Abstract

Introduction. The nuclear factor-kappaB (NF-κB) has been shown to upregulate pro-apoptotic mediators such as TRAIL-DR4/-DR5 receptors and the p53 transcription factor depending on the type of stimulus and the cell type involved. Previously, apple procyanidins (Pcy) have been shown to upregulate the expression of TRAIL-DR4/-DR5 and thereby overcoming the resistance of human colon cancer-derived metastatic SW620 cells to TRAIL. Objectives. NF-κB and p53 were investigated for their involvement in the Pcy-triggered apoptosis of human derived-metastatic colon cancer (SW620) cells. Materials and methods. Cell death, p53, TRAIL-DR4/-DR5 proteins were analyzed by flow cytometry. DR4/DR5 mRNA was analyzed by RT-PCR in real time. Activated p50/p65 and p53 forms were studied by ELISA and immunoblotting. Results. Pcy-triggered cell death was prevented by specific inhibitors of NF-κB and of p53: amino-4-(4-phenoxy-phenylethylamino) quinazoline (QNZ) and pifithrin μ (Pμ), respectively. QNZ and Pμ inhibited the Pcy-dependent activation of TRAIL-DR4/-DR5 death receptors. However, the upregulation of TRAIL-DR4 by Pcy was significantly decreased only when NF-κB and p53 inhibitors were used in combination; this effect was not observed with a single inhibitor. This effect was not observed for TRAIL-DR5 and suggested that the expression of each TRAIL-death receptor may be regulated differently. Conclusions. These data suggested that NF-κB and p53 are partially required in Pcy-triggered apoptosis of SW620 cells by up-regulating the expression of TRAIL-DR4/-DR5. In addition, the ratio between TRAIL-DR4/-DR5 may be a determining factor in the activation of TRAIL-death receptor mediated apoptosis.

Keywords

Apoptosis, colorectal neoplasms, flavonoids, tumor suppressor protein p53; receptors, TNF-related apoptosis-inducing ligand.