Drug and genetic material co-loaded liposomes for repairing chondrocytes in Osteoarthritic conditions

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Chronic knee and lower back pain due to osteoarthritis (OA) and intervertebral disc (IVD) degeneration (IVDD) have a global prevalence and impact human wellbeing by impairing mobility. Oxidative stress is a key factor in OA and IVDD pathogenesis. Non-viral gene therapy is a promising approach for safe and precise joint and disc restoration. Our study focuses on developing a liposomal formulation for efficient co-delivery of curcumin and therapeutic siRNA. Curcumin downregulates many inflammatory cytokines along with free radicals and upregulates collagen and aggrecan, therefore reducing pain and helping in regeneration. Luciferase siRNA was utilized for screening and prototyping, demonstrating effective transfection into luciferase-expressing chondrocytes (C28/I2 cells). Quality by Design principles guided formulation development, employing risk assessment, Design of Experiments (DoE), and optimization. Responses evaluated included particle size, polydispersity index, zeta potential, curcumin encapsulation efficiency, cell viability, siRNA complexation capacity, and luciferase activity. Statistical analysis using MODDE software helped us formulate optimum liposomes. The primary chondrocytes were then induced with oxidative stress and inflammatory conditions and treated with optimum liposomes. The effect of curcumin was analyzed through numerous biochemical tests like Total Antioxidant Capacity, Malondialdehyde levels, and qRTPCR for the cytokines. The optimum liposomes complexed with therapeutic siRNA like the IL-6 and IL-8 siRNA were evaluated by qRTPCR and ELISA on inflamed primary chondrocyte cells. These co-loaded liposomes effectively transfected chondrocytes with no toxicity and could be successfully carried forward for testing in vitro in OA and IVDD models. This study has yielded not only an optimum formulation but also serves as a platform for the incorporation of other lipophilic drugs and any negatively charged genetic material for various ailments.