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Summary of the original abstract

Effects of Three Avocado/Soybean Unsaponifiable Mixtures on Metalloproteinases, Cytokines and Prostaglandin E2 Production by Human Articular Chondrocytes
YE Henrotin, AH Labasse, JM Jaspar, DD De Groote, SX Zheng, GB Guillou, JYL Reginster
Clinical Rheumatology 1998, 17:31-39

General Introduction

Osteoarthritis at the chondrocyte level results in decreased matrix production, cartilage extracellular matrix (ECM) degradation, and inflammatory processes. Interleukin-1 (IL-1β) is the key cytokine implicated in these processes. The ECM degradation is mainly driven by the IL-1β–induced increase in metalloproteinase activity directly destroying the cartilage matrix. The inflammatory process is mainly supported by IL-1β–induced prostaglandin E2 (PGE2) and production of other cytokines (IL-6 and IL-8). Avocado Soybean Unsaponifiable (ASU) residues have been shown to increase matrix production by increasing proteoglycan and collagen production. The effect of ASU residues on the 2 other main processes at the chondrocyte level are unknown.

Main objective

The main objective of this study is to investigate the effects of ASU residues on cartilage ECM degradation and inflammatory molecules in human articular chondroyctes.

Methods

Human articular chondrocytes are obtained from the knee joints of normal young adults shortly after their death. Chondrocytes are cultured in suspension for a short time to maintain their phenotype, then in the presence or absence of IL-1β (17 ng/ml) for 72 hr. Three different qualities of ASU residues (A1S2, A2S1, A2S2) are used during the treatment period (72 hr) at 2 different concentrations (2 and 10 µg/ml). As well, avocado (A) and soybean (S) residues are tested separately at 3 different concentrations (3.3, 6.6, and 10 µg/ml). The ECM degradation process is evaluated in culture media by matrix metalloproteinase (collagenase and stromelysin) activity assays. The inflammatory process is evaluated by PGE2 and cytokine immunoassays.

Main results

In the presence or absence of IL-1β, only one of the 3 qualities of ASU residues, A1S2, is able to decrease matrix metalloproteinase (collagenase and stromelysine) activities and PGE2 production concomitantly. In the absence of IL-1β, production of IL-8 decreases with the S residue more potently than with the A residue. In the absence of IL-1β, production of IL-6 is decreased with the A residue at the 3 concentrations (3.3, 6.6, and 10 µg/ml) but with the S residue only at 10 µg/ml. When A and S residues are tested separately, in the absence of IL-1β, the decrease in PGE2 production is dose dependent with the A residue. This decrease is lower with the S than A residue. In the presence of IL-1β, A1S2 is potent in inhibiting IL-6 and IL-8 production. However, the downregulation of IL-6, IL-8 and PGE2 production is stronger with A1S2 than with the A or S residue alone.

Strengths of the study

This is the first study to demonstrate a beneficial biological effect of ASU residues on matrix degradation and inflammation in IL-1β–treated articular chondrocytes. Together with previous results showing upregulation of proteoglycan and collagen synthesis by ASU residues, these results support an interest in *in vivo* studies with osteoarthritis animal models. One of the strengths of this study is the use of human articular chondrocytes, in contrast to previous study, which involved rabbit articular chondrocytes. The other strength is the investigation of the effect of the quality and quantity of ASU residues on the biological activities observed.

Weaknesses of the study

The weaknesses of the study mainly relate to the usual criticisims of *in vitro* experiments. ASU-residue and IL-1β treatments are performed concomitantly. Comparison of ASU-residue pretreatment and posttreatment relative to IL-1β treatment would be of interest. The relevance of the ASU-residue doses used is not supported by previous pharmacological results. The qualititative evaluation of matrix components is lacking.

Conclusion and perspectives

ASU residues can decrease the activity of major actors of cartilage extracellular matrix degradation and inflammation in articular chondrocytes. The observed effects seem to depend on the quality and quantity of ASU residues used. These preliminary *in vitro* results are of interest but need to be enhanced by *in vitro* matrix study of the effects of ASU residues (proteoglycan and collagen) before *in vivo* experiments.