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**Modification of articular cartilage and subchondral bone pathology in an ovine meniscectomy model of osteoarthritis by avocado and soya unsaponifiables (ASU).**

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**OBJECTIVE:** To examine the effect of an oral preparation of avocado and soya unsaponifiables (ASU) on the development of joint pathology in an ovine model of osteoarthritis (OA), using computer-assisted histomorphometric methods.

**DESIGN:** OA was induced in ovine knee joints by bilateral lateral meniscectomy (N=32). ASU (900 mg/weekday) was given orally to half the group (MenX+ASU), the remainder receiving placebo (MenX). Sixteen animals were used as non-operated controls (NOC). At 3 and 6 months post-meniscectomy, histological sections from the medial and lateral femoral condyles (MFC, LFC), tibial plateaux (MTP, LTP) and trochlear groove (TG) were prepared from all joints. Sections were scored using traditional histopathological scales, and computerized image analysis, measuring total cartilage area, uncalcified cartilage (UCC) and subchondral bone plate (SCP) thickness, and intensity of articular cartilage toluidine blue staining (mean greyscale intensity, black=255) as an index of proteoglycan (PG) content. **RESULTS:** Computerized image analysis showed significant histological differences not detectable by traditional scoring methods. ASU-treated animals at 6 months showed reduced loss of toluidine blue stain in the MTP ( $P=0.015$ ) and LTP ( $P=0.001$ ), and significantly greater staining in the TG than either placebo or NOC groups ( $P=0.011$ ). UCC thickness increased after meniscectomy, but tended to be highest in ASU-treated animals, significantly so in the middle zone of the LFC (MenX+ASU:  $1.03+-0.21$  mm vs MenX:  $0.79+-0.14$  mm,  $P=0.018$ ; NOC:  $0.77+-0.17$  mm). Lateral compartment SCP thickness increased post-meniscectomy but was increased significantly less in the inner zone of the LTP in ASU-treated sheep (MenX+ASU:  $1.37+-0.23$  mm vs MenX:  $1.68+-0.28$  mm,  $P=0.033$ ; NOC:  $1.22+-0.33$  mm).

**CONCLUSIONS:** In this model ASU treatment following meniscectomy appeared to confer a subtle but statistically significant protective effect on articular cartilage. Although the drug failed to prevent focal cartilage lesions, characteristic of this model, histomorphometric analysis demonstrated greater PG content and UCC thickness in adjacent joint regions of ASU-treated animals. In addition, a statistically significant reduction of subchondral bone sclerosis was noted in the LTP region of the drug-treated group. An anabolic effect on chondrocytes, resulting in the stimulation of matrix production in regions distant to the insult, was also suggested by the data. These findings support other studies which have proposed that ASU may exhibit disease-modifying anti-OA activity.  
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