Luteolin>quercetin>crisina>kaempferol>apigenina>miricetina provocam apoptose e parada do ciclo celular em G2/M no carcinoma epidermóide de esófago

Cytotoxicity of flavones and flavonols to a human esophageal squamous cell carcinoma cell line (KYSE-510) by induction of G2/M arrest and apoptosis.


Source

Department of Food Science, Key Laboratory of Dairy Science of Ministry of Education, Northeast Agricultural University, Harbin, Heilongjiang 150030, PR China.

Abstract

In this study, cytotoxic effects of structurally related flavones and flavonols on a human esophageal squamous cell carcinoma cell line (KYSE-510) were determined, and the molecular mechanisms responsible for their cytotoxic effects were studied. The results of MTT assay showed that flavones (luteolin, apigenin, chrysin) and flavonols (quercetin, kaempferol, myricetin) were able to induce cytotoxicity in KYSE-510 cells in a dose- and time-dependent manner, and the cytotoxic potency of these compounds was in the order of: luteolin>quercetin>chrysin>kaempferol>apigenin>myricetin. Flow cytometry and DNA fragmentation analysis indicated that the cytotoxicity induced by flavones and flavonols was mediated by G(2)/M cell cycle arrest and apoptosis. Furthermore, the expression of genes related to cell cycle arrest and apoptosis was assessed by oligonucleotide microarray, real-time RT-PCR and Western blot. It was shown that the treatment of KYSE-510 cells with these compounds caused G(2)/M arrest through up-regulation of p21(waf1) and down-regulation of cyclin B1 at the mRNA and protein levels, and induced p53-independent mitochondrial-mediated apoptosis through up-regulation of PIG3 and cleavage of caspase-9 and caspase-3. The results of western blot analysis further showed that increases of p63 and p73 protein translation or stability might be contributed to the regulation of p21(waf1), cyclin B1 and PIG3.

PMID:19397994