Most or all of these were performed using Pharmascience’s prescription form of ASU called Piascledine® 300, not available in the US.

ABSTRACT

Objective: To investigate the effects of avocado (A)/soybean (S) unsaponifiables on the metabolism of human osteoarthritic (OA) chondrocytes cultured in alginate beads over 12 days.

Methods: Enzymatically isolated OA chondrocytes were cultured in alginate beads in a well defined culture medium for 12 days, in the presence or not of 10 - 10 M interleukin 1ß (IL-1ß). DNA content was measured using a fluorometric method. Production of aggrecan (AGG), stromelysin-1 (MMP-3), tissue inhibitor of metalloproteinases-1 (TIMP-1), macrophage inflammatory protein-1ß (MIP-1ß), IL-6, and IL-8 were assayed by specific enzyme amplified sensitivity immunoassays. Prostaglandin (PG) E 2 was measured by a specific radioimmunoassay and nitrite by a spectrophotometric method based on the Griess reaction. A commercial avocado and soybean mixture of unsaponifiables (A1S2) and each component separately were tested in a range of 0.625 to 40.0 µg/ml.

Results: After 12 days’ incubation, A1S2 increased AGG synthesis and accumulation in alginate beads in a dose and time dependent manner. A1S2 promoted the recovery of aggrecan synthesis after 3 days of IL-1ß treatment.
A1S2 was a potent inhibitor of basal and IL-1β stimulated MMP-3 production. The procedure also weakly reversed the inhibitory effect of IL-1β on TIMP-1 production. A1S2 inhibited basal production of MIP-1β, IL-6, IL-8, NO*, and PGE 2 by OA chondrocytes and partially counteracted the stimulating effect of IL-1 on PGE 2. Compared to avocado or soybean added separately, the mixture had a superior effect on NO* and IL-8 production.

**Conclusion.** A1S2 stimulated aggrecan production and restored aggrecan production after IL-1β treatment. In parallel, A1S2 decreased MMP-3 production and stimulated TIMP-1 production. These results suggest A1S2 could have structure-modifying effects in OA by inhibiting cartilage degradation and promoting cartilage repair.

---

**Title**
Effects of three avocado/soybean unsaponifiable mixtures on metalloproteinases, cytokines and prostaglandin E2 production by human articular chondrocytes.

**Authors**
Henrotin YE. Labasse AH. Jaspar JM. De Groote DD. Zheng SX. Guillou GB. Reginster JY.

**Institution**
Bone and Cartilage Metabolism Research Unit, Radioimmunoassay Laboratory, University Hospital, Liege, Belgium.

**Source**

**ABSTRACT**
The in-vitro effects of avocado and soybean unsaponifiable residues on neutral metalloproteinase activity, cytokines and prostaglandin E2 (PGE2) production by human articular chondrocytes were investigated. Avocado and soybean unsaponifiable residues were mixed in three ratios: 1:2 (A1S2), 2:1 (A2S1) or 1:1 (A2S2). Freshly isolated human chondrocytes were cultured for 72 h in the absence or presence of interleukin-1beta, (IL-1beta) (17 ng/ml), with or without unsaponifiable residue mixtures at a concentration of 10 microg/ml. A/S unsaponifiable residues were also tested separately at concentrations of 3.3, 6.6 and 10 microg/ml. All A/S unsaponifiable mixtures reduced the spontaneous production of stromelysin, interleukin-6 (IL-6), interleukin-8 (IL-8) and prostaglandin E2 (PGE2) by chondrocytes. At concentrations of 3.3 and 6.6 microg/ml, A/S residues, tested separately, were potent inhibitors of the production of IL-8 and PGE2. Nevertheless, only avocado residue inhibited IL-6 production at these concentrations. A/S unsaponifiable mixtures had a more
pronounced inhibitory effect on cytokine production than avocado or soybean residues added alone. As anticipated, IL-1beta induced a marked release of collagenase, stromelysin, IL-6, IL-8 and PGE2. A/S unsaponifiable mixtures partially reversed the IL-1 effects on chondrocytes. These findings suggest a potential role for A/S unsaponifiable extracts in mitigating the deleterious effects of IL-1beta: on cartilage.

Title
The Effect Of Avocado And Soybean Unsaponifies On Freshly Isolated Human Articular Chondrocytes

Authors

Source
Arthritis & Rheumatism. Volume 40(9) Supplement September 1997 pp S89-S89

ABSTRACT
In this in vitro study, avocado (A) and soybean (S) unsaponifiable extracts were separately tested or mixed in three A/S ratios; 1/3 avocado to 2/3 soybean (A1S2-Piascledine, laboratoire Pharmascience), 2/3 avocado to 1/3 soybean (A2S1) or 1/2 avocado to 1/2 soybean (A2S2). Freshly enzymatically isolated human chondrocytes were cultured for 72 hours in the absence or in the presence of IL-1 (10-9 M) and with or without unsaponifiable residues at the following concentrations (g/ml): A (3.3, 6.6, 10); S (3.3, 6.6, 10); A1S2 (10); A2S1 (10), A2S2 (10). Prostaglandin E2 (PGE2) and proteoglycans (PGs) were assayed by specific radioimmunoassays. IL-6 and IL-8 were quantified by EASIAAs (Medgenix). Stromelysin-like activity was measured by casein-resorufin test. Collagenase activity was assayed using (3H) type I collagenase as subtract. As anticipated, IL-1 induced a marked stimulation of collagenase, stromelysin, PGE2, IL-6, IL-8 and an important inhibition of proteoglycans syntheses. All A/S unsaponifiable mixtures reduced the spontaneous production of stromelysin, PGE2 and cytokines by chondrocytes and partially reversed the IL-1 effects. A1S2 and A2S2 partially inhibited the IL-1 stimulated collagenase production whereas A2S1 had no significant effect. Interestingly, A/S mixtures significantly increased the PGs content in the cellular phase but not the amount of PGs released in the culture supernatants. This finding suggests that A/S mixtures enhance the incorporation of the newly synthesised PGs in the cartilage matrix. Finally, A/S mixtures were more efficient on all parameters study than A and S added separately. In conclusion, these results suggest a potential role for A/S unsaponifiable extracts to mitigate the effects of IL-1 on cartilage.

[ASU may also inhibit the stimulating action of IL-1 on stromelysin, IL-6, IL-8, and prostaglandin E2 production as well as IL-1-stimulated collagenase synthesis]


[Demonstrated by reverse transcriptase-polymerase chain reaction, ASU could have an anabolic effect, stimulating transforming growth factor 1 and plasminogen activator inhibitor 1 expression by articular chondrocytes]


[In vivo, ASU significantly prevented the occurrence of lesions of contused cartilage in the postcontusive model of OA in rabbits]

Authors
Mauviel A. Loyau G. Pujol JP.

Institution
Laboratoire de Biochimie du Tissu Conjonctif, CHU, Caen.

Title
[Effect of unsaponifiable extracts of avocado and soybean (Piascledine) on the collagenolytic action of cultures of human rheumatoid synoviocytes and rabbit articular chondrocytes treated with interleukin-1]. [French]
ABSTRACT
In this work, the authors have studied the effect of advocate/soya-bean extracts (Piascledine) on the collagenolytic activity of cultured rabbit articular chondrocytes and human rheumatoid synovial cells. Incubation of these cells for 48 h with 10 micrograms/ml of Piascledine show that this drug slightly increases collagenase production. As expected, incubation of these cells with interleukin-1 (100 pg/ml) induces an important release of collagenase. Piascledine partially reverses the effect of interleukin-1 on synovial cells and totally abolishes its action on chondrocytes. Moreover, incubation of the two cell types for 5 days with Piascledine prior to a 48 h-exposure to interleukin-1 prevents partially the effect of interleukin-1. These data suggest a potential role for Piascledine to limit the deleterious effects of interleukin-1 in osteoarticular diseases by reducing the capacity of this cytokine to stimulate collagenase production by synoviocytes and chondrocytes.


[In vitro model, ASU partially prevented the deleterious effect of IL-1 on human synovial cells and abolished its effects on rabbit articular chondrocytes]


[In vitro, ASU had an inhibitory effect on interleukin-1 (IL-1) and stimulated collagen synthesis in articular chondrocyte cultures]

Periodontal Diseases and ASUs
**Title**
Morphometric analysis of human gingival elastic fibres degradation by human leukocyte elastase protective effect of avocado and soybean unsaponifiables (ASU).

**Authors**
Kut C. Assoumou A. Dridi M. Bonnefoix M. Gogly B. Pellat B. Guillou GB. Godeau G.

**Institution**
Faculty of Dental Surgery University Rene Descartes Paris V, Laboratoire de Physiopathologie des tissus non mineralises, Montrouge, France.

**Source**
Pathologie Biologie. 46(7):571-6, 1998 Sep.

**ABSTRACT**
Degradation of preelastic fibres (oxytalan and elaunin) and mature elastic fibres by human leukocyte elastase (HLE) was investigated using automated image analysis. Specimens from two young healthy adults were used. Although HLE hydrolyzed both fibre types, mature elastic fibres exhibited greater susceptibility to this effect than pre-elastic fibres. Avocado and soybean unsaponifiables are widely prescribed in rheumatology and parodontology and have also been the focus of ex vivo experiments aimed at determining whether they protect elastic fibres against degradation by HLE. Findings from the present study indicate that avocado and soybean unsaponifiables protect all types of gingival elastic fibres from degradation by HLE. Avocado and soybean unsaponifiables may be beneficial in patients with gingival inflammation and parodontitis, since HLE plays a major role in these disease states.

------------------------------------

**Title**
[Treatment of periodontal diseases with a combination of nonsaponifiable avocado and soybean oils]. [French]

**Authors**
Bourgeois G.

**Source**