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Summary of the original abstract

Avocado/Soya Unsaponifiables Enhance the Expression of Transforming Growth Factor β1 and β2 in Cultured Articular Chondrocytes
K Boumediene, N Felisaz, P Bogdanowicz, P Galera, GB Guillou, JP Pujol
Arthritis and Rheumatism 1999, 42:148-156

General introduction

Osteoarthritis (OA) is the result of an imbalance between the catabolic and anabolic pathways of extracellular matrix production. Previous studies have shown that Avocado and Soybean oil Unsaponifiable (ASU) residues can stimulate the production of collagen in cell cultures and facilitate the wound healing process involving collagen fibers. These results suggest a potential stimulating effect of ASU residues on the anabolic pathway. However, the cellular and molecular mechanisms of the ASU positive effect on collagen production have not been studied. Transforming growth factor β (TGF-β) is one of the major growth factors identified in the chondrocyte anabolic pathway. The hypothesis of the present study is that TGF-β could be the master molecule in the observed ASU protective effect on collagen production.

Main objective

The main objective of this study is to investigate the molecular effects of ASU residues on TGF-β production in chondrocytes.

Methods

Articular chondrocytes are obtained from calf cartilage and used in primary cultures to minimize phenotype modulation. They are incubated with ASU at various doses (from 5 to 25 μg/ml), and the expression of both TGF-β isoforms, 1 and 2, and their receptors is determined by Northern blot and RT-PCR analysis. TGF-β1 protein level is quantified by immunoassay. To elucidate the mechanism of ASU on TGF-β production, chondrocytes are transfected with a TGF-β promoter construct to isolate a potential responsive region or element in the promoter. Finally, plasminogen activator inhibitor 1 (PAI-1), known to be induced by TGF-β in chondrocytes and leading to a substantial reduction in OA cartilage lesions in animal models, is evaluated by Northern blot analysis and protein radiolabeling.

Main results

An amount of 10 μg/ml ASU residues induces the expression of both TGF-β1 and TGF-β2 isoforms. The increase in TGF-β1 expression is time dependent, peaks after 48-hr incubation and leads to increased protein level of TGF-β1. ASU and exogenous TGF-β1 treatment has a synergistic effect on TGF-β1 production, which suggests an amplification loop phenomenon. Using various constructs of TGF-β1 promoter, the authors identify the DNA sequences, between -1132 and -732, responsible for the ASU stimulating effect on TGF-β1 mRNA expression. In addition, ASU are able to increase the mRNA and protein levels of PAI-1.

Strengths of the study

This is the first study to demonstrate a potential molecular mechanism of the beneficial biological effect of ASU residues on articular chondrocytes. In addition, it identifies a putative ASU responsive element on the TGF-β1 promoter.

Weaknesses of the study

The weaknesses of the study mainly relate to the use of calf chondrocytes and the absence of experiments with interleukin-1β to evaluate the mechanism of ASU protection in an inflammatory environment.

Conclusion and perspectives

ASU residues can increase the production of a major actor of the anabolic cascade in chondrocytes: TGF-β. The ASU effect seems to involve upregulation of the TGF-β transcription process, which suggests a specific molecular mechanism. These *in vitro* results, coupled with previous results on the protective effect of ASU residues by downregulating inflammation, need to be confirmed *in vivo*. In addition, determining whether the effect of ASU on TGFβ is direct or indirect through an intermediate molecule is of interest.