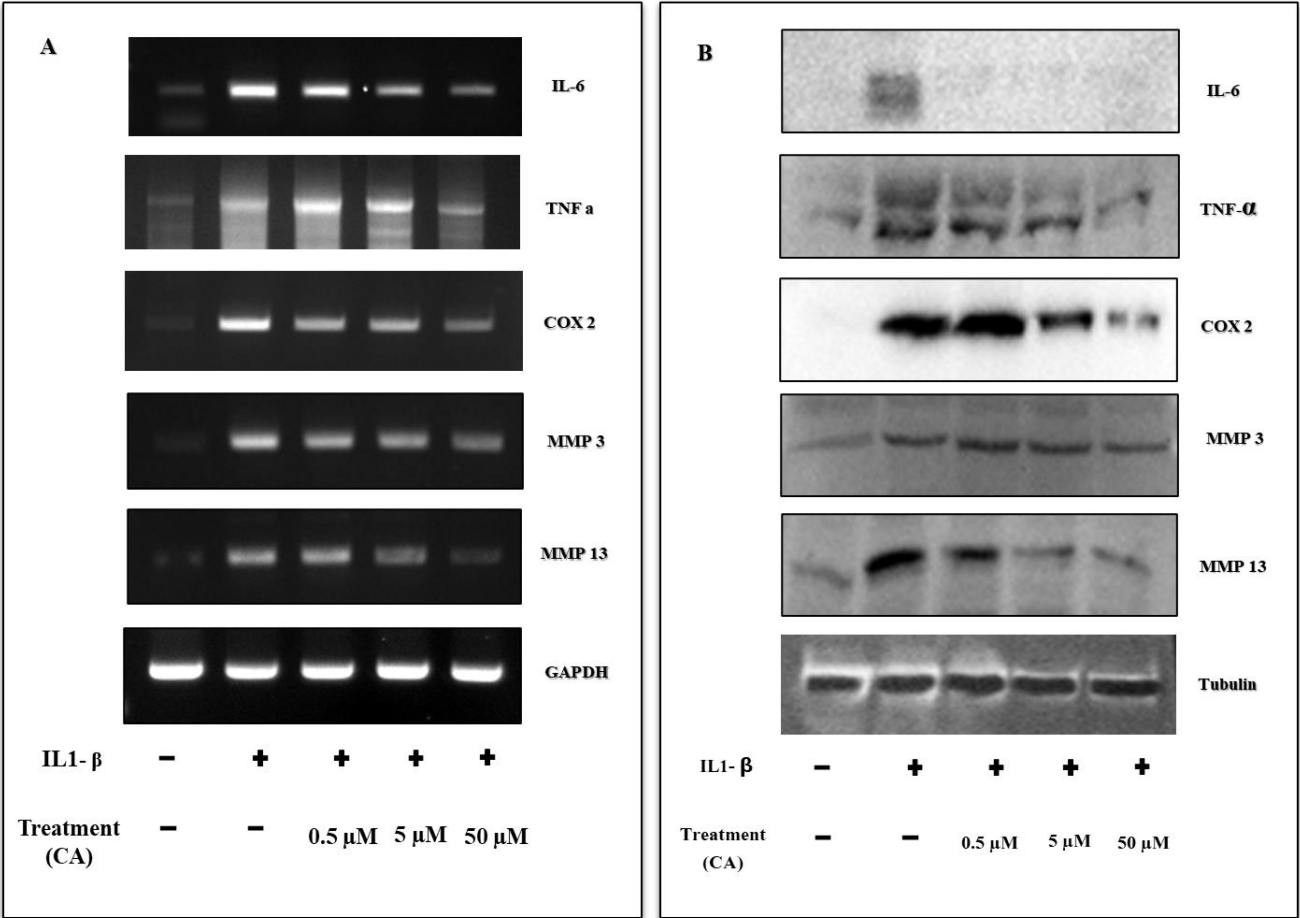


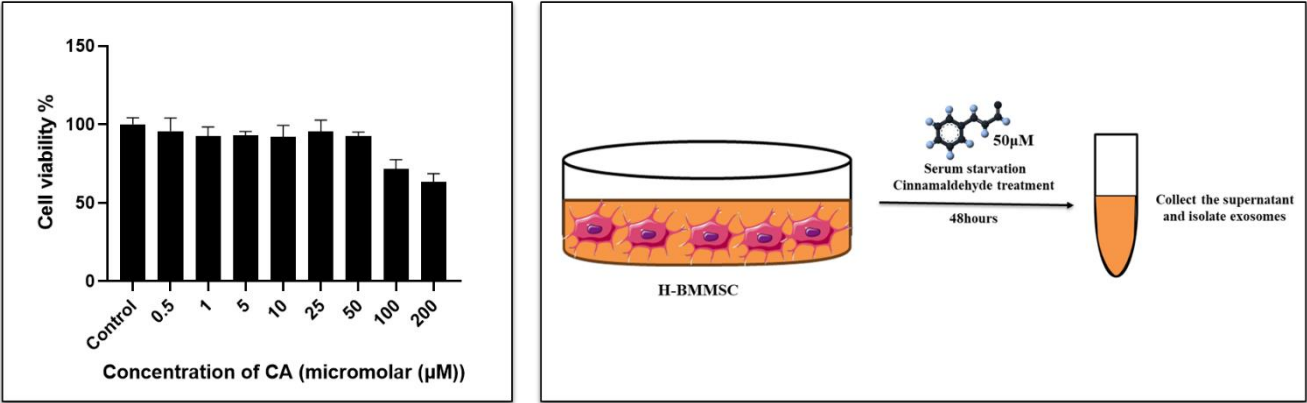
Cinnamaldehyde (CA) Treatment to Chondrocytes



Supplementary Figure S1. Effects of Cinnamaldehyde on inflammation specific mediators in a dose-dependent manner. (A) Gene

expression levels of IL-6, TNF- α , COX 2, MMP 3, and MMP 13 were analyzed using RT-PCR (B) Protein expression levels of IL-6, TNF- α , COX 2, MMP 3, and MMP 13 were analyzed using Western blot.

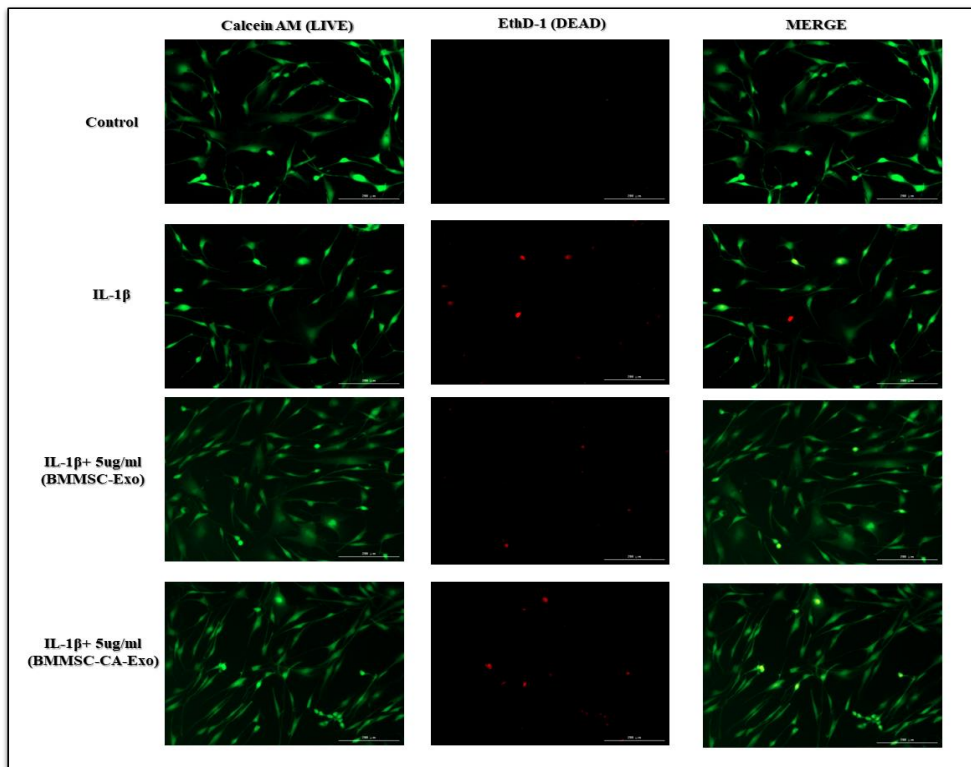
Cinnamaldehyde treatment to cells to determine the cellular toxicity.



Supplementary Figure S2. Cellular cytotoxicity of chondrocytes treated with different concentrations of cinnamaldehyde (CA).

The optimum concentration of cinnamaldehyde (CA) for treatment of chondrocytes appears to be 50 μM, as it does not significantly impact cell viability while still providing potential therapeutic effects.

Live-Dead staining assay



Supplementary Figure S3. Live-dead staining assay of chondrocytes using calcein and EthD-1 under different treatment conditions. The control group with no treatment shows no dead cells. The inflammation group stimulated with IL-1 β has significantly more dead cells stained by EthD-1. Treatment with BMMSC-derived exosomes (BMMSC-Exo) decreases the number of dead cells compared to the IL-1 β group. Treatment with cinnamaldehyde-activated BMMSC-derived exosomes (BMMSC-CA-Exo) also reduces the number of dead cells compared to the IL-1 β group, to a greater extent than BMMSC-Exo alone. These results indicate that exosomes derived from bone marrow mesenchymal stem cells, particularly those pre-treated with cinnamaldehyde, have a protective effect against inflammation-induced chondrocyte death.

Gene Expression (Primer details)

| Primer Name | Forward primer | Reverse Primer | Melting temp |
|--------------|---------------------------------|---------------------------------------|------------------|
| hCollagen II | TCTGCAACATGGAGACTGGC | GAAGCAGACCGGCCCTATGT | F 55.7 R 57.6 |
| hIL6 | GGATGCTTCCAATCTGGATTCAA TGAG | CGCAGAATGAGATGAGTTGTCAT GTCC \\ | F 63.5 R 63.6 |
| hCOX2 | TTC AAATGAGATTGTGGGAAA | AGATCATCTCTGCCTGAGTATCTT | F 51.9 R 52.0 |
| hMMP13 | GATGAAGACCCCAACCCTAAA | CTGGCCAAAATGATTTTCGTTA | F 54.3 R 54.1 |
| hGAPDH | ACCACAGTCCATGCCATCAC | TCCACCACCCTGTTGCTGTA | F 55 R 55.9 |

Supplementary Table S1. The primer sequences used in the following research.