Suppression of extracellular signals and cell proliferation by the black tea polyphenol, theaflavin-3,3'-digallate.

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Abstract

Previous studies in our laboratory have shown that the major green tea polyphenol, (-)-epigallocatechin-3-gallate (EGCG), suppressed autophosphorylation of epidermal growth factor (EGF) receptor induced by EGF in human A431 epidermoid carcinoma cells. In this study, we examined the inhibitory effects of black tea polyphenols, including theaflavin (TF-1), a mixture (TF-2) of theaflavin-3-gallate (TF-2a) and theaflavin-3'-gallate (TF-2b), theaflavin-3,3'-digallate (TF-3) and the thearubigin fraction on the autophosphorylation of the EGF and PDGF receptors in A431 cells and mouse NIH3T3 fibroblast cells, respectively. First, we examined the effects of these polyphenols on the proliferation of A431 and NIH3T3 cells. Both EGCG and TF-3 strongly inhibited the proliferation of A431 and NIH3T3 cells more than the other theaflavins did. In cultured cells with pre-treatment of tea polyphenol, TF-3 was stronger than EGCG on the reduction of EGF receptor and PDGF receptor autophosphorylation induced by EGF and PDGF, respectively. Other theaflavins slightly reduced the autophosphorylation of the EGF and PDGF receptors; furthermore, TF-3 could reduce autophosphorylation of the EGF receptor (or PDGF receptor) even with co-treatment with EGF (or PDGF) and TF-3, but EGCG was inactive under these conditions. In addition, TF-3 was stronger than EGCG in blocking EGF binding to its receptor. These results suggest that not only the green tea polyphenol, EGCG, but also the black tea polyphenol, TF-3, have an antiproliferative activity on tumor cells, and the molecular mechanisms of antiproliferation may block the growth factor binding to its receptor and thus suppress mitogenic signal transduction.