ROSMARINUS OFFICINALIS EXTRACT PROTECTS HUMAN CHONDROCYTES DIFFERENTIATED FROM MESENCHYMAL STEM CELLS BY PRO-INFLAMMATORY EFFECTS OF INTERLEUKIN-1 BETA

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Human osteoarthritis (OA), the most common form of joint disease, is characterized by degeneration of the articular cartilage (Suokas et al., 2012). OA results from an imbalance between chondrocyte-controlled anabolic and catabolic processes, and is characterized by progressive degradation of components of the extracellular matrix (ECM), associated with secondary inflammatory factors. In recent years, researchers have been working hard to elaborate surgical cartilage repair interventions for patients with articular damage, thus the regenerative medicine, involving the use of mesenchymal stem cells (MSCs) to produce tissues, has become an attractive new area of research. The discovery that adipose tissue is rich in adult stem cells capable of differentiating into many lines has led to consider their potential clinical applications. Moreover, MSCs were proved to be a useful cellular model to study the biological activity of some natural products. Rosmarinus officinalis L. (Lamiaceae) is used as a folk medicine around the world. In medicine, the extract is receiving increasing attention due to its anti-inflammatory constituents (Kuo et al., 2011). There are several reports that have established carnosic acid as the major phenolic diterpenoid present in R. officinalis leaves with interesting biological activity (Kuo et al., 2011).Thus, the aim of this research was to evaluate the chondroprotective effect of well-characterized R. officinalis methanolic extract, in which carnosic acid is a major compound (39.7%). For this purpose, MSCs derived from adipose tissue (AT) were differentiated in chondrocytes for 28 days. The chondrogenic differentiation of AT-MSCs was obtained applying a medium enriched with serum, supplements and factors that support the growth and cell-cell interaction and promote a stimulus toward chondrogenic lineage. After 28 days, the chondrogenic markers were verified and the cultures treated with 10 ng/mL of pro-inflammatory cytokine interleukin-1 beta plus or not 50 microg/mL of extract of Rosmarinus officinalis. After 24 hours, the anti-inflammatory activity of experimental extract was verified. For the determination of chondrogenic and inflammation markers Western blot was used. At 28 days, chondrocytes derived from AT-MSCs were able to produce significant quantity of transcription factorSOX-9, lubricin and collagen type II, suggesting hyaline cartilage formation. Rosmarinus officinalis extract was able to decrease markedly the expression of examined inflammation markers, such as membrane molecules (ICAM-1), cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS). Our study demonstrates that the pools of compounds extracted from Rosmarinus officinalis efficiently block the pro-inflammatory actions induced by interleukin-1 beta on human chondrocytes.

Suokas et al. (2012). Osteoarthr Cartil. 20, 1075–85

Kuo et al. (2011). J Agric Food Chem. 59, 3674-85.