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EVALUATION OF THE CHONDROPROTECTIVE EFFECT OF GLUCOSAMINE AND CHONDROITIN SULFATE BY A PROTEOMIC APPROACH

V. Calamia, C. Ruiz-Romero, V. Carreira, J. Mateos, B. Cillero-Pastor, E. Montell[1], J. Vergés[1], F.J. Blanco

Osteoarticular and Aging Research Laboratory. Proteomics Unit-Associated Node to ProteoRed. Biomedical Research Center (INIBIC). Hospital Universitario A Coruña. La Coruña. Spain.
[1]Medical Department. Bioiberica Pharma. Barcelona. Spain.

Glucosamine sulfate (GS) and chondroitin sulfate (CS) are symptomatic slow-acting drugs for osteoarthritis widely used in clinic, but with an unknown mechanism of action. The aim of this study is to evaluate the effects of both drugs GS and CS on cartilage cells (chondrocytes) to looking for cellular targets.

Chondrocytes obtained from healthy donors were treated with GS and CS, alone and in combination, and stimulated with IL-1β. Whole cell proteins were isolated 24 hours thereafter and resolved by 2-D electrophoresis. Gels were stained with SYPRORuby, and image analysis was performed using PDQuest software. Proteins of interest were identified by MALDI-TOF/TOF mass spectrometry. Real-time PCR and Western blot analyses were performed to validate our results.

We examined a mean of 500 protein spots that were present in each gel. Both qualitative and quantitative changes in protein expression patterns were studied. We identified 39 protein spots that were modulated by GS, 35 by CS and 48 by GS+CS compared to control ($p<0.05$). Database search showed that most of these proteins are involved in protein folding, stress response, cellular metabolism, protein targeting and oxidative stress. According to the essential role of oxidative stress balance that has been reported in osteoarthritis, we point out the effect of GS and CS (alone and combined) in counteracting the increase of mitochondrial superoxide dismutase that is caused by IL-1β.

In addition, the present study uses an *in vitro* model of inflammation (with IL-1β) to describe the effect of GS and CS on cartilage cells. We have identified several novel molecular targets of these compounds, such as SOD2, which may explain their reported good efficacy in osteoarthritis treatment. Our results highlight the synergic effect of the combined administration and point out the effectiveness of both molecules as anti-inflammatory drugs.