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Rugosin E, an ellagitannin, inhibits MDA-MB-231 human breast cancer cell proliferation and induces apoptosis by inhibiting nuclear factor-κB signaling pathway

Rugosin E，鞣花單寧酸，透過抑制 NF-κB 路徑而抑制人類乳癌細胞 MDA-MB-231 的細胞增生並誘導細胞凋亡

Yin-Yi Chen (陳胤伊)[1] Ya-Ling Hsu(許雅玲)[1] Ta-Chen Lin(林大楨)[2]
Wen-Sheng Tzeng(曾文盛)[3] Chun-Ching Lin(林俊清)[4,*] Po-Lin Kuo(郭柏麟)[1,*]

[1] Department of Biotechnology, Chia-Nan University of Pharmacy and Science, Taiwan
[2] Center of General Education, Central Taiwan University of Science and Technology, Taiwan
[3] Attending Diagnostic Radiologist, Chi-Mei Foundation Hospital, Tainan, Taiwan
[4] Faculty of Pharmacy, Kaohsiung Medical University, Kaohsiung 807, Taiwan

Abstract

Background and Purpose: We used a human breast cancer cell line, MDA-MB-231, to evaluate the potential of rugosin E as a chemopreventive agent against breast cancer. **Methods:** Cell proliferation assay (XTT); Cell cycle analysis (Flow cytometer); Apoptosis analysis; Caspase activity assay; Western blotting assay; Electrophoretic mobility shift assay (EMSA); NF-κb receptor assay; RT-PCR analysis. **Results:** Treatment with rugosin E decreased the cell proliferation of MDA-MB-231 cells in a dose-dependent manner and arrested MDA-MB-231 cells at G0/G1 phase. This effect was strongly associated with concomitant decrease in the level of cyclin D1, cyclin D2, cyclin E, cdk2, cdk4, and cdk6, and increase of p21/WAF1. In addition, rugosin E also induced apoptotic cell death. Rugosin E increased in the expression of Bax, Bak, and Bcl-Xs, but decreased the levels of Bcl-2 and Bcl-XL, and subsequently triggered mitochondria apoptotic pathway (release of cytochrome c, activation of caspase-9, and caspase-3). In addition, pre-treatment of cells with caspase-9 inhibitor blocked rugosin E-induced cell proliferation and apoptosis, indicating caspase-9 activation was involved in rugosin E-mediated MDA-MB-231 cells apoptosis. Rugosin E inhibited the constitutively activated and inducible NF-κb in both its DNA-binding activity and transcriptional activity. Furthermore, rugosin E also inhibited the TNF- -activated NF-κB-dependent reporter gene expression of cyclin D1, c-Myc, XIAP, Bcl-2, and Bcl-XL were all downregulated by rugosin E. **Conclusions:** Our results indicated that rugosin E inhibits the activation of NF-κB, and this may provide a molecular basis for drug development in the prevention and treatment of cancer by rugosin E.