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5,4'-二-正辛烷氧基-7-二氟亚甲基异黄酮抑制人乳腺癌细胞生长和诱导凋亡的作用

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Inhibition of Growth and Induction of Apoptosis in Human Breast Cancer Cell Line by 5,4'-Di-n-octoxyl-7-gem-Difluoromethylene-Genistein in Vitro

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摘要 目的 探讨金雀异黄酮(Genistein,Gen)衍生物5,4'-二-正辛烷氧基-7-二氟亚甲基异黄酮(5,4'-Di-n-octoxyl-7-gem-difluoromethylene-genistein, DODFMG)体外抑制人乳腺癌细胞系MCF-7细胞生长和诱导凋亡作用及机制,以寻找具有开发前景的肿瘤治疗新候选药物.方法 体外培养人乳腺癌细胞系(MCF-7)细胞,分别应用不同浓度的DODFMG处理人乳腺癌细胞系(MCF-7)细胞,软琼脂克隆形成法测定DODFMG对体外培养MCF-7细胞的锚定非依赖性增殖及生长作用的影响,PI染色流式细胞计分析(FCM)法检测DODFMG对MCF-7细胞诱导凋亡影响,western blotting法检测蛋白激酶CK2, NF-KB蛋白表达和活性的变化,初步探讨DODFMG抗乳腺癌作用的分子机制.结果 DODFMG对体外培养MCF-7细胞具有抑制增殖及生长作用,呈剂量依赖性.DODFMG诱导人MCF-7细胞凋亡.Western Blot分析结果显示: DODFMG 3.0, 10.0, 30.0 μmol/L处理人乳腺癌MCF-7细胞24 h后,比较于空白对照组,蛋白激酶CK2的表达下调12.50%, 41.50%, 67.30%, NF-KB的表达下调20.50%, 51.47%, 71.93%.DODFMG 30.0 μmol/L分别处理6, 12, 24 h后,比较于空白对照组,蛋白激酶CK2的表达下调27.73%, 44.8%, 65.2%, NF-KB的表达下调20.50%, 49.83%, 69.93%.这表明DODFMG以时间-剂量依赖方式引起蛋白激酶CK2、NF-KB下调,与先导化合物Gen比较, DODFMG更为有效(P<0.05).结论 DODFMG显著抑制人乳腺癌细胞系(MCF-7)细胞增殖及生长; DODFMG可诱导人乳腺癌细胞系(MCF-7)细胞凋亡;抑制蛋白激酶CK2,下调NF-KB的表达可能是DODFMG诱导凋亡的分子机制之一.

关键词: 乳腺癌 金雀异黄酮 5,4'-二-正辛烷氧基-7-二氟亚甲基异黄酮 蛋白激酶CK2

Abstract: PURPOSE To investigate the effect and mechanism of the Genistein derivative 5,4'-Di-n-octoxyl-7-gem-difluoromethylene-genistein(DODFMG) on the growth and apoptosis of human breast cancer(MCF-7) cells line in vitro.and provide a molecular mechanism of this effect so as to find a new candidate for tumor chemotherapy.METHODS Soft agar-colon assay was used to test colon formation inhibitory effect of MCF-7 by DODFMG.PI stain flow cytometry(FCM) was used to analyse the apoptosis after being treated with DODFMG.Western blotting assay was used to detect the effect of DODFMG on the CK2 and NF-kB protein expression level of breast cells.Results: DODFMG significantly inhibited proliferation and growth of MCF-7 cells in dose-dependent manner.DODFMG significantly induced apoptosis. Western-blotting analysis indicated that after exposures to DODFMG3.0,10.0,30.0μmol/L for 24h,the protein expressions of CK2 were down-regulated by 12.50%,41.50%,67.30%, the protein expressions of NF-kB were down-regulated by 20.50%,51.47%,71.93% respectively in comparison with the control group.After MCF-7 cells were treated with DODFMG at 30.0 μmol/L for 6,12 and 24 h,the protein expressions of CK2 were down-regulated by 27.73%,44.8%,65.2%, the protein expressions of NF-kB were down-regulated by 20.5%,49.83%,69.93% respectively in comparison with the control group.These showed that the expressions of CK2, NF-kB were decreased in a time and dose-dependent manner after treatment with various concentrations of DODFMG..In comparison with the lead compound Gen,DODFMG was more effective.CONCLUSION DODFMG possesses a significant inhibitory effect on the cell proliferation and growth of human breast carcinoma cell(MCF-7) in vitro DODFMG significantly induced apoptosis of human breast cancer (MCF-7) cell line.The mechanism might be associate d with down-regulation of ck2 and NF-kB.

Key words: breast cancer Genistein 5,4'-Di-n-octoxyl-7-gem-Difluoromethylene-genistein CK2

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