Development and Printability of Dynamic Hydrogels for Personalized Chronic Wound Treatment – FORCE REPAIR Project

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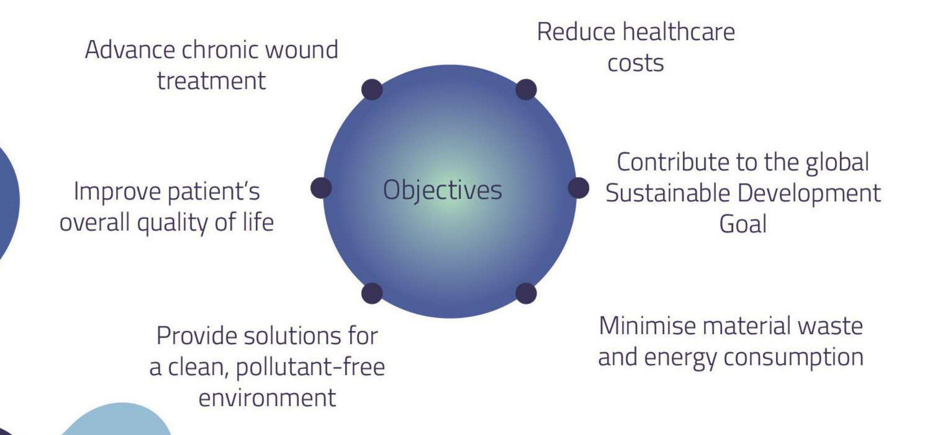
1. Background

FORCE REPAIR Aims

Chronic wounds affect up to 2% of the population in the industrial world, with an expected increase in the next years. However, current therapies remain insufficient and costly.

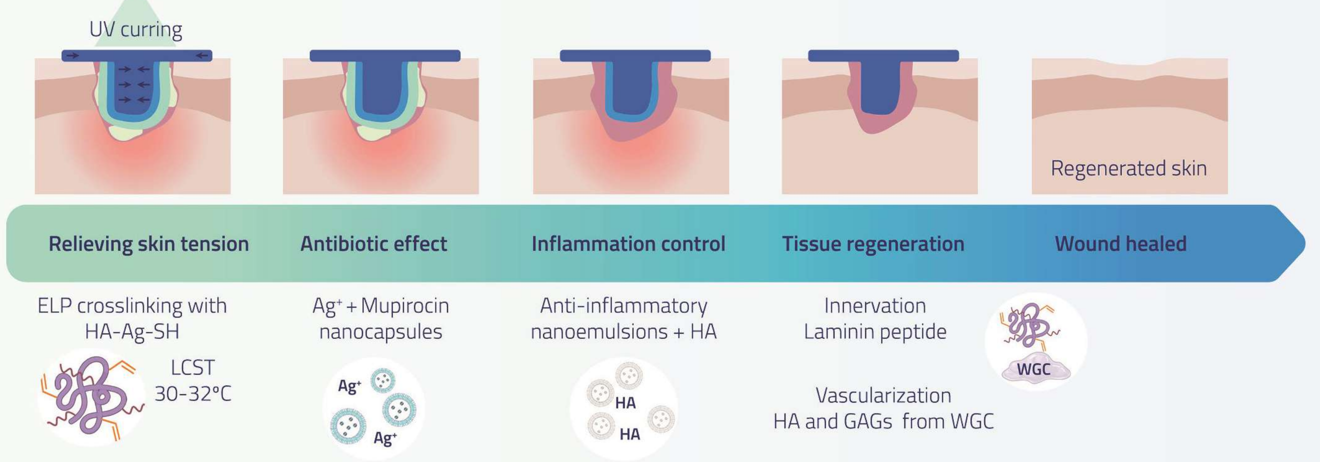
The FORCE REPAIR team sets out to advance chronic wound management by developing a smart, multifunctional, and cost-effective 3D-printed wound dressing to help i) fight bacterial infection, ii) control inflammation, iii) relieve skin tension and iv) stimulate healing.



Scientific Approach

The FORCE REPAIR concept is based on a unique 3D printable hyaluronic acid-based self-healing hydrogel (HA-Ag-DH) with the placement of each component in a strategic location:

Special trajectory software of the 3D printed materials will help inducing contractile force withing the dressing to help wound closure.



1 antibacterial and bioadhesive layer in contact with the wound

2 anti-inflammatory to recreate the environment of healthy tissue

3 regenerative core to facilitate healing using elastin-like polypeptide (ELP) and Wharton Gel Complex® (WGC)

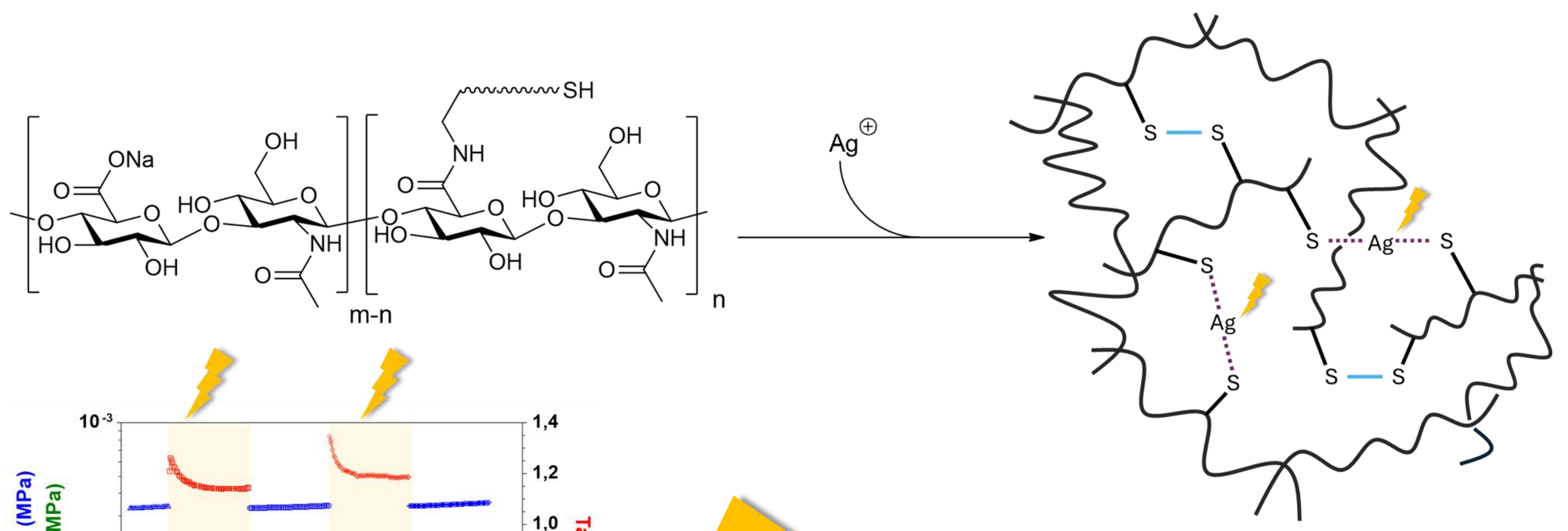
Regulatory frameworks, health technological assessment and marketability studies of the dressing validated on wound animal models will be taken into account.

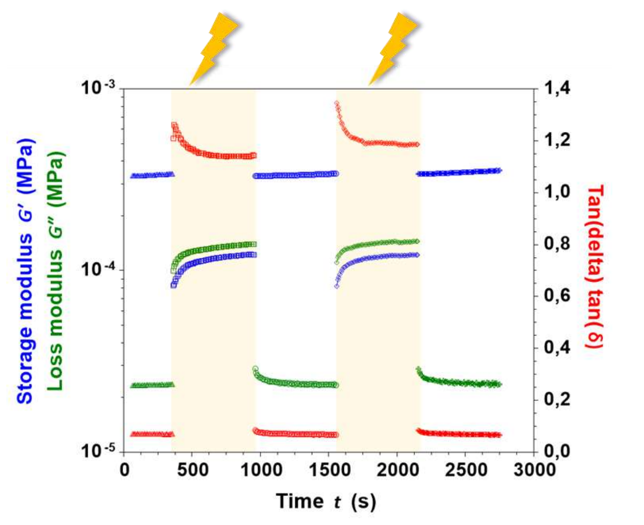
2. Introduction

Hydrogels are commonly used as printable biomaterials; however, most require post-processing treatments, typically additional cross-linking after printing.

Dynamic hydrogels (DHs), with their shear-thinning and self-healing properties, are a great opportunity to be printed without additional treatment.

This study reports the design and formulation of a DH based on **thiol-functionalized hyaluronic acid (HA-SH) with silver ions dynamic interactions**.





Within DH structure, Ag^+ ions introduce predefined rupture points by inhibiting the oxidation of thiols to disulfides

3. Materials and methods

The HA-SH and silver concentrations were varied (**Table 1**) to study their effects on the mechanical properties and printability of the hydrogel.

Table 1. Formulations tested

	[Ag], mol% per SH	[HA-SH], wt%
Ag1.5-C3	1.5	3
Ag3-C3	3	3
Ag4.5-C3	4.5	3
Ag3-C2	3	2
Ag3-C2.5	3	2.5

Rheometer

bIDO-I bioprinter

4. Results and discussion

- **Printability Assessment**

All formulations printed well, giving place to fully manipulable structures without needing additional cross-linking steps (**Figure 1**). The most successful ink was Ag3-C2, as it was less lumpy and less rigid than other 3wt% HA-SH formulations, making it ideal for dressing applications. It also showed better adhesive properties, warranting further detailed study.

Ag1.5-C3, Ag3-C3, and Ag4.5-C3 were initially lumpier and more cross-linked, leading to irregular filaments and rougher surfaces. However, their appearance improved significantly after overnight self-repair, enhancing structure definition.

- **Rheological Analysis:**

For the same [HA-SH] percentage, Ag1.5-C3 exhibited higher tan(delta), indicating lower mechanical stability, while Ag3-C3 and Ag4.5-C3 demonstrated higher mechanical stability with similar elastic behaviour, likely due to saturated silver ion binding. On the other hand, when changing the [HA-SH] percentage, Ag3-C3 showed the highest elastic behaviour, while Ag3-C2.5 and Ag3-C2 displayed intermediate stability with more viscous behaviour, supporting their suitability for flexible, adhesive dressings.

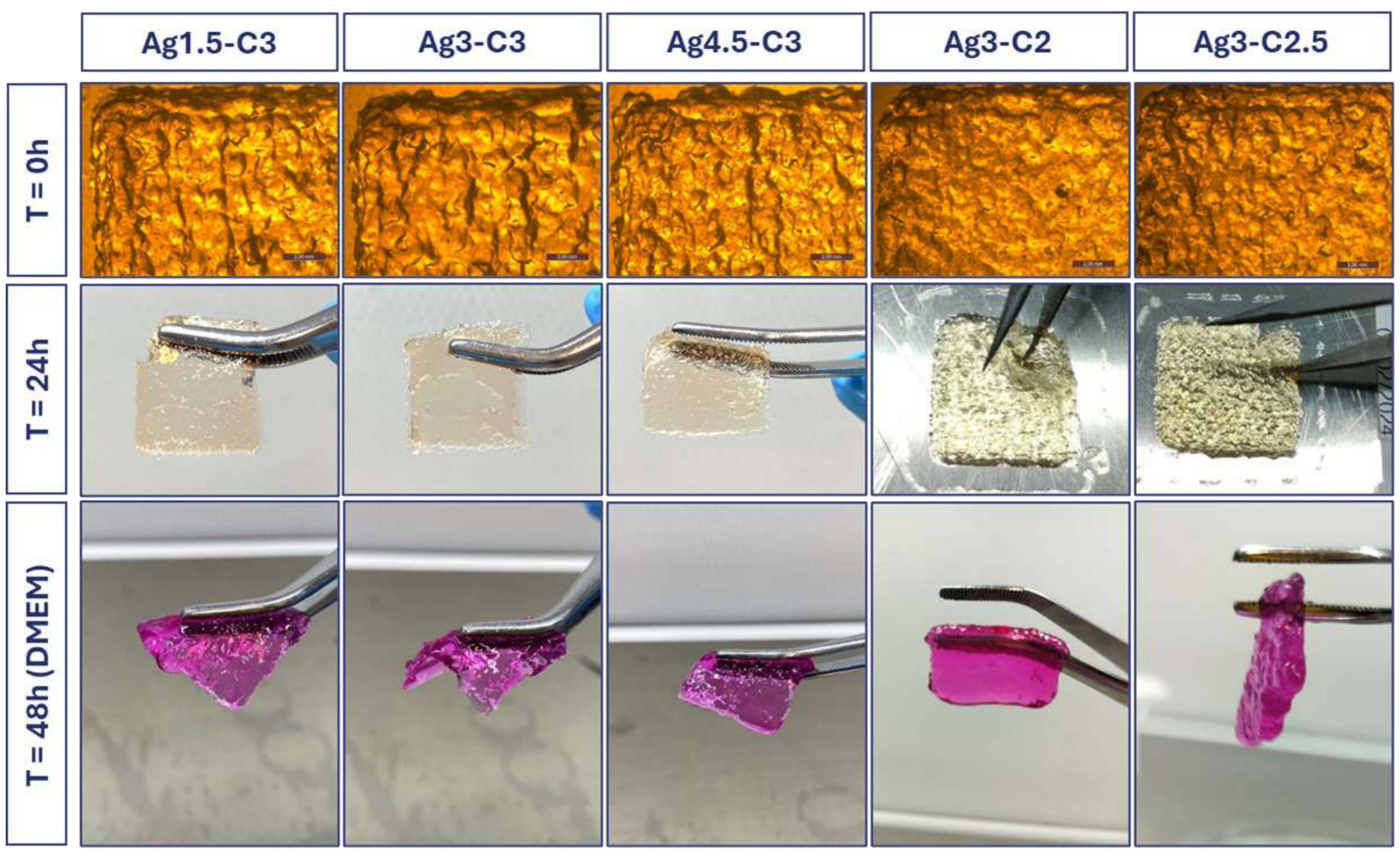


Figure 1. Printed structures: handling and swelling in DMEM

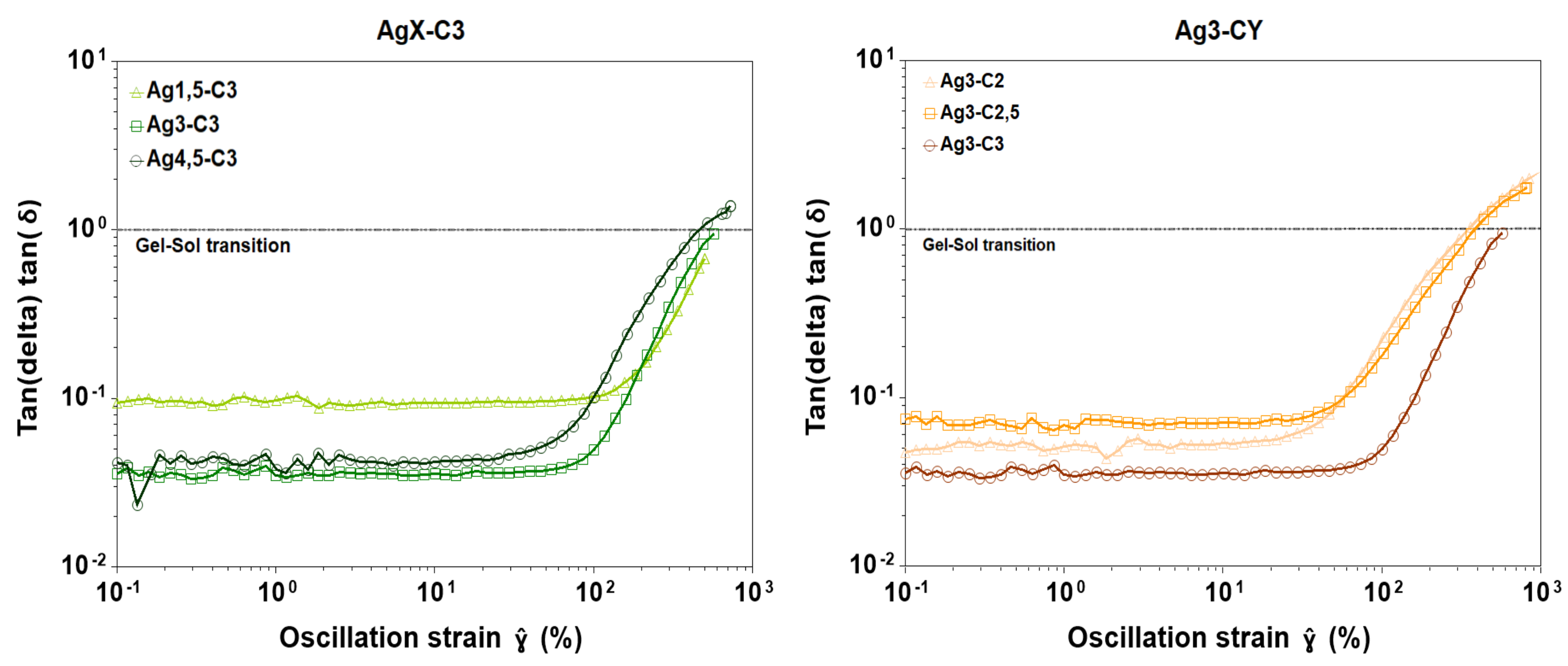


Figure 2. Tan(delta) vs oscillation strain (%) to evaluate the effect of [Ag^+] and [HA-SH]

5. Conclusions

The obtained results provide a foundation for predicting the printability of these DHs by extrusion-based 3D printing based on their chemical composition. This knowledge facilitates the selection of the best biomaterial formulations for further developments within the **FORCE REPAIR** project. Additionally, the 3D printing community can benefit from a deeper understanding of the relationship between rupture points and printability in this novel class of dynamic soft materials.

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