

Antarctic Krill Oil improves articular cartilage degeneration via activating chondrocyte autophagy and inhibiting apoptosis in osteoarthritis mice**Kai Wang**

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Osteo Arthritis (OA) is a major debilitating disease characterized by cartilage degeneration. In the current study, the in vivo effects of Antarctic Krill Oil (AKO) on cartilage degeneration in destabilization of the Medial Meniscus (DMM) model mouse were investigated. Results showed that AKO clearly improved the cartilage structure as evidenced by increased cartilage thickness and cartilage area and decreased histological OARSI scores. Safranin O/Fast Green staining showed that AKO remarkably inhibited the loss of cartilage matrix in mice with OA. Chondrocytes play important roles in regulation of cartilage homeostasis. AKO maintained the normal chondrocyte phenotype by downregulating hypertrophy markers such as *Ihh*, *Col10a1*, *Runx2*, and *MMP-13* and restoring the expression of chondrocyte-specific genes, including *Acan*, *Col2a1*, and *Sox9*. Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) staining analysis showed that AKO significantly inhibited abnormal apoptosis in articular cartilage. Autophagy is a self-protective metabolic process required for maintaining cartilage homeostasis. We observed that mTOR (negative regulator of autophagy) transcription was reduced, which was consistent with high PPAR- γ levels. In addition, expression of key genes related to autophagy, including LC-3B, Beclin-1, ATG-5, and BNIP-3 were significantly enhanced after treatment with AKO. The p53-dependent mitochondrial apoptotic pathway plays an important role in regulating chondrocyte apoptosis. We observed that AKO suppressed the expression of key genes expression in this pathway, such as p53, Bax, Bid, cytochrome c, caspase-9, and caspase-3. Furthermore, AKO enhanced the expression of anti-apoptotic genes, including Bcl-2 and Bcl-xl. These findings might provide a theoretical basis for the application of AKO as a potential chondroprotective bioactive compound or functional food.