

Chemical modification of hyaluronan: Improving hyaluronan as a wetting agent for contact lenses

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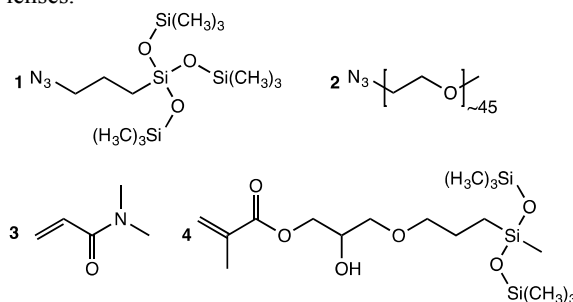
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Introduction: It has been estimated that around 125 million people use contact lenses, which represents around 5% of the population who require vision correction.¹ The low numbers of contact lens wearers is a result of issues of compatibility in the general population with current silicone-based contact lens design. Two issues that limit the widespread use of current generation silicone-based contact lenses are dry eye and protein and/or lipid adsorption; these issues have also been reported to affect up to 50% of the current contact lens wearing population. Dry eye and protein adsorption can, in part, be related back to the use of hydrophobic silicone-based contact lenses. One way to minimize dry eye and protein adsorption is to decrease the hydrophobicity by increasing the water content and surface wettability of the lens through the incorporation of a wetting agent. Hyaluronan (HA) is a biopolymer that has shown potential to act as a wetting agent in contact lenses.² However, despite preliminary success, HA is only sparingly soluble in the pre-polymer mixtures used for contact lens synthesis, and this relatively small amount of HA that can be incorporated leads to only small increases in the water content of the lens and limits HA's widespread use as a wetting agent. The aim of this study was to increase the solubility of the HA in the pre-polymer mixtures by modifying HA using click chemistry. Modified HA was then incorporated in model contact lens materials to ascertain the potential for modified HA to act as a wetting agent.

Methods: HA (LifeCore Biomedical) was modified with propargylamine using a modified procedure.³ Azido-containing silicone (**1**) or poly(ethylene glycol) (**2**) groups were synthesized using their halide or tosylate precursors, respectively, and sodium azide. Conjugation of alkyne-modified HA with azido-silicone or azido-poly(ethylene glycol) groups was carried out using typical copper-catalyzed reaction conditions followed by dialysis against methanol and saturated aqueous EDTA. For polymerization studies, modified HA was dissolved in a minimum amount of water and DMF, then diluted with N,N'-dimethylacrylamide (DMA, **3**) and (3-methacryloxy-2-hydroxypropoxy)propyl-bis(trimethylsiloxy)methylsilane (TRIS-OH, **4**) and polymerized using UV. The water content and transparency of the resulting materials were examined to establish what type(s) of modified HA are suitable wetting agents.

Results: HA (7.5 kDa and 28.5 kDa) was successfully modified using click chemistry with either **1** or **2**. When HA with a molecular weight of 28.5kDa was modified with **1**, it was soluble in the pre-polymer solution via the

addition of a 1:2 H₂O:DMF solution (10 vol.% with respect to monomer vol.). Interestingly, when 7.5 kDa HA was modified with **1**, it was not soluble in the pre-polymer solution even with the addition of 1:2 H₂O:DMF. Unfortunately, materials that contained **1**-modified 28.5kDa HA were opaque to nontransparent post-polymerization. Despite the lack of transparency, the addition of modified HA increased the water content of the materials from 59% (for materials diluted by 10 vol.% with 1:2 H₂O:DMF solutions but contained no modified HA) to 75%. When HA (7.5 kDa or 28.5 kDa) was modified with **2**, only 2 vol.% (with respect to total monomer volume) of a 1:1 H₂O:DMF solution was needed to be fully solubilize modified HA. Also, the materials were transparent post-polymerization. Incorporation of **2**-modified HA increased the water content of polymers from 37% to over 50%. While these values are not as high as polymer prepared with **1**-modified HA, these materials are transparent and they also have water contents similar to current silicone-based lenses.



Conclusions: HA was successfully modified using click chemistry with either silicone-containing or poly(ethylene glycol)-containing groups. The presence of silicone or poly(ethylene glycol) made HA more soluble in model pre-polymer contact lens mixtures compared to unmodified HA, which only formed dispersions. While the presence of silicone groups led to opaque to non-transparent materials, the presence of poly(ethylene glycol) resulted in the formation of transparent materials. In any case, the presence of modified-HA increased the water content of the polymers regardless of their transparency. This work highlights the potential for modified-HA to act as a wetting agent in contact lenses and other applications.

References: (1) Barr, J.T. Cont. Lens Spect. 1st January 2005. (2) Weeks, A. J. Biomat. Appl. 2012. DOI: 10.1177/08853282124446936. (3) Goh EJ. Biomacromolecules. 2012;13:2554-2561.