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ISOTHIOCYANATES ARE CHEMOPREVENTIVE COMPOUNDS AND REDUCE THE MDR PHENOMENON – STUDY ON NORMAL AND COLON CANCER CELLS

Lubelska Katarzyna1, Wiktorśka Katarzyna2, Śliwka Lidia3, Mlczarek Małgorzata4, Chilmonczyk Zdzisław1

1National Medicines Institute, Warsaw, Poland
2National Medicines Institute, Warsaw, Poland
3Medical University, Faculty of Pharmacy with the Laboratory Medicine Division, Warsaw, Poland
4Medical University, Faculty of Pharmacy with the Laboratory Medicine Division, Lublin, Poland

Introduction: Isothiocyanates (ITC) are compounds with proved chemopreventive properties [1]. According to epidemiological data, diet rich in isothiocyanates reduces the risk of colon cancer [2]. Induction of transport proteins such as multidrug resistance-associated proteins (MRP) is one of the factors responsible for chemopreventive effect of ITC. This also results in efficient disposal of carcinogenic substances. MPR are also one of the factors responsible for multidrug resistance (MDR) in tumor cells. Therefore, their induction in these cells is undesirable [4]. For this reason, the compounds that will selectively strengthen the protective processes in normal cells and weaken them in cancer cells are sought. In this study we investigated whether ITC selected by us exhibit selectivity between normal and cancer human colon cells. We examined the effect of ITC - SFN, which is already the subject of clinical trials and the new analog - ITC 2-oxoheptyl (HPT). We searched for changes in MRP1 and MRP2 gene expression, protein levels and total MRP transport activity. According to the literature MRP1 and MRP2 proteins play a major role in the induction of MDR phenomenon in many types of cancer cells [5]. 1. Navarro SL, Li F, Lampe JW (2011) Food Funct 2:579-587.2. Chung FL, Conaway CC, Rao CV et al (2000) Carcinogenesis 21:2287-2291.3. Shen G, Kong A-N (2009) Biopharm Drug Dispos 30:345-355.4. Sharom FJ (2008) Pharmacogenomics 9:105-127.5. Konno T1, Ebihara T, H isaeda K, et al (2003) J Biol Chem 278:22908-22917.

Methods: The experiments were conducted with the use of CRL1790 normal human colon cells and Caco2 colon human cancer cells. We examined the expression of genes encoding MRP1 and MRP2 using quantitative real-time PCR (qPCR). The protein level was examined by immunocytochemistry using confocal microscope. We used test with calcine (Calcein AM) to study total MRP transport activity.

Results: We have shown that in normal CRL170 cells, both compounds: SFN and HPT increased total MRP transport activity. We have found that this increase in normal cells is associated with increased expression of gene encoding MRP1 and subsequent increase in the level of MRP1 protein. In contrast to SFN, HPT showed selectivity and decreased total MRP transport activity in Caco2 cancer cells. Both compounds increased expression of gene encoding MRP2, but in case of HPT, a decrease in MRP2 protein level was observed.

Conclusion: In the Caco2 cancer cells, SFN and HPT acted in different ways on their molecular targets. This may explain the differences observed in the effect on total MRP transport activity and greater selectivity of HPT in these cells. This researches has been co-financed with the European Union funds by the European Social Fund.