



Inhibitory Effect of Nutrient Synergy, A Specific Formulation of Nutrients Containing Lysine, Proline, Ascorbic Acid, and Epigallocatechin Gallate, on Matrix Metalloproteinase Activity and Invasion of Human Fibrosarcoma HT-1080 Cells

Roomi MW, Ivanov V, Netke SP, Niedzwiecki A, Rath M.

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Abstract

Introduction:

Cancer turns deadly when it invades and metastasizes to other parts of the body. Matrix metalloproteinases (MMPs) play a crucial role in tumor invasion and metastasis, due to their ability to digest basement membrane and extracellular matrix components. We have been interested in natural products that inhibit MMP activity. Nutrient Synergy (NS), a specific mixture of nutrients and natural products containing lysine, proline, ascorbic acid, and epigallocatechin gallate, was formulated on the basis that such a combination of nutrients would exert a very potent synergistic effect on MMP activity and stop the spread of cancer cells.

Objective:

In the current study, we have investigated the effect of Nutrient Synergy on human fibrosarcoma HT-1080 cells, specifically on: cell proliferation/cytotoxicity; expression of matrix metalloproteinases (MMPs); Matrigel invasion assay; and Hematoxylin and Eosin staining.

Method and Materials:

Human fibrosarcoma HT-1080 cells were obtained from ATCC and cultured in modified Eagle media supplemented with 10% heat-inactivated fetal bovine serum and antibiotic in 24-well culture plates. At near confluence, the cells were treated with NS at 0, 10, 100, 200, 500 and 1000 µg/ml in triplicate at each concentration for 24 hours. Proliferation/cytotoxicity was evaluated by MTT assay, MMP assay by gelatinase zymography in condition media, and invasion through Matrigel.

Results:

Nutrient Synergy was not toxic to human fibrosarcoma HT-1080 cells even at

100 µg/ml, but showed slight toxicity at 200 µg/ml (20% of the control) and at 1000 µg/ml (40% of the control). NS inhibited the expression of both MMP-2 and MMP-9 in dose dependent fashions, which were significantly inhibited at 1000 µg/ml. The invasion of human fibrosarcoma HT-1080 cells through Matrigel was inhibited by 40%, 50%, 70% and 100% at 10, 100, 200 and 1000 µg/ml, respectively. H&E stains of human fibrosarcoma HT-1080 cells did not indicate any changes in morphology with different concentrations of NS.

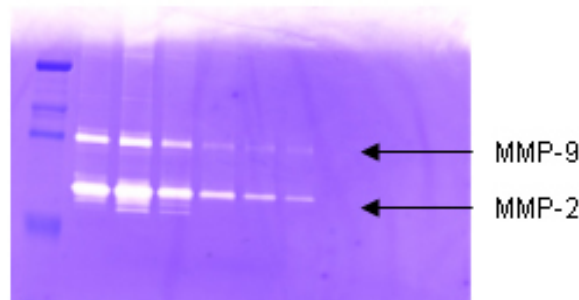
Conclusion:

In conclusion, Nutrient Synergy is considered to be an agent with promising potential for anti-metastatic activity by inhibiting invasion and MMP activity.

Comment:

To reproduce and spread to other parts in the body, cancer cells degrade the extracellular matrix (ECM) by secreting various matrix metalloproteinases (MMPs), which have been correlated with the aggressiveness of tumor growth. In this study, Nutrient Synergy, a specific mixture of nutrients, including lysine, proline, ascorbic acid, and epigallocatechin gallate, significantly inhibited the expression of both MMP-2 and MMP-9, and the invasion of human fibrosarcoma HT-1080 cells through Matrigel in a dose dependent fashion, without toxic effect to cells. These results suggest that Nutrient Synergy has great potential as a natural, non-toxic therapeutic regimen based on its antimetastatic activity.

Nutrient Synergy (NS) Inhibited Fibrosarcoma HT-1080 Cellular Expression of MMP-2 and MMP-9



1. Markers 2. Control 3-7 NS 10, 100, 200, 500, and 1000 µg/ml

Nutrient Synergy (NS) Inhibited Matrigel Invasion by Human Fibrosarcoma HT-1080 Cells

