Bioadhesion Reduction Revealed in Tissue-on-Tissue Testing of Ophthalmologic Formulations

Robert E. Baier[1], Anne E. Meyer[1], Huagang Chen[2], Masood Chowhan[2]
[1]University at Buffalo, [2]Alcon Research, Ltd.

Statement of Purpose: The surface properties of cornea and eyelid tissues [Meyer & Baier 1997, 1998], determined by a combination of contact angle and infrared spectroscopic methods, are well-matched by the intimal wall properties of glutaraldehyde-preserved human umbilical cord vein grafts (UCVG). Use of this surrogate tissue system was explored for lubricity testing of ophthalomologic formulations, wherein coefficients of friction were monitored under reciprocating motion and increasing loads.

Methods: Saline-lubricated and "artificial tears" formulation-lubricated systems were used to determine intrinsic lubricity of the formulations and substantivity of components bound to the articulating materials [Meyer et al., in press]. Testing was carried out with a reciprocating pin-on-disc device constructed and donated by Spire Corporation (Bedford, MA), that allowed controlled relative motions for different surface-to-surface couples [Meyer et al. 2006]. One test surface was always attached to a vertically loaded "pin", and the opposing test surface fixed horizontally to a "disk" that oscillated through an arc length of 25 mm at 1 Hz. Friction between the two surfaces was monitored via a strain gauge and strip chart recorder system.

Lubricity measurements evaluated tissue-on-tissue, tissue-on-synthetic [tissue-on-germanium, Ge], and synthetic-on-synthetic [Ge-on-Ge] couples. All experiments were conducted at ambient laboratory temperature (approx. 21°C) in a Class 100 clean room. Tissue-on-tissue experiments were performed in triplicate. Other experiments with donated human corneas employed multiple serial measurements. Supporting analyses included MAIR-IR spectroscopy, comprehensive contact angle measurements, light microscopy, and SEM. Tissues used as surrogates for the corneal and conjunctival surfaces of the eye were segments of stabilized human umbilical vein grafts, ("Biograft", UCVG), with established intimal surface and micro-architectural features. Corneas were obtained from the Central Florida Lions Eye & Tissue Bank and from Upstate NY Transplant Services, Inc. after approval for research use of the tissue by the appropriate regulatory review process.

Results/Discussion: When tissue was articulated against smooth Ge plates, rather than against other tissue, much less effective lubrication was found for the formulations tested (Fig.1). Tissue uptake of the aqueous formulations led to direct tissue contact with the high-surface-energy Ge substratum, and formation of a transfer film from tissue to plate. Post-friction critical surface tension values and infrared spectra of residues on the Ge were consistent with this interpretation. The high coefficients of friction recorded in tissue-on-Ge couples were indicative of bioadhesion and surface damage that did not occur in tissue-to-tissue couples lubricated with the same formulations.

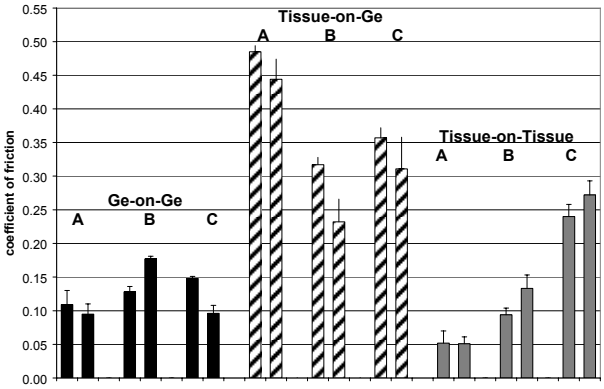

Figure 1. Coefficients of Friction for 3 Formulations. In each pair, first bar is condition just before a saline rinse; second bar is condition just after saline rinse.

Among the formulations tested, preparations containing active demulcents, as well as a gellable HP guar, (e.g. A in Fig.1) were found to be immediately and persistently capable of reducing the tissue-on-tissue coefficient of friction by nearly 80% from the values displayed when only saline was used as the liquid lubricant. Formulations using hydroxyl-propylmethyl-cellulose (B in Fig.1) or carboxy-methyl-cellulose (C in Fig.1) were not as effective.

Friction coefficients indicated a significant maintenance (substantivity) of the friction-reducing components from the HP guar "artificial tear" systems, even after rinsing away of the original formulation with saline. SEM photos and gross physical inspection showed very little tissue damage occurred during articulation in the most effectively lubricated couples.

Conclusions: Retention of some macromolecular components in articulating tissue-on-tissue interphase zones produces low frictional coefficients indicative of minimized bioadhesion. Results for experiments with donated human corneas confirmed the potential generality and relevance of these findings to actual in-the-eye situations.

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