World Academy of Science, Engineering and Technology
International Journal of Environmental and Ecological Engineering
Vol:17, No:04, 2023

Re-Differentiation Effect of Sesquiterpene Farnesol on De-Differentiated Rabbit Chondrocytes

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Abstract : Articular cartilage is composed of chondrocytes and extracellular matrix, such as collagen fibers, glycosaminoglycans, etc., which play an important role in lubricating and cushion joint activities. The phenotypic expression and metabolic activity of chondrocytes are extremely important in maintaining the functions of articular cartilage. In in vitro passaged culture of chondrocytes, chondrocytes gradually lose their original cell phenotype and morphology, which is called dedifferentiation. After continuous passaged culture of chondrocytes or induction by inflammatory factor IL-1, chondrocytes changed their phenotype and morphology. Also, the extracellular matrix type II collagen and GAG secretion were significantly reduced, while type I and X collagen were synthesized. Farnesol is an anti-inflammatory and antioxidant sesquiterpene compound that has the specific property of promoting collagen production. The purpose of this study was to investigate whether farnesol could restore the original type II collagen synthesis and, furthermore, the mechanisms of farnesol on the synthesis of type II collagen from the de-differentiated chondrocytes. The obtained results showed that the de-differentiated chondrocytes significantly restored to secret type II collagen and GAG (2.5-folds increases), and the secretion of collagen I and X and PGE2 synthesis were also significantly reduced after being treated with farnesol, indicating that farnesol had a restoration/re-differentiation effect on de-differentiated chondrocytes. The de-differentiated chondrocytes exhibited decreased expression of PPAR-γ and upregulated TGF-β expression to increase the MMP-13 expression. Higher expression of MMP-13 caused chondrocytes to secret type X collagen. On the contrary, increasing the expression of PPAR-γ would benefit the production of type II collagen. As shown, the PPAR-γ expression increased, and MMP-13 expression decreased after being treated with farnesol, indicating a possible signal pathway of farnesol to restore the production of type II collagen. However, more detailed mechanisms still need to evaluate.

Keywords : chondrocytes, de-differentiation, farnesol, re-differentiation
Conference Title : ICSBFM 2023 : International Conference on Sustainable Biomaterials and Functional Materials
Conference Location : Tokyo, Japan
Conference Dates : April 17-18, 2023