

Hyaluronic acid-based hydrogels for suprachoroidal administration in glaucoma treatment: influence of precursors characteristics on hydrogels properties

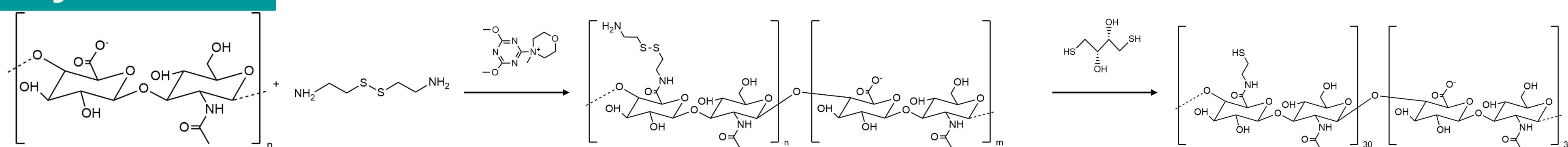
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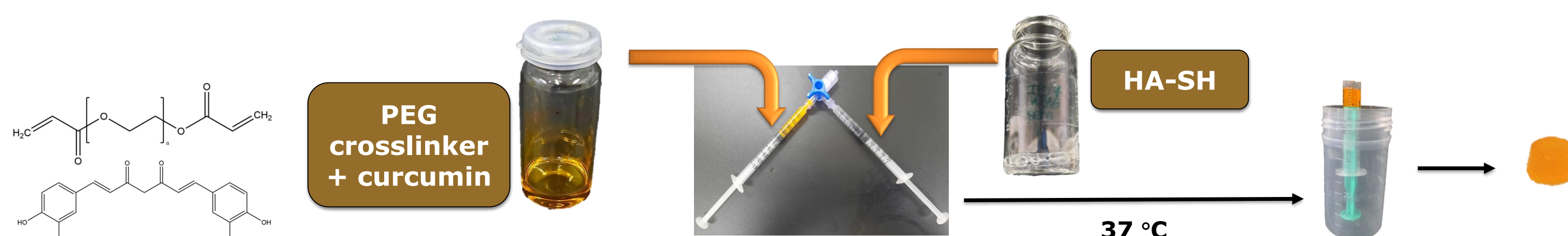
Introduction

- Glaucoma is a leading cause of vision loss that is associated with the increase in intraocular pressure.
- The injection of a hydrogel into the suprachoroidal space (SCS) is a promising treatment, decreasing intraocular pressure and allowing drug delivery.
- Hydrogels of hyaluronic acid crosslinked with PEG were prepared and studied as potential drug delivery vehicles.

Synthesis



Scheme 1. Synthesis of thiolated hyaluronic acid via a two-step process.



Scheme 2. Synthesis of HA-based hydrogels.

Chemical structure

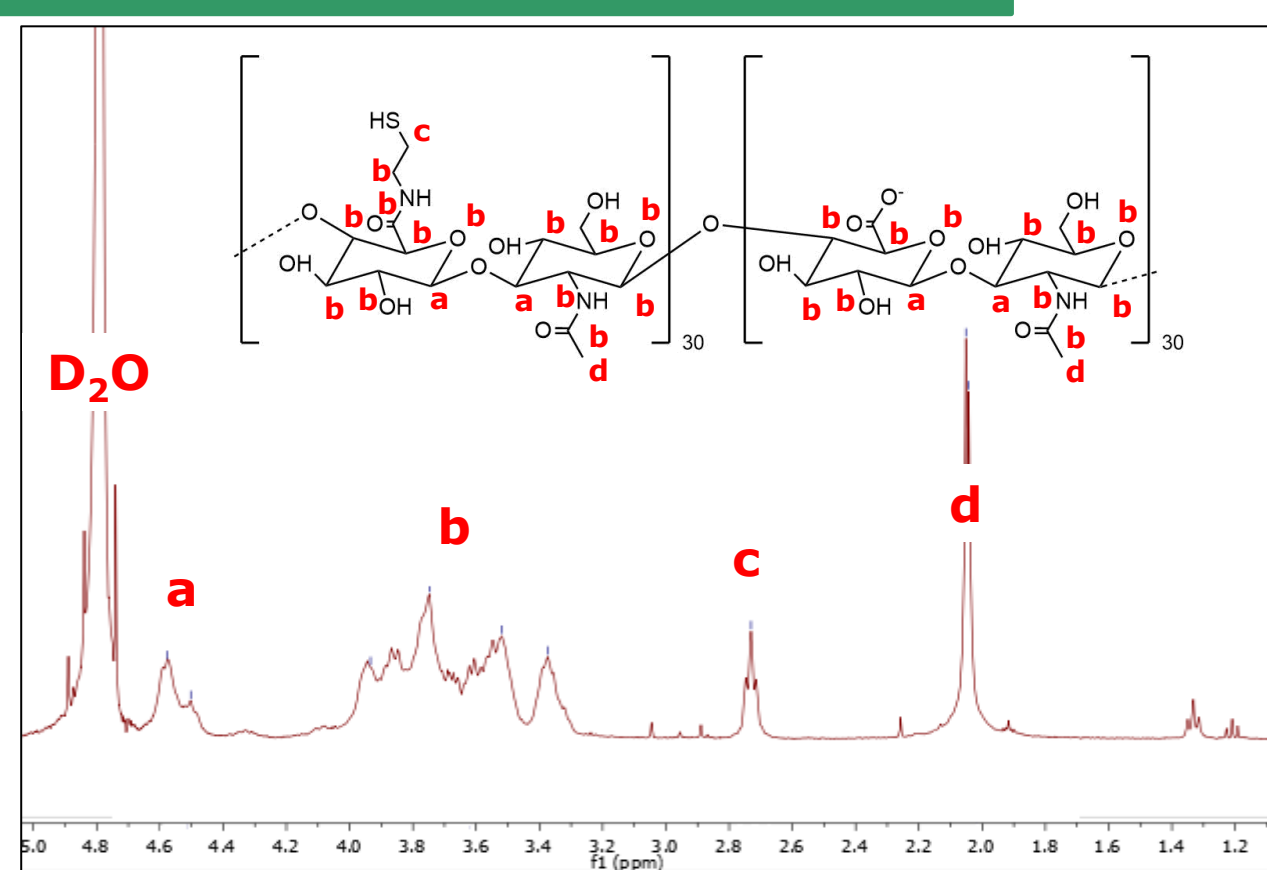


Figure 1. 400MHz ¹H NMR spectra of representative HA-SH.

- HA modification is successful
- Different modification degrees were achieved

Rheology

Table 1. Storage modulus and critical strain.

Crosslinker	<i>MW</i>	<i>G'</i> (Pa)	Critical Strain (%)
HCUR1	575	210	65
HCUR2	302	190	60
HCUR3	214	160	35

- HA with a modification degree of 26% yields gels with the best properties
- The sturdiness of the hydrogel depends on the crosslinkers MW
- Higher MW crosslinker creates a more robust gel

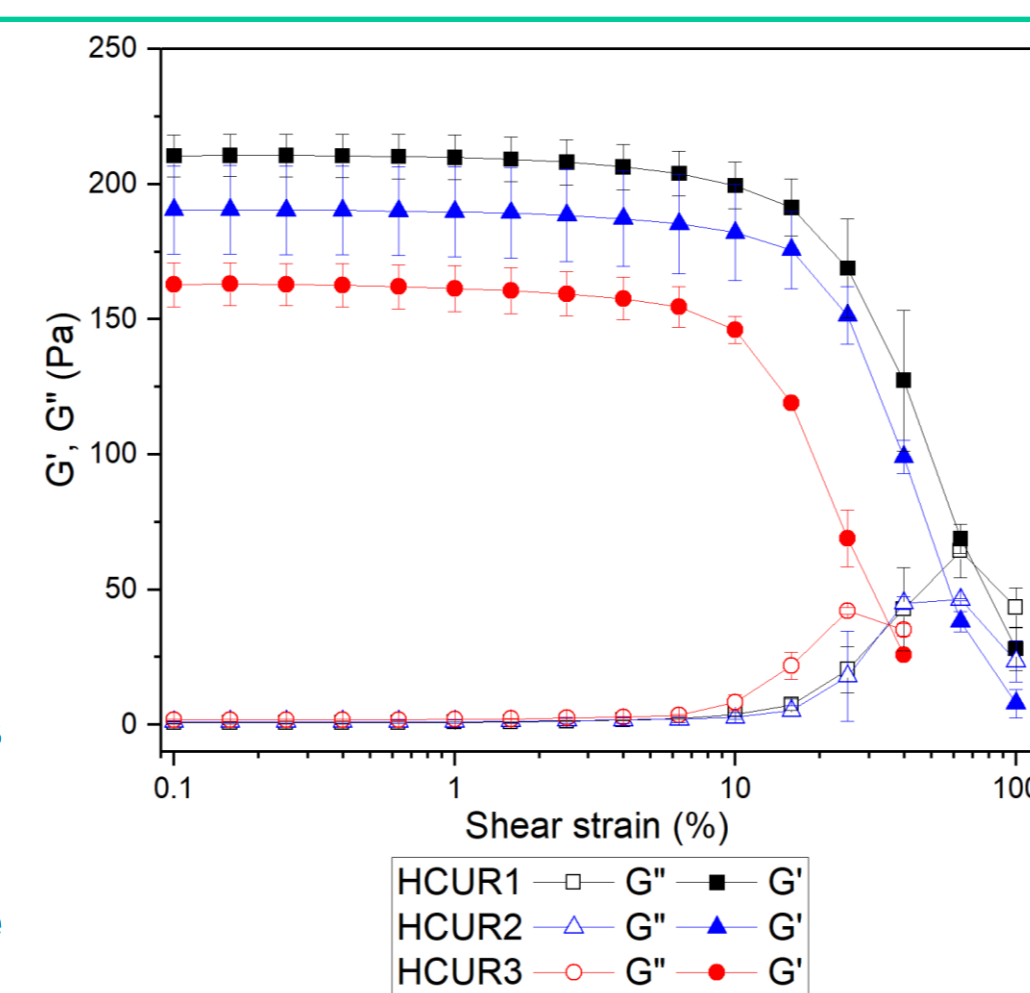


Figure 2. Amplitude sweep for the curcumin loaded hydrogels.

Gel Time

Table 1. Gel time for hydrogels with and without curcumin, for different PEG crosslinkers.

<i>n</i> _{SH} : <i>n</i> _{acrilate}	Crosslinker	<i>t</i> _{gel} (min)	
	<i>MW</i>	No curcumin	curcumin
5,00	575	1,83	2,33
3,00	302	2,75	3,08
4,00	214	2,42	2,58

- Curcumin addition increases gel time
- Steric hindrance effects due to curcumin are more evident in formulations with Low MW crosslinkers
- Fast gelling times were obtained for all formulations

In vitro curcumin release

- Curcumin release was assessed in vitro using PBS (1X concentration)
- Sink conditions require large volume of media due to low curcumin solubility

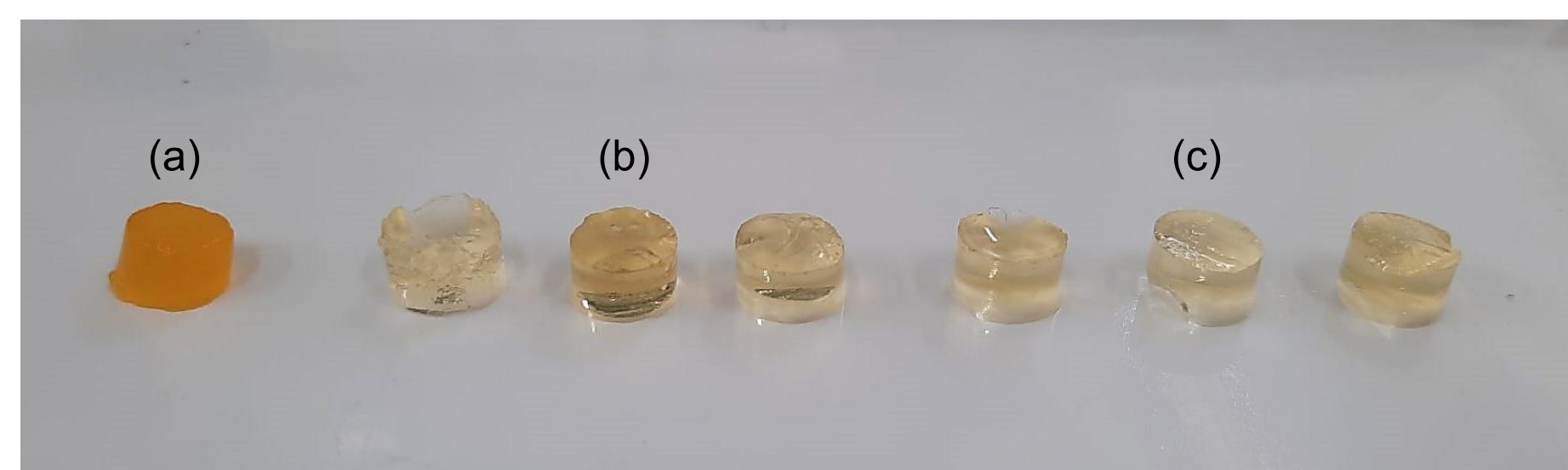


Figure 3. Aspect of hydrogels after synthesis (a) and after 1 month in PBS: HCUR1 (b) and HCUR3 (c).

- Curcumin is released but was not quantifiable due to high dilution in release medium;
- Future work requires the testing of more suitable release media.