New Product Highlights

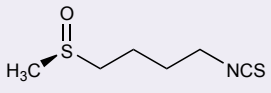
L-Sulforaphane: Antioxidant, anticarcinogen and antibiotic

Sigma-RBI has recently introduced **L-sulforaphane** (Prod. No. S 6317), a naturally occurring isothiocyanate found in high concentration in the SAGA (Mariner) variety of broccoli (*Brassica oleracea italica)*. Sulforaphane acts as a potent monofunctional inducer of detoxification enzymes involved in xenobiotic metabolism, an effect which may explain why the consumption of green and yellow vegetables, especially crucifers, is associated with lower cancer risk.

Detoxification enzymes are classified into two families: Phase I cytochrome p450 oxidoreductases, and Phase II conjugation enzymes that modify xenobiotic compounds by conjugating them with endogenous ligands including **glutathione** (Prod. No. G 6529), **glucuronic acid** (Prod. No. G 5269) and sulfate. Monofunctional inducers exhibit their protective function via the induction of Phase II enzymes, which can also activate procarcinogenic compounds to their carcinogenic metabolites. Sulforaphane has been shown to induce **quinone reductase** (Prod. No. D 1315) [1], **glutathione S-transferase** (Prod. No. G 5663) [1] and **glutathione reductase** (Prod. Nos. G 3664, G 3011, G 6004) [2]. Enzyme induction has been observed in cell lines, including murine hepatoma (Hepa 1c1c7) [1], the BPrc1 p450-deficient mutant [1] and human adult retinal pigment epithelial cells (ARPE-19) [2] as well as in liver, stomach, small intestine and lung of mice fed sulforaphane [1]. Protection against oxidative damage was observed as increased cell survival following *in vitro* treatment with oxidants such as **menadione** (Prod. No. M 5625), t-butyl hydroxide, hydroxynonenal and peroxynitrite [2]. Experimental chemical carcinogenesis with **DMBA** (9,10-dimethyl-1,2-benzanthracene, Prod. No. D 3254) in rats confirmed the efficacy of sulforaphane in reducing mammary tumor incidence, multiplicity and size [3]. Chemoprotection with sulforaphane also resulted in the delayed appearance of tumors [3].

A direct link has been proposed between the activity of sulforaphane and the cellular molecular sensor, Nrf2-Keap1 complex [5], which regulates the induction of Phase II enzymes. Nrf2, a member of the NF-E2 transcription factor family, induces Phase II enzymes by binding to the ARE (antioxidant response element) region of the promoter. Under normal conditions, Nrf2 is suppressed by binding to Keap1, a cytoplasmic protein anchored to the actin cytoskeleton. Sulforaphane, and other titrants of thiol groups, competes with the cysteine-rich intervening region of Keap1 for interaction with Nrf2 [5]. Disruption of the Nrf2-Keap1 complex by sulforaphane frees Nrf2 to translocate into the nucleus where it can heterodimerize with other transcription factors on ARE regions of phase II genes, leading to activation of transcription. It appears that, while sulforaphane is chemoprotective in wild type animals, it loses its efficacy in reducing benzo[a]pyrene-induced gastric tumors in Nrf2 deficient mice [6].

Sulforaphane is bactericidal to both the extracellular and intracellular forms of *H. pylori* in a human epithelial cell line [6]. Also significant is its bacteriostatic activity against three reference strains and 45 clinical isolates of *H. pylori* regardless of their resistance to conventional antibiotics [6]. Given the endemic nature of *H. pylori* infection in many developing countries and the etiologic connection between infection, gastritis, peptic ulcers and gastric cancer, sulforaphane holds promise as both an antibiotic and an anticancer agent.



L-Sulforaphane
(Prod. No. S 6317)

References

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