HPGuar Provides a Synthetic Glycocalyx for Superior Tissue Lubrication

Lindsay F. Springer, Robert E. Baier, Anne E. Meyer, Howard A. Ketelson, David L. Meadows

School of Dental Medicine, University at Buffalo, Buffalo, NY, USA: Alcon Ltd., Fort Worth, TX, USA

INTRODUCTION

Biological interfaces experiencing high coefficients of friction (CoF) are associated with tissue damage, inflammation and indications of pain *in vivo*. Clinical manifestations such as dry eye, xerostomia, and arthritis are often mitigated using replacement therapies, such as artificial tears, saliva substitutes, and synovial fluid supplements respectively. These synthetic lubricants must serve in place of their natural counterparts to maintain low CoFs and alleviate patient discomfort, but are often not as effective and less persistent.

Excellent in-the-eye lubricity has been reported for new ophthalmic products containing hydroxypropyl guar galactomannan (HPGG; Christensen et al., 2004). Although reported to be superior to all previous artificial tear preparations, the interfacial mechanism/s associated with demonstrated reduction of tissue-on-tissue coefficient of friction values to less than 0.1 have not been previously documented. To investigate HPGG mechanism/s of lubricity, we employed a tribological protocol that has been previously shown to correlate *in vitro* data to ophthalmic clinical outcomes (Meyer et al., 2006). This modified pin-on-disk device articulates collagenous tissue-on-tissue, chosen on the basis of similar Critical Surface Tension values to the anterior face of human cornea (Meyer et al., 2007), to provide relevant biological interfaces on which we could study HPGG formulations and their resulting lubricity.

MATERIALS and METHODS

- HPGG (MW 2.11 MDa) and Texas red labeled HPGG (MW 2.09 MDa) were obtained from Alcon Ltd.
- HPGG was formulated at varying concentrations, pHs and also with 0.15M calcium chloride, normal saline (NS, 0.9% NaCl), Unisol® 4 ophthalmic buffer, 6M urea and distilled water (dH20)
- Friction testing was carried out on a modified pin-on-disk device, coupled to a strain gauge, to articulate glutaraldehyde-tanned bovine or paraformaldehyde fixed porcine, pericardium
- Tissue couples oscillated through an arc length of 25mm at a rate of 32 cycles/minute and experienced a vertical load of about 25 grams under desiccating conditions
- Porcine pericardium was provided as a provision to University at Buffalo IACUC agreement (MED02011Y) for confocal microscope imaging with 0.2% Texas red labeled HPGG in NS
- Scanning electron microscope images were performed after articulating tissues for one hour with either NS or 0.2% HPGG in NS added at determined intervals
- Multiple attenuated internal reflection infrared (MAIR-IR) images were performed on germanium (Ge) prisms after drying the lubricant formulation, leaching with water, and rinsing.

RESULTS

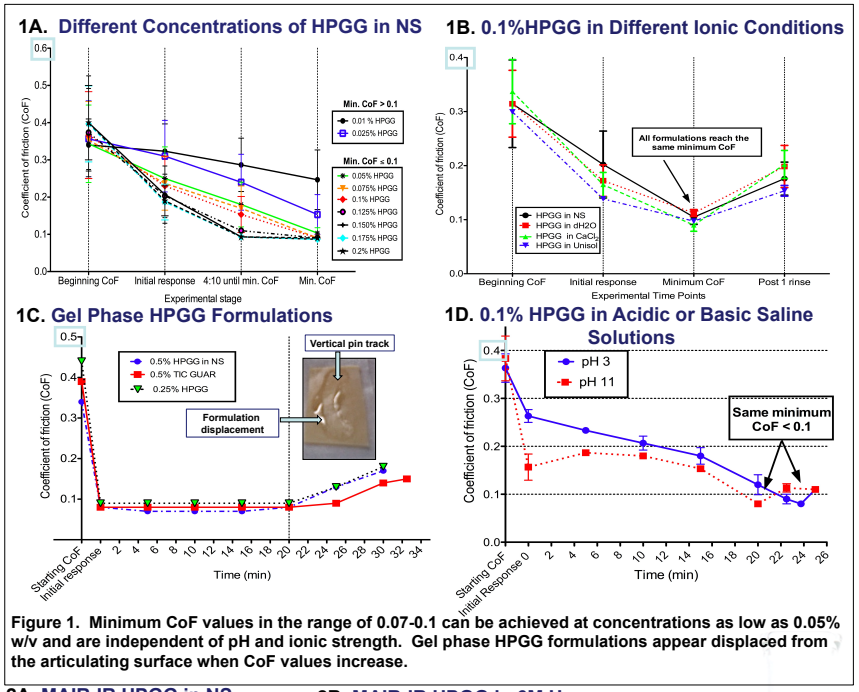

Figure 1. Minimum CoF values in the range of 0.07-0.1 can be achieved at concentrations as low as 0.05% w/v and are independent of pH and ionic strength. Gel phase HPGG formulations appear displaced from the articulating surface when CoF values increase.

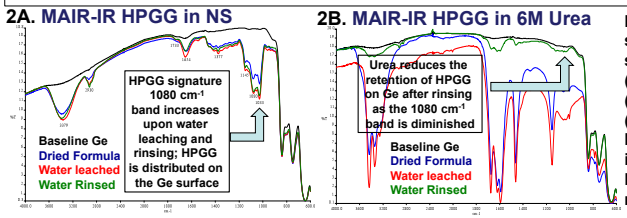

Figure 2. (A) HPGG in NS shows retention on the Ge surface throughout chemical (leaching) and mechanical (rinsing) efforts to displace it. (B) Adding urea disrupts the hydrogen bonding interaction between Ge and HPGG, resulting in easier removal.

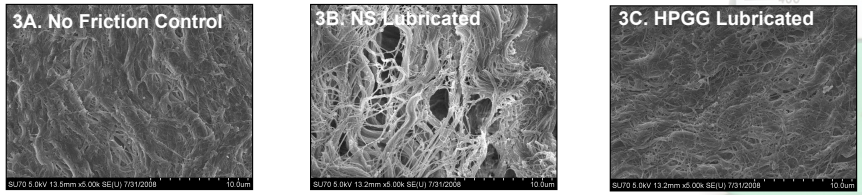

Figure 3: Scanning electron microscope images of fixed bovine pericardial tissue (A) without articulation, (B) articulated with NS for one hour, and (C) articulated with 0.2% HPGG in NS for one hour. Tissue was severely damaged when lubricated with NS alone while the HPGG lubricated tissue maintained its original fiber directionality and structure.

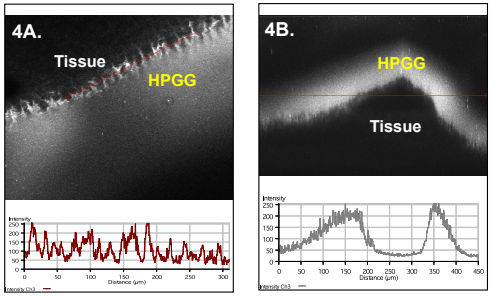

Figure 4. HPGG forms a protective overlayer (~0.7% w/v, calibration not shown) at low CoFs and does not interpenetrate tissue.

CONCLUSIONS

Using HPGG to lubricate fixed pericardial tissues demonstrated minimum static CoFs in the 0.07-0.1 range, resembling the CoF values of ice-on-ice, or highly structured water molecules. These minimum CoF values were found to be independent of ionic strength, pH and can occur at concentrations as low as 0.05%(w/v). HPGG gels formed synthetic glycocalyxes via hydrogen-bonding overlayers and diminished tissue friction-induced superficial damage without interpenetrating the tissue surface. The greatest lubricity was associated with superficial 0.7% w/v HPGG gel layers that spontaneously formed from an initially applied 0.2% concentration on both articulating surfaces. Higher starting concentrations of HPGG caused further gelation, stiffened the overlayers and promoted easier mechanical detachment, which limited longevity of the lubricant effect (Rodgers, 2010).

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ACKNOWLEDGEMENTS

We would like to acknowledge Dr. Wade Sigurdson for his time and expertise on the confocal microscope. We are grateful to Elaine Granica for performing numerous pericardectomies to retrieve the porcine tissues for our confocal microscope experiments. Peter Bush was a tremendous asset to our scanning electron microscope work.