



# Suppression of Human Rheumatoid Synovial Fibroblast MMP-2 Expression and Matrix Invasion by Nutrient Synergy

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## **Abstract**

### **Objective:**

In patients with rheumatoid arthritis and other inflammatory diseases, MMPs are expressed in synovial membranes and have been implicated in synovial tissue invasion into adjacent cartilage and bone. We investigated the effect of a unique nutrient mixture (NS) containing ascorbic acid, lysine, arginine, and epigallocatechin gallate on human synovial fibroblast growth, MMP expression, and invasive potential.

### **Materials and Methods:**

Human synovial fibroblasts (CHTN) were grown in DME medium supplemented with 10% FBS, penicillin (100 U/ml) and streptomycin (100 mg/ml) in 24-well tissue culture plates. At near confluence, the cells were treated with NS dissolved in media and tested at 0, 10, 100, 500, and 1000  $\mu$ g/ml in triplicate at each dose. Cell proliferation was evaluated by MTT assay, MMP expression by gelatinase zymography, and invasion through Matrigel.

### **Results:**

NS demonstrated dose-dependent inhibition of synovial fibroblast growth with maximum inhibition of 49% at 1000  $\mu$ g/ml ( $p < 0.0001$ ). NS was found to inhibit synovial fibroblast expression of MMP-2 in a dose-dependent manner, with complete inhibition at 500  $\mu$ g/ml. The synergistically acting nutrient mixture significantly reduced the invasion of human synovial fibroblasts through Matrigel in a dose-dependent fashion, with 89% inhibition at 100  $\mu$ g/ml and 100% at 500  $\mu$ g/ml NS ( $p = 0.01$ ). H&E staining demonstrated no major changes, even at the highest concentration of NS.

### **Conclusion:**

Our results suggest that this nutrient mixture has excellent potential as an anti-inflammatory agent to suppress synovial cell MMP-2 activity and tissue invasion.

## Comments

In patients with rheumatoid arthritis and other inflammatory diseases, MMPs are expressed in synovial membranes and have been implicated in synovial tissue invasion into adjacent cartilage and bone. Standard anti-arthritic drugs, used for prolonged periods, have been associated with serious side effects. We studied the in vitro effect of a mixture of nutrients containing ascorbic acid, lysine, arginine and epigallocatechin gallate on human synovial fibroblast growth, MMP expression, and invasive potential. Our results demonstrated complete inhibition of MMP-2 expression and invasive potential of synovial fibroblasts at 500 µg/ml, suggesting this nutrient mixture has excellent potential as a safe anti-inflammatory agent.

