Mogoltacin enhances vincristine cytotoxicity in human transitional cell carcinoma (TCC) cell line

F. Behnam Rassoulia, M.M. Matina,b,* M. Iranshahic, A.R. Bahramia,b, V. Neshatiia, S. Mollazadeha, Z. Neshatiia

aInstitute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran
bDepartment of Biology, Ferdowsi University of Mashhad, Mashhad, Iran
cDepartment of Pharmacognosy and Biotechnology, Biotechnology Research Center, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract

Bladder cancer is the second common cancer of the genitourinary system throughout the world and intravesical chemotherapy is usually used to reduce tumour recurrence and progression. Human transitional cell carcinoma (TCC) is an epithelial-like adherent cell line originally established from primary bladder carcinoma.

Here we report the effect of mogoltacin, a sesquiterpene coumarin from Ferula badrakema on TCC cells. Mogoltacin was isolated from the fruits of F. badrakema, using silica gel column chromatography and preparative thin layer chromatography. Mogoltacin did not have any significant cytotoxicity effect on neoplastic TCC cells at 16, 32, 64, 128, 200 and 600 μg ml⁻¹ concentrations. In order to analyse its combination effect, TCC cells were cultured in the presence of various combining concentrations of mogoltacin and vincristine. Cells were then observed for morphological changes (by light microscopy) and cytotoxicity using MTT assay. The effect of mogoltacin on vincristine toxicity was studied after 24, 48 and 72 h of drug administration. The results of MTT assay showed that mogoltacin can significantly enhance the cytotoxicity of vincristine and confirmed the morphological observations. Results revealed that combination of 40 μg ml⁻¹ vincristine with 16 μg ml⁻¹ mogoltacin increased the cytotoxicity of vincristine after 48 h by 32.8%.

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Introduction

Although bladder cancer can be treated successfully or controlled with combinations of surgery and intravesical chemotherapy, the treatment of recurrent and metastatic bladder cancer remains ineffective (Nicholson et al., 2004; Iaffaioli et al., 2007). The main reason for failure of chemotherapy is believed to be intrinsic or developed resistance to a wide range of chemically and functionally dissimilar chemotherapeutic agents by tumour cells, termed multidrug resistance (MDR) (Shoemaker et al., 1983; Gottesman, 1993).

Transitional cell carcinoma (TCC) is an epithelial-like adherent cell line originally established from primary bladder carcinoma of a 68-year-old man in 1974. TCC of the bladder makes up 90% of all bladder cancers (Lorusso and Silvestris, 2005). Despite advances in early diagnosis, TCC is still accompanied by high recurrence rates of 50–70% and frequent progression.