New
ALGINATE-CHITOSAN HYDROGEL
with anti-inflammatory and annabolic effects on human chondrocytes

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PURPOSE

Today here is no treatment to cure osteoarthritis (OA) or to delay effectively its progression. Current treatments are mainly based on the alleviation of painful symptoms but are unable to restore the cartilage lining the joint. The repair of cartilage lesion still remains a great challenge for orthopaedic surgeons. The development of new scaffolds for tissue engineering is a promising approach. Herein, we report the effects of alginate-chitosan hydrogel (AC) beads on the metabolism of chondrocytes. ■

METHODS

Human OA chondrocytes were cultured either in AC beads or in alginate (A) beads. AC beads were prepared using ultra-pure chitosan (KiOmedine-CsU from KitoZyme) with molecular weight of 20 K (AC20) or 40 K (AC40) and alginate from Sigma. The two polymer solutions were prepared separately before being mixed together. Cells were added to the polymer mixture and the cell-containing beads prepared by precipitation in a calcium chloride solution. The chondrocytes embedded in the beads (0.5 to 1 x 10^5 cells/bead) were then cultured in a well defined culture medium for 28 days. Histological staining of the paraffine embedded beads was performed with hematoxyline-eosine. Interleukin (IL)-6 and -8, matrix metalloProteinase (MMP)-3 and aggrecan were measured by specific sandwich enzyme-linked immunoabsorbent assays (ELISA). A spectrophotometric method based upon the Griess reaction was used to quantify nitric oxide (NO) product. ■

RESULTS

AC (*Figure 1A*) and A beads were successfully prepared. Histological analysis of AC beads showed a homogeneous distribution of chitosan trabeculae in the alginate matrix and the presence of chondrocytes in contact with chitosan trabeculae (*Figure 1B*).

By comparaison with cultured in A beads (= 100 % = control), chondrocytes cultured in AC20 or AC40 produced significanly higher amounts of aggrecan after 28 days of culture. But significanly lower levels of MMP-3, IL-6, IL-8 during 21 days of culture and lower NO during the 7 first days of culure. The amount of NO was indetectable after the 8th day (*Figure 2*).

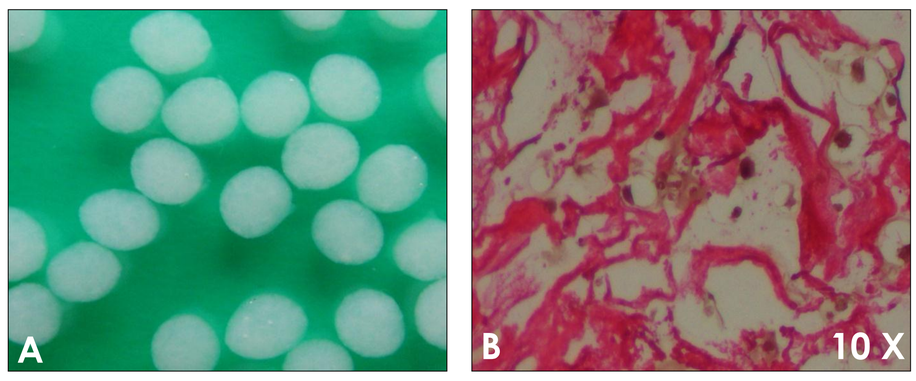


Figure 1:
A Gross observation of AC 20 beads. B Histological appearance of chondrocytes cultured in AC 20

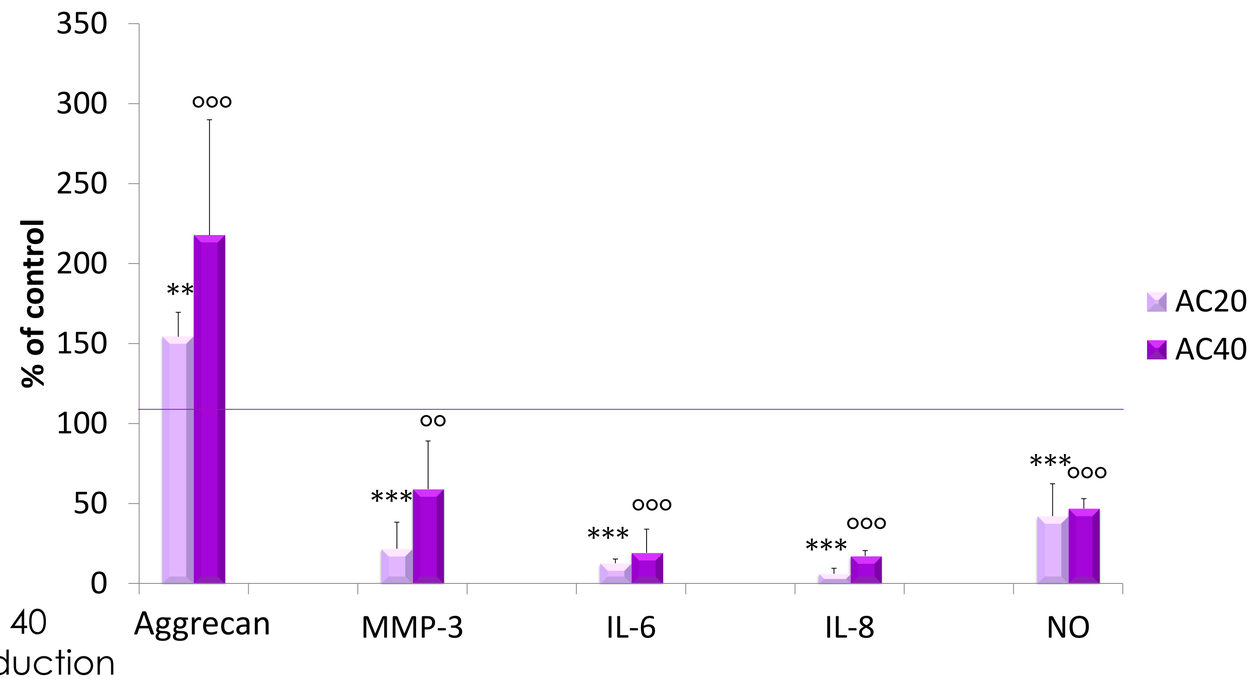
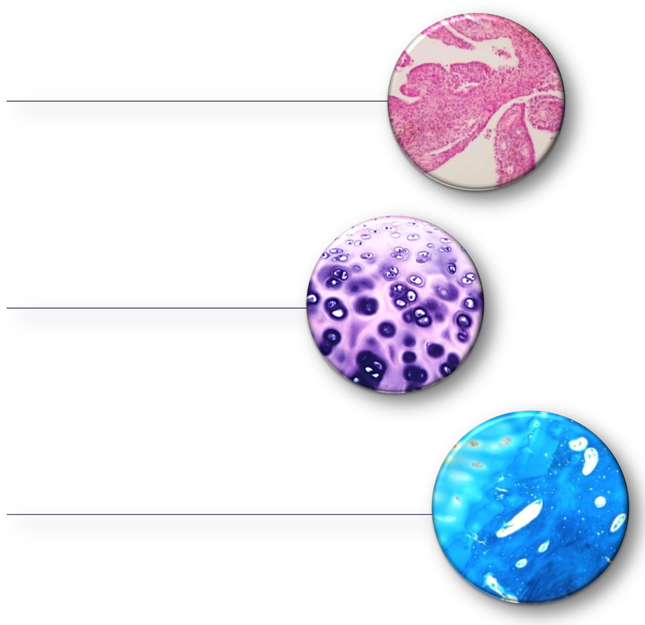


Figure 2: Aggrecan, MMP-3, IL-6, IL-8 and NO production of chondrocyte in AC20 and AC 40 beads. Results were represented as % of production of chondrocytes in A beads. Results were expressed as mean ± SEM of 3 independent experiments (n=9). A vs AC20 : ** $p < 0.01$; *** $p < 0.001$. A vs AC40 : °° $p < 0.01$; °°° $p < 0.001$

CONCLUSIONS

AC beads reduce the production of inflammatory and catabolic mediators by OA chondrocytes and promote the synthesis of cartilage-specific matrix componemts. These particular effects indicate that AC beads are a potential carrier for cell transplantation and particularly to repair cartilage defects.



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