Effects of Concentration on Synergistic Hyaluronan-PRG4 Cartilage Boundary Lubrication

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Abstract

Introduction: Proteoglycan 4 (PRG4) and hyaluronan (HA) are constituents of synovial fluid (SF) that act synergistically to contribute to the boundary lubrication of articular cartilage in a dose-dependent manner\(^1\). However, the potential concentration dependency of this HA-PRG4 synergism remains to be elucidated. The objective of this study was therefore to evaluate the in vitro cartilage boundary lubricating ability of PRG4+HA at varying concentrations of each.

Methods: Cartilage boundary lubricating ability was assessed using bovine osteochondral samples in a cartilage-on-cartilage friction test, as previously described\(^1\). Test sequences were as follows: Test 1 (PRG4 dose response, + constant HA = 3.33 mg/mL, n=6): PBS, 150\(\mu\)g/mL PRG4 + HA, 450\(\mu\)g/mL PRG4 + HA, 1500\(\mu\)g/mL PRG4 + HA, SF. Test 2 (HA dose response, + constant PRG4 = 450 \(\mu\)g/mL, n=5): PBS, 0.3mg/mL HA + PRG4, 1.0mg/mL HA + PRG4, 3.33mg/mL HA + PRG4, SF. Static, \(\mu_{\text{static}}N_{eq}\), and kinetic, \(\mu_{\text{kinetic}}N_{eq}\), friction coefficients were then calculated\(^2\).

Results: In all tests, \(\mu_{\text{static}}N_{eq}\) values were consistently highest in PBS and lowest in SF, with all PRG4+HA combinations tested being similar to SF. Test 1: \(\mu_{\text{kinetic}}N_{eq}\) values in varying PRG4 concentrations + constant HA were not significantly different from each other, nor from SF. Test 2: \(\mu_{\text{kinetic}}N_{eq}\) values in varying HA concentrations + constant PRG4 were not significantly different from each other, nor from SF.

Discussion: These results demonstrate that HA+PRG4 lubrication synergism is maintained provided that either PRG4 or HA is present at a physiologically normal concentration, and that these combinations provide lubricating ability approaching that of SF. Intra-articular PRG4 has been shown to be chondroprotective in animal injury models of osteoarthritis\(^3-6\). Therefore, clarifying the PRG4+HA synergism will contribute to the potential application of PRG4, with or without HA, as an improved biotherapeutic treatment. (Acknowledgements: AI, CAN, NSERC (CREATE), TAS).

References


