demonstrate cartilage destructive properties as expressed by an increased release and a decreased synthesis rate and content of cartilage proteoglycans. The synovial tissue destructive properties increase with time after the experimental haemorrhage (+168%±260%; -76%±83%; -18%±23% respectively, for 24/48 hours).

Conclusions: Although intra-articular blood is cleared within 2 days from the canine knee joint (<10% left), adverse effects on cartilage and synovium are already initiated within 1 day, and they are more severe 2 days after the experimental haemorrhage. Although these are only short-term effects in the canine joint, it is clear that only a small amount of blood in a joint for a short period of time can result in a condition significantly compromising the joint.

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OXIDIZED LDL ENHANCES MCP-1 EXPRESSION IN CULTURED HUMAN CHONDROCYTES THROUGH ACTIVATION OF NF-kappaB

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Purpose: Recently, it has been demonstrated that lectin-like ox-LDL receptor-1 (LOX-1) is expressed on chondrocytes and suggested in vitro and vivo that its ligand ox-LDL play some role in degeneration of articular cartilage. To investigate whether oxidized low-density lipoprotein (ox-LDL) binding to lectin-like ox-LDL receptor 1 (LOX-1) enhances monocyte chemoattractant protein 1 (MCP-1) expression in cultured human articular chondrocytes (HACs). Furthermore, to ascertain whether the ox-LDL-induced MCP-1 upregulation is mediated by NF-kappaB activation.

Methods: The time course and dose response of MCP-1 mRNA expression and MCP-1 protein release into medium following ox-LDL stimulation were investigated using RT-PCR and ELISA, respectively. HACs were prepared, and NF-kappaB activation (p65 DNA binding activity) following ox-LDL stimulation was investigated by ELISA. LOX-1 mRNA expression in HACs was confirmed by RT-PCR. Ox-LDL significantly increased MCP-1 mRNA and protein expression levels in a time- and dose-dependent manner, which was suppressed markedly by pretreatment with TS92 and NF-kappaB inhibitors (Fig. 1). Ox-LDL stimulation activated NF-kappaB in HACs in a dose-dependent manner, which was suppressed by TS92 pretreatment (Fig. 2). NF-kappaB inhibitors significantly suppressed ox-LDL-induced MCP-1 expression.

Conclusions: It has been reported that chemokines produced by chondrocytes and chemokine receptors expressed on chondrocytes play an important role in pathogenesis of arthritis through intra-articular recruitment of monocytes/macrophages and the activation of matrix degrading enzymes. Our results suggest that the ox-LDL binding to LOX-1 enhances MCP-1 expression in human articular chondrocytes through activation of NF-kappaB and supports the hypothesis that ox-LDL deposition in cartilage and its receptor LOX-1 expression on chondrocytes are involved in degeneration of cartilage in osteoarthritis and rheumatoid arthritis.

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DIACERHEIN EXERTS A PARTIAL CONTROL ON THE CATABOLIC PROGRAM OF HUMAN OSTEOARTHRITIC CHONDROCYTES BUT NOT ON SYNOVIAL FIBROBLAST IN CULTURE

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Purpose: It has been proposed that diacerein acts as a slow-acting, symptom-modifying and perhaps as a disease-structure modifying drug in the treatment of osteoarthritis (OA), although its effects on cartilage and synovial catabolic program remain poorly studied. This work was designed to simultaneously study the effects of diacerein and that of conventional symptomatic drugs, like NSAIDs, on the synthesis of inflammation and structural mediators in OA chondrocytes and synoviocytes in culture.

Methods: Chondrocytes and synoviocytes were obtained from joint specimens of OA patients who underwent total knee replacement surgery. We used quiescent cells stimulated with 10 U/ML IL-1β, and studied the effects of diacerein (10-5M), celecoxib (CBX, 10-6M), diclofenac (DCF, 10-6M), meloxicam (MXC, 10-6M) and indomethacin (IND, 10-6M) in the release of prostaglandin (PG) E2 and nitric oxide (NO), the expression of cyclooxygenase (COX)-2, the accumulation of metalloproteinase (MMP)-1 and MMP-13, and the activation of the nuclear factor kappa B (NF-κB). All drugs were tested at the mean peak plasma concentration (Cmax) observed after oral administration of a therapeutic dose.

Results: The activation of NF-kB binding induced by IL-1β was inhibited by diacerein, both in chondrocytes and synoviocytes. All of the NSAIDs used in these experiments also inhibited the activation of NF-kB induced by IL-1β, although IND only showed this effect on chondrocytes. Regarding the prostaglandin system, we showed that diacerein did not revert the increase in COX-2