

Source

Department of Food and Nutrition, Hungkuang University, Taichung County, Taiwan, Republic of China.

Abstract

Antioxidants have been suggested to inhibit the expression of matrix metalloproteinases (MMPs), especially MMP-9, which plays a critical role in tumor metastasis. Because of its antioxidant activity and the ability to chelate divalent cations, L-carnosine (LC) was tested for inhibition of MMP-9 in a highly invasive hepatocarcinoma, SK-Hep-1 cells. We found that LC (50-1,000 microM) did not directly inhibit the activity of MMP-9 in a cell-free system. However, LC significantly inhibited the expression and activity of MMP-9 protein in SK-Hep-1 cells [inhibitory concentration of 50% (IC(50))] = 105 and 63 muM, respectively). Whereas LC did not inhibit the viability of SK-Hep-1 cells at concentrations up to 1,000 microM within 3 days of incubation, this dipeptide significantly inhibited cell migration (IC(50) = 82 microM) and invasion (IC(50) = 113 microM). LC significantly (P < 0.05) and dose dependently enhanced the expression of an antimetastatic gene, nonmetastatic cells 1, protein (nm23)-H1, at both protein and messenger ribonucleic acid (mRNA) levels. MMP-9 activity inversely correlated significantly with the expression of protein (r(2) = 0.77, P < 0.001) and mRNA (r(2) = 0.65, P < 0.001) of nm23-H1 in LC-treated cells. Thus, LC can inhibit the migration and invasion of SK-Hep-1 cells, and the effect is likely associated with upregulation of nm23-H1 and downregulation of MMP-9 expression.

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