6-(METHYLSULFINYL)HEXYLISOTHIOCYANATE AS POTENTIAL CHEMOPREVENTIVE AGENT: MOLECULAR AND CELLULAR PROFILE IN LEUKEMIA CELL LINES

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Numerous laboratory and epidemiological studies show that the risk of developing several types of cancer can be reduced with the employment of natural substances that act by multiple mechanisms. In this context an important role is played by the isothiocyanates. Recently, the 6-(methylsulfinyl) hexyl isothiocyanate (6-MITC), present in the root of Wasabia Japonica has stimulated the interest of researchers due to the demonstrated anti-inflammatory, antioxidants and neuroprotective properties, which permit to hypothesize its potential use as a chemopreventive agent. This work is focused on the evaluation of 6-MITC cytotoxic, cytostatic, cytodifferentianting activities and pro-apototic potential in vitro. These effects were investigated by flow cytometric analysis on Jurkat and HL-60 cells and in parallel, on healthy lymphocytes extracted from the blood of AVIS donors, in order to verify a potential selectivity of action. The results demonstrate that 6-MITC exerts a stronger cytotoxic effect on tumor cells than on healthy cells. The apoptosis induction exerted by the 6-MITC on transformed cells is triggered by extrinsic pathway, as demonstrated by the statistically significant increase in the percentage of cells with activated caspase 8, while the intrinsic pathway does not seem to be involved, as demonstrated by the number of cells with depolarized mitochondrial membrane potential cells and by the level of bax and cytochrome c that remain comparable to those found in the controls. Furthermore, the apoptosis induction resulted in tumor cells is dose- and time-related, p53 indipendent and statistically significant at lower concentrations than those required for exert the same effect on non-transformed cells. In addition, it was observed that 6-MITC is able to limit tumor growth by slowing down and blocking the cell cycle of Jurkat and HL-60 cells respectively, in a dose- and time-related manner, while it does not exert any kind of activity on replication of healthy cells. Finally, by measuring the expression levels of CD-14 and CD-15, 6-MITC showed the ability to induce cytodifferentiation of HL-60 into the macrophage and granulocytic phenotype. In conclusion it is possible to conjecture for 6-MITC a potential use as chemopreventive agent and a range of concentrations to act selectively.