

Dietary indoles and isothiocyanates

Dietary indoles and isothiocyanates that are generated from cruciferous vegetables can both stimulate apoptosis and confer protection against DNA damage in human colon cell lines.

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The natural indoles 3,3'-diindolylmethane (DIM), ascorbigen (ASG), indole-3-carbinol (I3C), and indolo[3,2-b]carbazole (ICZ), as well as the natural isothiocyanates sulforaphane (SUL), benzyl isothiocyanate (BITC) and phenethyl isothiocyanate (PEITC), all possess cancer chemopreventive properties.

It is now shown that DIM, ICZ, SUL, and BITC can each stimulate apoptosis in human colon adenocarcinoma LS-174 and Caco-2 cells. Treatment of LS-174 cells with nontoxic doses of DIM, ASG, I3C, or ICZ affected an increase of up to 21-fold in cytochrome P450 1A1 (CYP1A1).

None of these indoles caused an elevation in either aldo-keto reductase 1C1 (AKR1C1) or the gamma-glutamylcysteine synthetase heavy subunit (GCS(h)), but DIM, I3C, and ICZ produced a very modest increase in NAD(P)H:quinone oxidoreductase 1 (NQO1). By contrast, nontoxic doses of SUL, BITC, or PEITC failed to induce expression of CYP1A1 in LS-174 cells, but caused an increase of between 11- and 17-fold in the protein levels of AKR1C1, NQO1, and GCS(h). Treatment of the colon cell line with ICZ or SUL caused increases in the levels of mRNA for CYP1A1, AKR1C1, and NQO1 that were consistent with the enzyme data.

Exposure of Caco-2 cells to media containing indoles or isothiocyanates gave similar results to those obtained using LS-174 cells. Evidence is presented that the ability of indoles and isothiocyanates to stimulate either xenobiotic response element- or antioxidant response element-driven gene expression accounts for the two groups of phytochemicals inducing different gene batteries.

Pretreatment of LS-174 cells for 24 h with ICZ and SUL before exposure for 24 h to benzo(a)pyrene (BaP) reduced to <20% the number of single-strand DNA breaks produced by the carcinogen. Neither ICZ alone nor SUL alone were able to confer the same degree of protection against DNA damage produced by BaP as they achieved in combination. Similar results were obtained with H₂O₂ as the genotoxic agent.

Together, these phytochemicals may prevent colon tumorigenesis by both stimulating apoptosis and enhancing intracellular defenses against genotoxic agents.

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