Increased Cytotoxicity of Doxorubicin in HT20 Colon Cancer Cells by Combination with 7-geranyloxycoumarin

Seyed Mahdi Moussavi¹, Farhang Haddad¹, Fatemeh B. Rassouli¹,²*, Mehrdad Iranshahi³, Shokouhozaman Soleymanifard⁴

¹Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran
²Cell and Molecular Biotechnology Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran
³Department of Pharmacognosy and Biotechnology, Biotechnology Research Center, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
⁴Department of Medical Physics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding author’s e-mail: behnam3260@um.ac.ir

Abstract
Cancer is known as one of the most challenging diseases in management and therapy, especially in developing countries. In Iran, for instance, high mortality of colon carcinoma is mainly due to their poor diagnosis and inefficacy of current therapeutic strategies. doxorubicin is a anticancer agent commonly prescribed for colon carcinoma. To investigate whether natural compounds such as coumarins could enhance the efficacy of chemical drugs, the synergic effects of 7-geranyloxycoumarin has been examined in present study in vitro. In this regard, 7-geranyloxycoumarin was synthesized by a reaction between 7-hydroxy coumarin and transgeranyl bromide in acetone at room temperature and then purified by column chromatography. Afterwards, HT-29 cells, a colon carcinoma cell line, were treated with increasing concentrations of 7-geranyloxycoumarin and doxorubicin, and their viability was assessed by MTT test. After determining the IC₅₀ of 7-geranyloxycoumarin and doxorubicin, HT-29 cells were treated with combining concentrations, including 20 µg/ml 7-geranyloxycoumarin with 1, 2 and 4 µg/ml doxorubicine. Then, effect of each combination was assessed on cells’ morphology and viability after 24, 48, 72 h. After cell treatments, the IC₅₀ of 7-geranyloxycoumarin and doxorubicin were determined as >40 µg/ml and >9 µg/ml in HT-29 cells, respectively. Studying HT-29 cells treated with combining concentrations revealed that combination of 20 µg/ml 7-geranyloxycoumarin with 1 µg/ml doxorubicin increased the toxicity of doxorubicin up to 14.5%. As 7-geranyloxycoumarin enhances the cytotoxicity of doxorubicin, it is worth to study its synergic effects on other anticancer drugs.

Key words: Doxorubicin, 7-geranyloxycoumarin, HT-29 cells, Cytotoxicity