

# Inflammatory and Non-Inflammatory Synovial Fluids Exhibit New & Distinct Tribological Phenotypes

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**INTRODUCTION:** Inferior synovial lubrication is a hallmark of osteoarthritis (OA)<sup>1,2</sup>. Recent studies suggest that changes in synovial lubrication and composition are highly dependent on the type of OA<sup>3,4</sup>, though a loss of high molecular weight hyaluronic acid (HA) and reduction in synovial fluid viscosity is common. HA viscosupplementation is a widely used therapy for managing the symptoms of OA. However, it is unclear how the effectiveness of HA viscosupplements varies with OA phenotype. The objective of this study was to investigate the effects of the HA viscosupplement, Hymovis®, on the lubricating properties of diseased synovial fluid from patients with non-inflammatory and inflammatory OA.

**METHODS:** Synovial fluid was collected with patient consent from the knee joints of donors with noninflammatory OA (n=10, age 62±10 years) and inflammatory OA (n=10, age 44±26 years) where inflammatory patients were defined as having white blood cell counts above 2000/μL and a polymorphonuclear neutrophil percentage >25%. Synovial fluid samples' biophysical properties were assessed alone or in a 1:1 mixture with Hymovis®, a modified HA viscosupplement. Cartilage explants (6mm diameter x 2mm thick) were harvested from the condyles of neonatal bovine stifle joints and loaded onto a custom tribometer in a bath of the fluids. Explants were compressed to 40% strain against a glass counter-face, which was slid at speeds of 10-0.1mm/s as normal and shear loads were recorded. The viscous properties were quantified for all fluids by shearing the fluid continuously at rates ranging from 1000-1x10<sup>-4</sup> 1/s on an Anton-Paar MCR702 rheometer using a 25mm cone-and-plate fixture. Stribeck curves were created to examine the frictional properties of the lubricants across different modes of lubrications including high friction boundary mode, mixed, and low-friction elastoviscous lubrication modes. To create the curves, friction coefficients were plotted versus Sommerfeld Number, a dimensionless parameter calculated as  $\eta v a / L_N$  that accounts for the lubricant viscosity ( $\eta$ ), sliding speed ( $v$ ), cartilage contact width ( $a$ ), and contact load ( $L_N$ ). A 3-factor ANOVA was performed to compare viscosities followed by a Tukey's HSD test to detect differences at specific shear rates between samples with and without HA.

**RESULTS:** Inflammatory and non-inflammatory OA samples exhibited similar shear-thinning viscous behavior. The addition of HA significantly increased the viscosity (p<0.001) of the fluids by a factor of over 100 at low shear rates Figure 1A,B). In non-inflammatory OA samples (Figure 2B), HA reduced the overall magnitude of friction coefficients. However, for inflammatory OA samples, HA did not always reduce friction coefficients (Figure 2 C,D, patient samples matched by shape). Non-inflammatory OA samples exhibited typical Stribeck behavior (Figure 2A vs. 2B) in which friction coefficients decreased with increasing Sommerfeld number. The addition of HA shifted the Stribeck curve toward higher Sommerfeld numbers, and also revealed a high-friction boundary mode plateau at low Sommerfeld numbers. The boundary mode was not evident for noninflammatory OA samples without HA. In contrast, inflammatory OA samples showed inconsistent Stribeck behaviors (Figures 2C, D); while several samples exhibited a similar magnitude of friction coefficients and Stribeck behavior like the non-inflammatory OA groups, a subset showed a vastly different behavior in which friction coefficients were higher, more variable, and also increased with Sommerfeld number. This non-Stribeck like behavior was preserved when HA was added.

**DISCUSSION:** The viscosity of inflammatory and non-inflammatory OA synovial fluids was significantly enhanced by the addition of HA. Interestingly, our results show that HA viscosupplementation was effective in reducing friction coefficients for non-inflammatory OA samples, but this was not necessarily the case for inflammatory OA samples. For some patients, friction coefficients were increased by the addition of HA. Furthermore, our Stribeck analysis revealed a subset of inflammatory OA samples that exhibited higher friction and follow an atypical Stribeck behavior where friction coefficients increased with Sommerfeld numbers. Interestingly, these atypical behaviors were not explained by the viscosity of the fluids. This suggests that compositional differences in the fluids may be causing this behavior such as the native concentrations of HA and lubricin, a critical boundary lubricant. Future analyses will be focused on identifying these and other markers that may be driving this phenomenon.

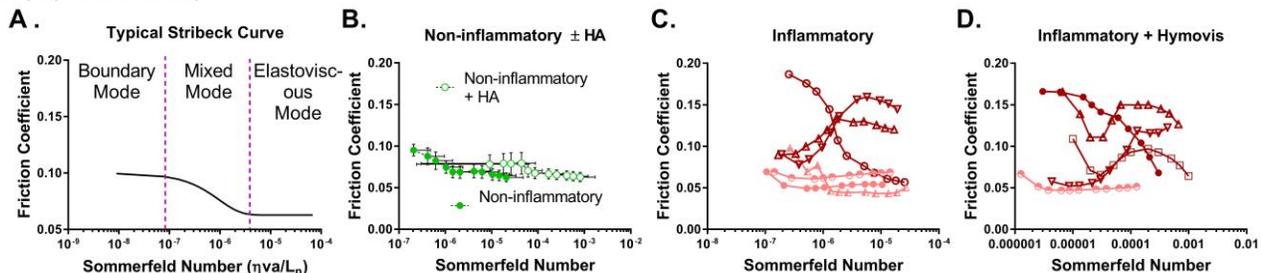
**SIGNIFICANCE:** We have identified tribological phenotypes within inflammatory and non-inflammatory human OA synovial fluids. This suggests that distinct HA viscosupplement strategies or different tribosupplements may be advised for specific phenotypes.

**REFERENCES:** 1. Elsaid KA et al. Arthritis Rheum. 2005. 2. Neu CP et al. Arthritis Rheum. 2010.

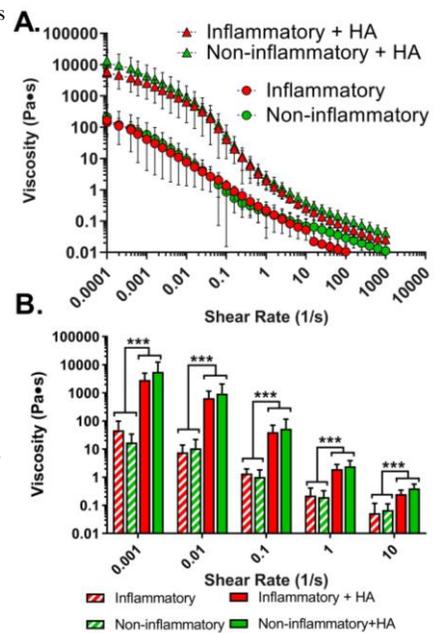
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**IMAGES AND TABLES:**



**Figure 2.** (A) Example of a Stribeck curve for lubricated cartilage. (B) Non-inflammatory OA samples exhibit a Stribeck-like behavior in which the addition of Hymovis shifts the transition to elastoviscous mode to higher Sommerfeld numbers. Individual inflammatory OA samples (C,D) show unique lubrication phenotypes; some patients (pink) exhibit typical Stribeck behavior similar to non-inflammatory OA samples in (B), while others (maroon) show increasing friction coefficient with increasing Sommerfeld numbers and a larger variability in friction coefficients. Note that each shape represents a single patient (C,D). (n=6-7).



**Figure 1:** Inflammatory and non-inflammatory OA synovial fluid exhibit similar shear-thinning viscous behavior (A), which is significantly enhanced by the addition of Hymovis (B, p<0.001, n=6-7).