Introduction:

Knee Osteoarthritis (OA) is a leading cause of disability worldwide, characterized by progressive cartilage degradation, chronic inflammation, and subchondral bone remodeling. Current treatments are largely symptomatic. Hyaluronic acid (HA) has shown promise as a disease-modifying agent by modulating inflammation, maintaining extracellular matrix integrity, and protecting chondrocytes from catabolic stress. This study evaluated the therapeutic effects of HA in a co-culture model comprising chondrocytes and osteoclast precursors designed to mimic the OA microenvironment.

Methods:

Inflammatory stress was induced with lipopolysaccharide (LPS, 1 μg/mL) in a direct co-culture of chondrocytes and osteoclast precursors. Cultures were treated with HA at 100, 200, and 500 μg/mL. Cell viability was assessed by MTT assay; osteoclastogenesis by TRAP staining; and inflammatory and matrix markers by Western blotting. Cell-cycle distribution was analyzed by flow cytometry, and cytokine and enzyme expression were evaluated using qPCR and ELISA.

Results:

HA treatment significantly reduced osteoclast differentiation and suppressed NF-κB and TRAP expression. Chondrocyte G0/G1 cell-cycle arrest was restored, and anabolic markers such as collagen II and aggrecan were upregulated. Inflammatory and osteoclastic markers were downregulated in a dose-dependent manner.

Conclusions:

Hyaluronic acid exerted dual protective effects in an OA co-culture model by mitigating inflammation and promoting chondrocyte homeostasis. These findings support HA as a biologically active, disease-modifying therapy for OA. Further in vivo and long-term studies are warranted to confirm its therapeutic efficacy and safety.