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New Methods for the functionalisation of UHMW-Polyethylene to develop implants for the plastic and reconstructive surgery in combination with tissue engineered bone and cartilage

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In the plastic and reconstructive Surgery there is an increasing demand for replacement material to fill defects especially in bone and cartilage. The aim of this study is to create an implant which interacts actively with the biological system and provoke exactly the same reactions as the corporal tissue. The implant based on ultra high molecular weight polyethylene (UHMW-PE) which will be coated with biological tissue (bone and cartilage) which will be directed to the implant surface through a collagen interface. A direct functionalisation of the UHMW-PE was carried out by means of plasma in order to increase the collagen adsorption capacity. On this modified surface osteoblast and chondrocytes were cultured. Environmental scanning electron microscopy, confocal scanning electron microscopy and immunohistochemical studies were carried out to investigate the tissue engineered osteoblast and chondrocytes. All methods used to functionalise the surface of the UHMW-PE, shows a homogenous immobilisation of collagen and homogenous biological tissue growth on the modified UHMW-PE surface. There are new possibilities for developing special kinds of implants, which can be used in the plastic and reconstructive surgery.

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Diacerein by its metabolite rhein, down-regulates stromelysin and nitric oxide productions and up-regulates aggrecan production by human chondrocytes in alginate beads.

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Rhein (1,8-dihydroxy-3-carboxyantraquinone) is the active metabolite of the drug diacerein which has proved to be effective in the treatment of osteoarthritis (OA). We investigated the long-term effects (12 days) of rhein on human OA chondrocytes cultured in alginate beads. In this purpose, enzymatically isolated OA chondrocytes were cultured in alginate beads for twelve days in the absence or in the presence of IL-1beta (10-10 M) and with or without rhein at the concentrations ranged among 10-6 to 2.10-5 M. Interleukin (IL)-6 and -8, stromelysin (MMP-3) and aggrecan (AGG) productions were quantified by immunoassays. NO production was determined by quantifying nitrite in the supernatants using a spectrophotometric method based on the Griess reaction. As expected, IL-1beta drastically depressed AGG production and upregulated IL-6, IL-8, MMP-3 and NO production. In the basal conditions, rhein (10-5 M) increased by 25% the synthesis of AGG and significantly reduced NO, IL-6 and MMP-3 productions by more than 30%. When IL-1b was added to the supernatant, rhein did not modify the inhibition of AGG, but partially reversed the IL-1 stimulatory effect on IL-6 and NO. Rhein had no significant effect on both basal and IL-1b-stimulated IL-8 productions. In conclusion, we have demonstrated that rhein, an active metabolite of diacerein, increases the production of AGG and decreases the synthesis of MMP-3 and NO. These findings provide a piece of evidence towards the mechanism of action by which rhein could exert a protective effect on cartilage.

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Long-term effects of nonsteroidal antiinflammatory drugs on human chondrocytes in alginate beads.

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This study was designed to compare the long-term effects (12 days) of non-steroidal anti-inflammatory drugs (NSAID) on the metabolism of human osteoarthritic (OA) chondrocytes cultured in alginate beads. Interleukin-6 and -8 (IL-6, IL-8), stromelysin (MMP-3), aggrecan (AGG) and prostaglandin E2 (PGE2) productions were assayed by specific immunoassays. All NSAID were tested at the mean peak plasma concentration (Cmax) obtained after oral administration of a therapeutic dose. Interestingly, aceclofenac, diclofenac, indomethacin, nimesulide and ibuprofen significantly inhibited both basal and IL-1beta-stimulated IL-6 production, whereas rofecoxib, celecoxib and piroxicam had no significant effects. No NSAID showed significant effects on basal and IL-1beta-stimulated IL-8 production, excepted ibuprofen which slightly increased basal IL-8 production. Aceclofenac and indomethacin increased by 25% AGG content in the alginate beads, while the other NSAID were without significant effect. At the therapeutic concentration, all NSAID tested fully blocked PGE2 production. Furthermore, none NSAID were able to modify the inhibitory effect of IL-1beta on AGG production. Finally, NSAID did not modify MMP-3 production. From this study, we can conclude that the mechanism of action of NSAID seems to be multifactorial and not limited to the inhibition of cyclooxygenases. Furthermore, by comparison with other NSAID, ACECLO and INDO show a advantageous profile of activity. They fully block PGE2 production, inhibit IL-6 synthesis and increase aggrecan synthesis. These effects would appear to be advantageous for the long-term treatment of chronic joint diseases such as osteoarthritis.

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Long-term effects of avocado/soybean unsaponifiable on human chondrocytes metabolism.

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To investigate the long-term effects (12d) of avocado/soybean unsaponifiable (ASU; 1 part avocado and 2 parts soybean, Piascléline, Pharmascience-Expanscience, Courbevoie, France) mixture on the metabolism of human osteoarthritic (OA) chondrocytes cultured in alginate beads. The DNA content was measured according to a fluorimetric method. Interleukin-6 and -8 (IL-6, IL-8), stromelysin (MMP-3), aggrecan (AGG) and prostaglandin E2 (PGE2) productions were assayed by specific immunoassays. In the basal conditions, ASU at 10 microg/ml, increased by 35 % the AGG contained in the alginate beads. Furthermore, ASU significantly inhibited IL-6, IL-8 and MMP-3 syntheses. IL-1beta stimulated IL-6, IL-8, PGE2 and MMP-3 productions and fully blocked AGG synthesis. When it was added simultaneously with IL-1, ASU partially reversed the IL-1beta-stimulatory effect on IL-6, IL-8, PGE2 and MMP-3 productions but did not modify the AGG inhibition. Nevertheless, ASU promoted the restoration of AGG synthesis after a 3-days pre-treatment with IL-1. From this work, we can conclude that ASU shows anti-inflammatory properties by inhibiting PGE2, IL-6 and IL-8. Furthermore, it stimulates AGG production and accumulation in the extracellular matrix and promotes matrix formation after IL-1 treatment. In parallel, it decreases MMP-3 production in both untreated and IL-1-treated cultures. Taken together, these results suggest that ASU could have a structural effect in OA by decreasing matrix degradation and restoring its formation.