



Preferred Nutrition is pleased to pass along the following information:

Sulforaphane

What does it do?

Sulforaphane is a compound that was identified in broccoli sprouts by scientists at the Johns Hopkins University School of Medicine in Baltimore, MD.¹

These researchers were investigating the [anticancer](#) compounds present in [broccoli](#) when they discovered that broccoli sprouts contain anywhere from 30 to 50 times the concentration of protective chemicals that are found in mature broccoli plants.² Sulforaphane is one of a class of chemicals called isothiocyanates. Sulforaphane and other isothiocyanates are [antioxidants](#) and potent stimulators of natural detoxifying enzymes in the body. These compounds are believed to be responsible for the lowered risk of cancer that is associated with the consumption of broccoli and other cruciferous [vegetables](#), such as [cauliflower](#), [cabbage](#), and [kale](#).^{3 4 5 6 7 8 9}

Feeding sulforaphane-rich broccoli-sprout extracts to laboratory rats exposed to a carcinogen dramatically reduced the frequency, size, and number of the rats' tumors.^{10 11 12} Human studies with sulforaphane and other cruciferous-vegetable components have shown that these compounds stimulate the body's production of detoxification enzymes and exert antioxidant effects.^{13 14 15}

Preliminary studies suggest that in order to cut the risk of cancer in half, the average person would need to eat about two pounds of broccoli or similar vegetables per week. Since the concentration of sulforaphane is much higher in broccoli sprouts than in mature broccoli, the same reduction in risk theoretically might be had with a weekly intake of just over an ounce of sprouts.

Where is it found?

Sulforaphane is found in highest concentrations in broccoli sprouts, but it is also found in mature [broccoli](#) and other cruciferous [vegetables](#), such as [cauliflower](#), [cabbage](#), and [kale](#).

Sulforaphane has been used in connection with the following conditions (refer to the individual health concern for complete information)

Who is likely to be deficient?

Sulforaphane is not an essential nutrient, and thus no deficiency state exists.

How much is usually taken?

The optimal level of intake is not known, but some doctors recommend 200 to 400 mcg of sulforaphane daily from [broccoli](#)-sprout extracts.

Are there any side effects or interactions?

No side effects or drug interactions have been reported, although sulforaphane and dietary consumption of cruciferous [vegetables](#) does interact with drug detoxifying [enzymes](#).¹⁶ People taking prescription drugs should therefore consult a doctor before taking sulforaphane or [broccoli](#)-sprout extracts.

At the time of writing, there were no well-known drug interactions with sulforaphane.

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High cellular accumulation of sulphoraphane, a dietary anticarcinogen, is followed by rapid transporter-mediated export as a glutathione conjugate.

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Sulphoraphane (SF), a naturally occurring isothiocyanate, is a potent anticarcinogen in animal experiments. The mechanism of action of sulphoraphane includes induction of Phase 2 detoxification enzymes, inhibition of carcinogen-activating Phase 1 enzymes, induction of apoptosis and cell cycle arrest, and anti-inflammation. We have recently found that it was accumulated in mammalian cells by up to several hundred-fold over the extracellular concentration, primarily by conjugation with intracellular GSH. The intracellular accumulation levels of SF can reach millimolar concentrations. The anticarcinogenic activity of SF is at least partly dependent on its accumulation levels in cells. Here we show, however, that the accumulated SF was rapidly exported mainly in the form of GSH conjugate (GS-SF) in cultured human cells. It appeared that to sustain the intracellular accumulation levels required a continuous uptake of SF to offset the rapid export of SF/GS-SF. These findings may have important implications for the development of an effective dosing regimen for SF. Moreover, the export was temperature-sensitive and was inhibited by known inhibitors of membrane pumps, suggesting the involvement of such a pump in exporting accumulated SF/GS-SF. Indeed, studies with human leukemia cells (HL60) with or without overexpression of multidrug resistance associated protein-1 (MRP-1) and human myeloma cells (8226) with or without overexpression of P-glycoprotein-1 (Pgp-1) indicated that both MRP-1 and Pgp-1 are involved in the export of intracellular SF/GS-SF.

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Isothiocyanates as substrates for human glutathione transferases:

structure-activity studies.

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The catalytic properties of four human glutathione transferases (GSTs), A1-1, M1-1, M4-4 and P1-1, were examined with 14 isothiocyanate (R-NCS) substrates. The compounds include aliphatic and aromatic homologues, some of which are natural constituents of human food, namely sulforaphane [1-isothiocyanato-4-(methylsulphinyl)butane], erucin [1-isothiocyanato-4-(methylthio)butane], erysolin [1-isothiocyanato-4-(methylsulphonyl)butane], benzyl-NCS, phenethyl-NCS and allyl-NCS. All isothiocyanates investigated were substrates for the four GSTs. The enzymes promote addition of the thiol group of GSH to the electrophilic central carbon of the isothiocyanate group to form dithiocarbamates [R-NH-C(=S)-SG] which have high UV absorption at 274 nm. Molar absorption coefficients and non-enzymic rate constants as well as standardized enzyme assay conditions for all compounds were established. Of the four isoenzymes investigated, GSTs M1-1 and P1-1 were generally the most efficient catalysts, whereas GST M4-4 was the least efficient. Isothiocyanates are among the GST substrates that are most rapidly conjugated. On the basis of rate-enhancement data and binding energies, the isothiocyanates were compared with 4-hydroxyalkenals, another class of natural GST substrates previously subjected to systematic kinetic analysis. The incremental transition-state stabilization attributable to an increased number of methylene groups in homologous alkyl isothiocyanates is similar to that previously noted for homologous 4-hydroxyalkenals.

Antimicrob Agents Chemother. 2003 Dec;47(12):3982-4.

Efficacy of sulforaphane in eradicating Helicobacter pylori in human gastric xenografts implanted in nude mice.

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Sulforaphane, an isothiocyanate abundant in the form of its glucosinolate precursor in broccoli sprouts, has shown in vitro activity against Helicobacter pylori. We evaluated the effect of sulforaphane in vivo against this bacterium by using human gastric xenografts in nude mice. H. pylori was completely eradicated in 8 of the 11 sulforaphane-treated grafts. This result suggests that sulforaphane might be beneficial in the treatment of H. pylori-infected individuals.

Colorectal Dis. 2004 Jan;6(1):28-31.

Sulforaphane inhibits growth of a colon cancer cell line.

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OBJECTIVE: The consumption of cruciferous vegetables has a protective effect on the development of colorectal cancer. The phytochemical Sulforaphane is an isothiocyanate found almost exclusively in cruciferous vegetables. We have studied the effect of Sulforaphane on cell proliferation of an HT-29 colon cancer cell line. **MATERIALS AND METHODS:** HT-29 colon cancer cells were cultured in 96-well microtitre plates. Sulforaphane (in concentrations ranging from 0.01 to 0.1 mmol) were added to the wells. Cell proliferation was measured using the colourimetric assay technique. **RESULTS:** The proliferation of colon cancer cells was significantly reduced by Sulforaphane at concentrations of ≥ 0.02 mmol. **CONCLUSION:** These findings may help explain the epidemiologically proven protective effect of vegetables against colon cancer.

Cancer Lett. 2004 Jan 8;203(1):35-43.

Induction of medulloblastoma cell apoptosis by sulforaphane, a dietary anticarcinogen from Brassica vegetables.

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There is increasing evidence that a variety of natural substances derived from the diet may act as potent chemopreventive agents. In this work, we show that DAOY cells, a widely used model of metastatic medulloblastoma (MBL), are highly sensitive to sulforaphane, a naturally occurring isothiocyanate from Brassica vegetables. Sulforaphane induced DAOY cell death by apoptosis, as determined by DNA fragmentation and chromatin condensation. DAOY apoptosis correlates with the induction of caspase-3 and -9 activities, resulting in the cleavage of PARP and vimentin. Both the cytotoxic effect and apoptotic characteristics induced by sulforaphane were reversed by zVAD-fmk, a broad spectrum caspase inhibitor, demonstrating the important role of caspases in its cytotoxic effect. These results identify sulforaphane as a novel inducer of MBL cell apoptosis, supporting the potential clinical usefulness of diet-derived substances as chemopreventive agents.

Cancer Res. 2003 Nov 1;63(21):7520-5.

Effects of glutathione on antioxidant response element-mediated gene expression and apoptosis elicited by sulforaphane.

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Sulforaphane (SFN) and its N-acetyl-L-cysteine (NAC) conjugate are effective inhibitors of tumorigenesis in animal models. These compounds induce the expression of the antioxidant response element (ARE)-related genes and cause apoptosis. We studied the role of reduced glutathione (GSH) in the activations of ARE-mediated gene expression, apoptosis, and the activation of c-Jun NH(2)-terminal kinase (JNK) in HepG2-C8 cells. The cellular level of GSH decreased transiently when cells were exposed to SFN and then increased from 4 h, reaching 2.2-fold over control at 24 h. In contrast, SFN-NAC did not change the GSH level substantially during the time of incubation. ARE expression was increased in a dose-dependent manner up to 35 micro M SFN and 75 micro M SFN-NAC, respectively. The induction of ARE by SFN was 8.6-fold higher than that by SFN-NAC. Pretreatment with L-buthionine sulfoximine increased SFN-induced ARE expression significantly. The decrease in ARE expression at higher concentrations of SFN and SFN-NAC was correlated with accelerated apoptotic cell death, with a dose-dependent activation of caspase 3 activity by SFN. On addition of extracellular GSH within 6 h of treatment with SFN, the effect on ARE expression was blocked almost completely. SFN was able to activate JNK1/2, and that activation was blocked by treatment with exogenous GSH. Taken together, these results suggest that the biological effects of SFN and SFN-NAC on the induction of ARE-related gene expression and apoptosis could be different from each other; however, the different effects on ARE-related gene expression and apoptosis elicited by SFN can be blocked by the addition of GSH. *Carcinogenesis*. 2003 Oct 24 [Epub ahead of print].

Sulforaphane: a naturally occurring mammary carcinoma mitotic inhibitor which disrupts tubulin polymerization.

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Sulforaphane (SUL), an isothiocyanate found in broccoli and other cruciferous vegetables, has been shown to induce phase II detoxification enzymes, inhibit chemically-induced mammary tumors in rats, and more recently to induce cell cycle arrest and apoptosis in cancer cells of the colon. Here, we provide evidence that SUL also acts as a breast cancer antiproliferative agent. The BALB/c mouse mammary carcinoma cell line F3II was treated with SUL at concentrations up to 15 micro M and examined for markers of cell cycle arrest and apoptosis. Treatment of asynchronous F3II cells with 15 micro M SUL resulted in G2/M cell cycle arrest, elevated p34(cdc2) (cdc2) kinase activity, Bcl-2 downregulation, evidence of caspase activation, and aggregation of condensed nuclear chromatin. Subsequent exposure of synchronized cells to 15 micro M SUL resulted in elevated numbers of prophase/prometaphase mitotic figures, indicating cell cycle

progression beyond G2 and arrest early within mitosis. Moreover, cells treated with 15 micro M SUL displayed aberrant mitotic spindles, and higher doses of SUL inhibited tubulin polymerization in vitro. In addition, BALB/c mice injected s.c. with F3II cells and subsequently injected daily i.v. with SUL (15 nmol/day for 13 days) developed significantly smaller tumors (approximately 60% less in mass) than vehicle-treated controls. Western blot analysis of tumor proteins demonstrated significantly ($P<0.05$) reduced PCNA and elevated PARP fragmentation in samples from animals dosed with SUL. Taken together, these results indicate that SUL has mammary cancer suppressive actions both in cell culture and in the whole animal. Inhibition of mammary carcinogenesis appears in part to involve perturbation of mitotic microtubules and early M-phase block associated with cdc2 kinase activation, indicating that cells arrest prior to metaphase exit

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Chemoprevention of cancerogenesis--the role of sulforaphane.

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Isothiocyanates are a group of naturally occurring compounds with interesting medical properties, such as antimicrobial, antioxidant and antitumor activities. In our work we were trying to present the tumoricidal activity of new synthesized derivatives of one isothiocyanate: 1-isothio-cyanato-(4R)-(methylsulfinyl) butane [sulforaphane]. Many chemical substances derived from plants, undoubtedly have protective properties. The effectiveness of sulforaphane is based on induction of hepatic detoxifying enzymes.

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The effect of indole-3-carbinol and sulforaphane on a prostate cancer cell line.

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BACKGROUND: Cruciferous vegetable consumption is inversely related to the incidence of prostate cancer. We examined the effect of indole-3-carbinol (I3C) and of sulforaphane (constituents of cruciferous vegetables) on cell proliferation of a PC-3 prostate cancer cell line, in order to observe if an inhibitory effect might be detected in vitro. **METHODS:** PC-3 prostate cancer cells were cultured in 96-well microtitre plates. Indole-3-carbinol concentrations ranging from 0.1 mmol/L to 0.8 mmol/L or sulforaphane concentrations ranging from 0.01 mmol/L to 0.06 mmol/L were added to the wells. Cell proliferation was measured by colorimetric

assay and results were based on the mean value of triplicate experiments. Data are presented as medians and interquartile ranges and were analysed using the Mann-Whitney U-test. RESULTS: Cell proliferation in PC-3 prostate cancer cells was significantly inhibited by I3C and sulforaphane at media concentrations of 0.2 mmol/L and 0.02 mmol/L, respectively. CONCLUSION: Both compounds inhibited the proliferation of prostate cancer cells in a dose-dependent manner. These findings may help explain the observed protective effect of cruciferous vegetables in relation to prostate cancer.