Cyclin-dependent Kinase Inhibitor p21 is a Crucial Molecular Target for the Potential Antitumor Efficacy of Erucin from Rocket Salad Species against Prostate Cancer

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It is becoming increasingly clear that many dietary agents, such as isothiocyanates (ITCs) from Cruciferous vegetables, can retard or prevent the process of carcinogenesis by multiple mechanisms perturbing the three major steps, initiation, promotion and progression, as well as the later stages, angiogenesis and metastasis [1]. Erucin (ER) is a dietary isothiocyanate present in cruciferous vegetables, such as rocket salads (*Eruca sativa* Mill., *Diplotaxis* sp.), that has been recently considered a promising cancer chemopreventive phytochemical [2]. In this study, the potential protective activity of ER against prostate cancer was investigated using a human carcinoma prostate (PC3) cell line, in order to analyze its effects on molecular pathways involved in cell growth regulation, such as the cyclin-dependent kinase (CDKs) inhibitor $p21^{WAF1/CIP1}$ (p21) pathway. p21 is an inhibitor of CDKs that regulates the cell cycle by inhibiting both the G1-to-S and G2-to-mitosis transitions [3]. It has been previously demonstrated in many cancer cell lines that the inhibitory effects of ITCs on cell cycle progression is strongly related to their inductive effects on p21 expression [4-5]. Results obtained from our study indicate that the isothiocyanate ER may up-regulate p21 protein expression to inhibit the proliferation of human adenocarcinoma prostate PC3 cells. We have shown for the first time that ER caused a significant increase of p21 levels in a dose-dependent manner on human prostate cells. Compared to the structurally related sulforaphane (SF), a well-studied broccoli-derived ITC, the isothiocyanate ER showed lower potency in inhibiting proliferation of PC3 cells, as well as in modulating p21 protein expression. Several studies have showed that the tumor suppressor protein p53 plays a key role in cellular response to DNA damage leading to apoptosis in case of unrepaired DNA damage, or indirectly to the block of cell cycle progression by transactivating p21 [6]. Because PC3 cells do not express functional p53, our data suggest that the up-regulation of p21 by ER occur through a p53-independent pathway. The ability of dietary compounds, such as ER, to modulate molecular mechanisms that affect cancer cell proliferation is certainly a key point of the potential cancer prevention by functional foods.

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