Synthesis & Characterisation of Hyaluronic Acid (HA) based Hydrogels for Biomedical Applications

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Introduction

Hydrogels, as a result of their numerous and flexible synthesis methods, biocompatibility, advantageous physical and chemical properties, have been the material of choice for numerous biomedical applications. As such, naturally derived hydrogels such as hyaluronic acid (HA) have received increasing attention due to their inherent biocompatibility. In order to reduce HA’s rapid as vivo enzymatic degradation, it is necessary to introduce synthetic crosslinks. The synthesis of such a macromolecular network in the form of a hydrogel has the property of swelling in the presence of water, and can be tailored to possess superior rheological and viscoelastic properties than native HA solutions. The objectives of this project are to synthesise and characterise novel HA based hydrogels for potential biomedical applications in the field of drug delivery or cell encapsulation. Both chemical and photo-crosslinking approaches shall be considered in synthesising these hydrogels.

Hyaluronic Acid (HA)

- Hydrophilic natural polyionic linear polysaccharide
- Present in all the connective tissues, high molecular mass (10⁴ - 10⁶ Da)
- Key role in wound healing, promoting cell motility and differentiation

Chemical-crosslinking

Motivation

As a result of its carboxyl, acetamido and multiple hydroxyl groups, HA may be functionalised and subsequently crosslinked using a range of approaches.

Method

Step 1 – Functionalisation
Objective: Functionalise HA with amine groups, by grafting adipic dihydrazide (ADH).

- HA
- RT pH 4.8
- EDC (Coupling agent)
- ADH
- HA-ADH

Step 2 – Crosslinking
Objective: Crosslink HA-ADH with butanediol diglycidyl ether (BDDGE) via an epoxy-amine reaction.

- BDDGE
- HA-ADH
- Crosslinked HA

Results

- HA:PEGDA-sIPN: A photo-crosslinked HA:PEGDA sIPN hydrogel system, yielding opaque hydrogels with swelling ratios ranging from 5 - 20.

Conclusions and Perspectives

Future works may include optimising the mixing process so as to reduce the reaction time and limit the amount of excess crosslinker. HA:PEGDA-sIPN: A photo-crosslinked HA:PEGDA sIPN hydrogel system, yielding opaque hydrogels with swelling ratios ranging from 5 - 20. Future works may include photo-calorimetry studies so as to optimise the PEGDA crosslinking kinetics.

Photo-crosslinking

Motivation

Hydrogels may be synthesised on the basis of a copolymer crosslinking, a semi-interpenetrating network (sIPN) or an interpenetrating networks (IPN).

Hyaluronic acid will be incorporated into a PEG network, forming a sIPN, so as to enhance elasticity, biocompatibility and provide a suitable physiological environment.

Method

PEG network

- Poly ethylene glycol diacrylate (PEGDA) is widely used synthetic polymers for network synthesis, due to its biocompatibility, ease of photo-polymerisation and tailoring of mechanical properties. The photo-initiator employed is Irgacure 2959 due to its biocompatibility.

Results

- PEGDA governs hydrogel swelling
- No statistically significant difference in swelling ratio between days 1 and 7 suggesting that HA leaching is also inducing water loss

Cryo-SEM

- 3D porous network structure
- Pores size ranging 10-30 µm
- Post 7 days immersion in water
- Interior morphology change due to HA leaching

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