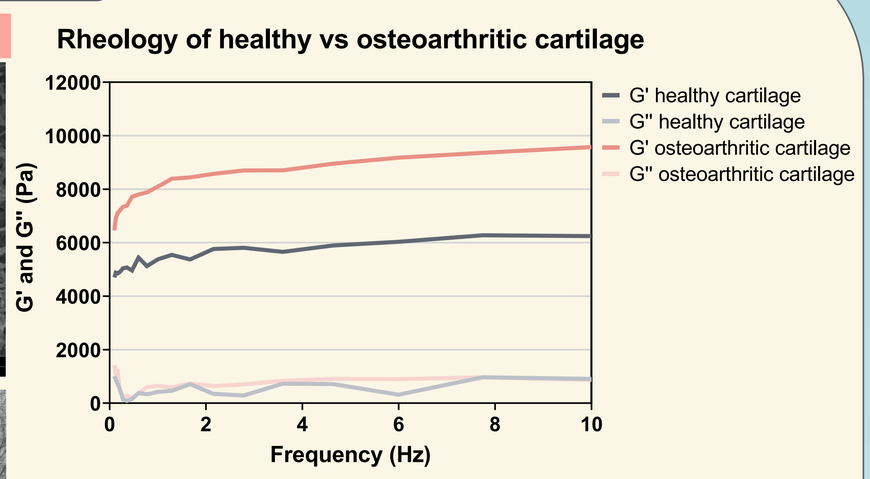
Background

Osteoarthritis (OA) is a degenerative joint disease characterized by **progressive cartilage degradation and loss of function**, affecting millions of people worldwide. Its complex pathology involves **structural and mechanical alterations of cartilage**, highlighting the need for experimental models that accurately reproduce **native tissue properties**.

In this work, cartilage from OA patients was characterized by comparing **macroscopically healthy and osteoarthritic regions**. Based on these insights, **collagen–hyaluronic acid (HA) biomimetic hydrogels** were developed, and their **structural, mechanical, and biological performance** was evaluated for **3D cell culture applications**.

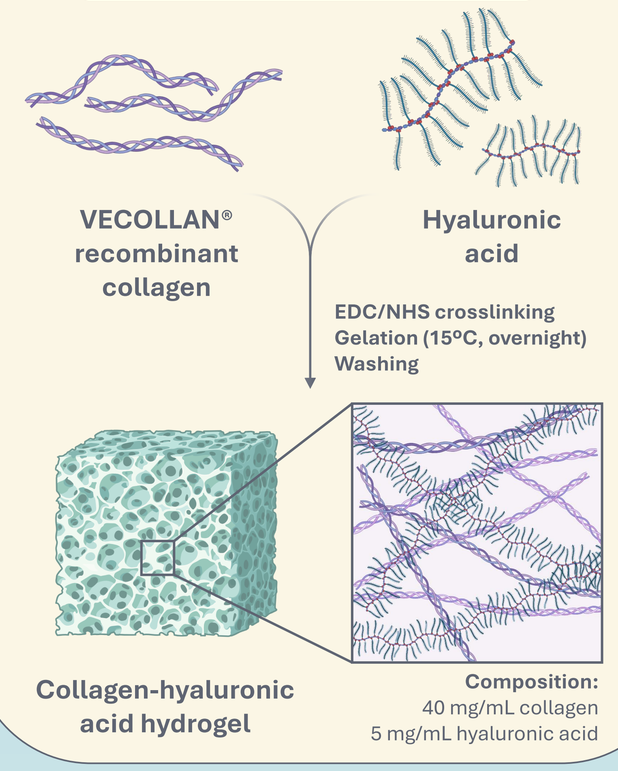
Cartilage characterization



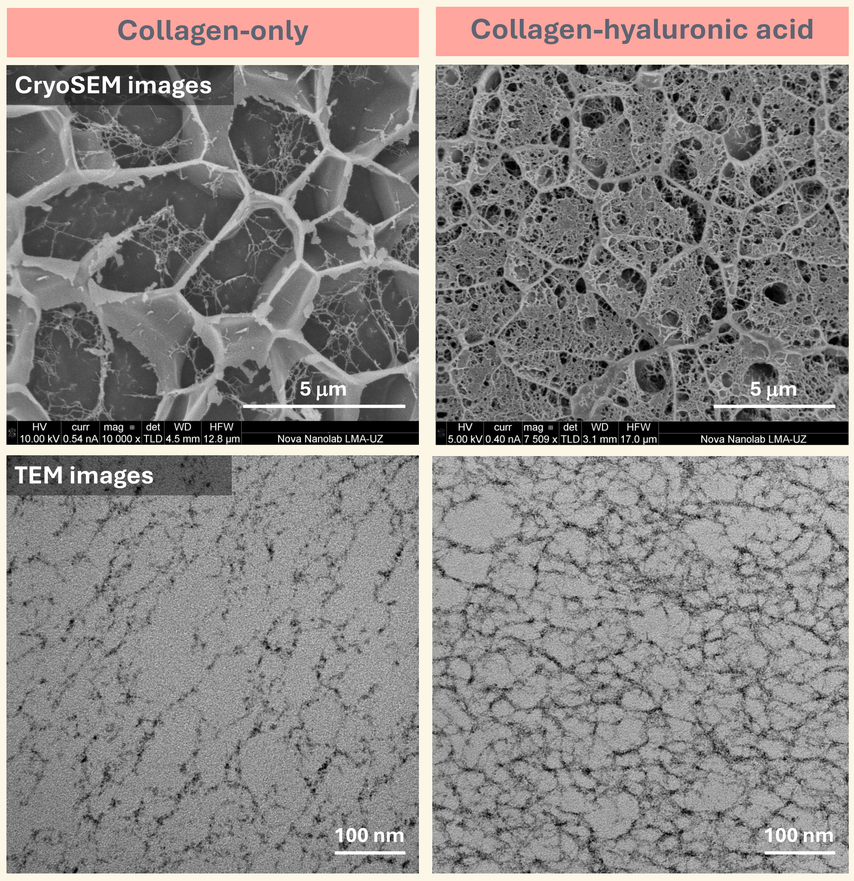


Representative TEM and cryoSEM images (left) and rheological data (top) of healthy and osteoarthritic cartilage. Healthy tissue shows a compact structure with low degree of porosity, while osteoarthritic cartilage exhibits an open and porous architecture, allowing clearer visualization of collagen fibers. Rheological analysis revealed **higher G'/G" values in osteoarthritic samples**, suggesting an elastic-dominant behavior. Despite increased porosity, this may be related to matrix remodeling and loss of proteoglycan-driven viscoelasticity.

Hydrogel design

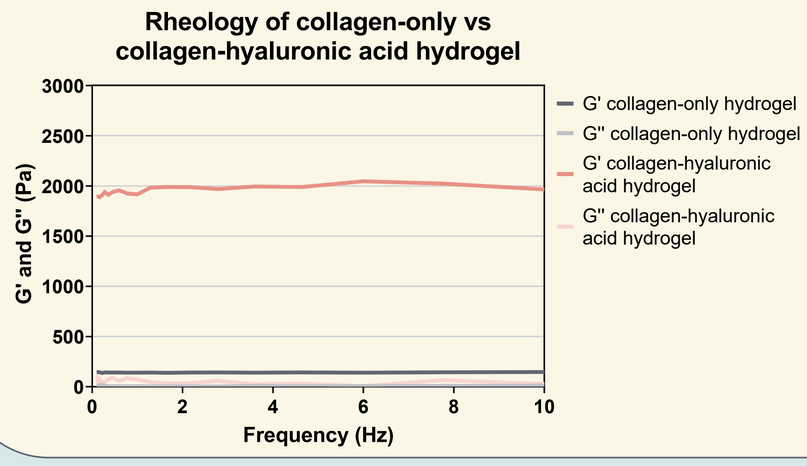


Hydrogel structure



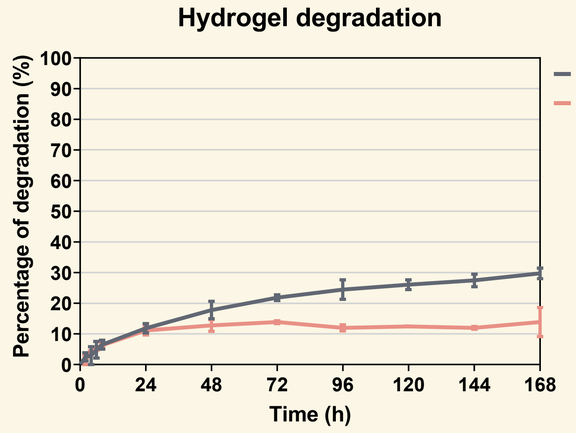
Representative images of collagen-only and collagen–hyaluronic acid hydrogels. The collagen-only hydrogel exhibits an open and porous structure, whereas the addition of hyaluronic acid **reduces porosity and promotes a denser architecture**, more closely resembling native cartilage.

Hydrogel mechanics



Rheological characterization of collagen-only and collagen–hyaluronic acid hydrogels. The addition of hyaluronic acid to the collagen-only hydrogel **increases G'/G" values**, indicating a shift towards an elastic behavior. Although the levels of native cartilage were not reached, the values fall within a **similar range**.

Hydrogel stability



Degradation of collagen–hyaluronic acid hydrogels in PBS and culture medium. Swelling results are not shown due to the absence of significant changes. The hydrogel exhibits a **slow degradation profile**, with **lower mass loss in culture medium**, where degradation stabilizes at **approximately 10%**, indicating **improved stability** under these conditions.

Conclusions

1. The incorporation of **hyaluronic acid into collagen-based hydrogels** modulates their **structural and mechanical properties**, reducing their **porosity** and increasing **G'/G" values**, resulting in a **denser and more elastic network** than those lacking hyaluronic acid mimicking **native cartilage**.
2. The collagen–hyaluronic acid hydrogel exhibits a **slow degradation profile under physiological conditions**, maintaining **structural integrity** while allowing **remodeling**, which supports its suitability for **3D cell culture applications**.

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Instituto de Investigación Sanitaria Aragón

INMA INSTITUTO DE NANOCIENCIA Y MATERIALES DE ARAGÓN

Departamento de Ingeniería Química y Tecnologías del Medio Ambiente
Universidad Zaragoza