



# Matrix Metalloproteinase-2 Inhibition and Invasion Potential in Human Chondrocytes by Nutrient Synergy – A Specific Mixture of Nutrients Containing Lysine, Proline, Ascorbic Acid and Epigallocatechin Gallate (2002)

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## Abstract

Cartilage erosion as well as variable degrees of synovial inflammation are two crucial features of osteoarthritis. Current thinking is that these changes are due to up-regulation of chondrocytes mediated matrix metalloproteinases (MMPs), which in turn lead to a breakdown of cartilage macromolecules. We have been investigating different biological active components from natural products that inhibit MMP activities. Nutrient Synergy (NS), a specific mixture of nutrients and natural products containing lysine, proline, ascorbic acid and epigallocatechin gallate, was formulated on the premise that such a combination of nutrients would exert a very potent synergistic effect on MMP activities. Recently, we have reported that NS inhibits MMP activity and invasion potential in a number of human cancer cell lines. In the present study we have investigated the effect of NS on human chondrocytes, specifically on the expression of MMP-2, cell proliferation/cytotoxicity and matrix invasion potential. MMP-2 activity was assayed by zymography, invasion potential by the ability to invade through reconstituted basement membrane (Matrigel) and cytotoxicity by MTT assay. The results indicated that NS inhibits the expression of MMP-2 in a dose dependent manner. The expression of MMP-2 was significantly inhibited at a concentration of 100 µg/ml of NS and virtually not detected at a concentration of 200 µg/ml. In addition, it was also found that invasion of chondrocytes through Matrigel was inhibited by 50%, 85% and 95% at 10 µg/ml, 100 µg/ml and 200 µg/ml, respectively. At 500 µg/ml the invasion was complete. Interestingly, NS was not toxic to chondrocytes even at a concentration of 200 µg/ml. In fact, NS exerted a cell proliferative effect, a 70% increase in cell proliferation, with 200 µg/ml, 70% more than the control. These results demonstrate that NS is very effective in inhibiting the expression of MMP-2 in chondrocytes and in preventing their ability to invade through Matrigel. Taking into account the safety record of nutritional supplements and the encouraging results of this study with NS, this nutrient

combination should be considered a novel anti-inflammatory candidate for a natural approach to inhibit MMP production and ECM degradation in osteoarthritis and other problems related to excessive cartilage degradation.

### Comments

The processes of cartilage erosion and synovial inflammation associated with osteoarthritis are thought to result from increased MMP expression by chondrocytes. The synergistic inhibitory effects of the nutrient mixture of lysine, proline, ascorbic acid and epigallocatechin gallate (from green tea extract) on human chondrocyte MMP-2 expression and matrix invasion without cell toxicity demonstrated in this study suggest that this nutrient combination has potential as an anti-inflammatory agent for safe, natural therapeutic use in osteoarthritis.

