Study on the Therapeutic Effect of a Co-delivery System for Curcumin and Catalase in the Treatment of Knee Osteoarthritis

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INTRODUCTION:This study aims to construct a targeted nano co-delivery system for Curcumin (CUR) and Catalase (CAT) to delay the progression of knee osteoarthritis (KOA) through anti-inflammatory and antioxidant effects, thereby providing a theoretical basis and experimental foundation for the precise treatment of KOA.

METHODS:The co-delivery system for CUR and CAT was first constructed and subjected to quality control. The TFCC nano-drug delivery system was prepared using metal-organic framework (MOF) drug carrier technology based on ferric ions and tannic acid. Hyaluronic acid (HA) was conjugated to the surface to construct TFCC@H. The drug content, activity, and encapsulation efficiency were determined using high-performance liquid chromatography (HPLC) and ultraviolet spectrophotometry, while characteristics such as particle size and morphology were analyzed using transmission electron microscopy and laser particle size analysis. For in vitro experiments, an inflammatory chondrocyte model induced by IL-1β was established. Cellular uptake and apoptosis were observed using confocal laser scanning microscopy and flow cytometry, and the molecular mechanisms were further investigated through transcriptomics. For in vivo experiments, a KOA mouse model was established using the destabilization of the medial meniscus (DMM) surgery. Multiple control groups were set up, and treatments were administered via tail vein injection. Changes in the knee joint and the expression of related proteins were evaluated using micro-CT and Safranin O-Fast Green staining, while the targeting and retention effects of TFCC@H were observed using a small animal in vivo imaging system.The animal experiment has been approved by the institutional review committee that complies with the laws and regulations of the country of origin.

RESULTS SECTION:The characterization of the drug delivery system showed stable physicochemical properties, including particle size, PDI, and Zeta potential, with the encapsulation efficiency meeting expectations. Cellular experiments confirmed that both TFCC and TFCC@H systems could be effectively taken up by chondrocytes, reduce ROS levels, improve mitochondrial function, and inhibit apoptosis. In animal experiments, the TFCC@H group demonstrated superior effects in improving the bone microstructure of the knee joint, reducing cartilage damage, and regulating the expression of metalloproteinases, antioxidant enzymes, and inflammation-related proteins compared to other experimental groups, while also exhibiting targeting and retention capabilities.

DISCUSSION:The TFCC@H nano-drug delivery system constructed in this study, through MOF encapsulation and HA modification, achieves targeted delivery and sustained release of CUR and CAT. It delays the progression of KOA through multiple pathways, including anti-inflammatory, antioxidant, and mitochondrial function improvement. This system overcomes the low bioavailability of curcumin and provides a novel strategy for the prevention and treatment of KOA, demonstrating significant theoretical value and clinical translation potential.

SIGNIFICANCE/CLINICAL RELEVANCE: Provide new references for the clinical treatment of knee osteoarthritis; Develop a new type of nano-targeting material