ERK-modulated intrinsic signaling and G(2)/M phase arrest contribute to the induction of apoptotic death by allyl isothiocyanate in MDA-MB-468 human breast adenocarcinoma cells.


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Abstract

Allyl isothiocyanate (AITC), a member of the isothiocyanate (ITC) family found in a constituent of cruciferous vegetables, possesses anticancer activity and induces apoptosis in various types of human cancer cell lines. However, no available information showed antitumor effects in human breast adenocarcinoma cells. The current study was focused on exploring the mechanisms underlying AITC-induced apoptosis in MDA-MB-468 human breast cancer cells in vitro. We found that AITC reduced the cell number and viability using trypan blue staining with the Countess Automated Cell Counter and the MTT assay, respectively. AITC also was found to induce apoptotic cell morphological changes by a contrast-phase microscope and cell cycle arrest at G(2)/M phase by flow cytometric assay in MDA-MB-468 cells. Intrinsic apoptosis-associated factors such as caspase-9 and caspase-3 activities were performed, and reactive oxygen species (ROS) production, loss of mitochondrial membrane potential (ΔΨm) occurred in AITC-treated MDA-MB-468 cells. AITC also stimulated mitochondria-related signaling, including p-Bcl-2 (Ser-70), cytochrome c and Apaf-1 in MDA-MB-468 cells. We found that the p-ERK signal was upregulated in AITC-treated cells. Importantly, NAC (a ROS scavenger) and U0126 (an ERK inhibitor) abolished AITC-reduced viability in MDA-MB-468 cells. AITC downregulated CDK1 activity and altered the expression of G(2)/M phase-modulated associated protein levels by western blotting in MDA-MB-468 cells. In summary, our findings demonstrated that AITC-promoted G2/M phase and AITC-triggered apoptosis correlate with the activation of phosphorylation of ERK in MDA-MB-468 cells. AITC is a potential agent for application in the treatment of human breast cancer.

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