Inhibition of melanoma growth and metastasis by combination with (-)-epigallocatechin-3-gallate and dacarbazine in mice

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摘要

Abstract

(-)-Epigallocatechin-3-gallate (EGCG), a major polyphenol in green tea, was shown to have cancer chemopreventive activity. In this study, we examined the antimetastatic effects of EGCG or the combination of EGCG and dacarbazine on B16-F3m melanoma cells in vitro and in vivo. First, the antimetastatic potentials of five green tea catechins were examined by soft agar colony formation assay, and the results show that EGCG was more effective than the other catechins in inhibiting soft agar colony formation. Second, EGCG dose-dependently inhibited B16-F3m cell migration and invasion by in vitro Transwell assay. Third, EGCG significantly inhibited the spread of B16-F3m cells on fibronectin, laminin, collagen, and Matrigel in a dose-dependent manner. In addition, EGCG significantly inhibited the tyrosine phosphorylation of focal adhesion kinase (FAK) and the activity of matrix metalloproteinase-9 (MMP-9). In animal experiments, EGCG alone reduced lung metastases in mice bearing B16-F3m melanomas. However, a combination of EGCG and dacarbazine was more effective than EGCG alone in reducing the number of pulmonary metastases and primary tumor growths, and increased the survival rate of melanoma-bearing mice. These results demonstrate that combination treatment with EGCG and dacarbazine strongly inhibits melanoma growth and metastasis, and the action mechanisms of EGCG are associated with the inhibition of cell spreading, cell-extracellular matrix and cell-cell interactions, MMP-9 and FAK activities.