Glucoraphanin, the bioprecursor of the widely extolled chemopreventive agent sulforaphane found in broccoli, induces phase-I xenobiotic metabolizing enzymes and increases free radical generation in rat liver.

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Abstract

Epidemiological and animal studies linking high fruit and vegetable consumption to lower cancer risk have strengthened the belief that long-term administration of isolated naturally occurring dietary constituents could reduce the risk of cancer. In recent years, metabolites derived from phytoalexins, such as glucoraphanin found in broccoli and other cruciferous vegetables (Brassicaceae), have gained much attention as potential cancer chemopreventive agents. The protective effect of these micronutrients is assumed to be due to the inhibition of Phase-I carcinogen-bioactivating enzymes and/or induction of Phase-II detoxifying enzymes, an assumption that still remains uncertain. The protective effect of glucoraphanin is thought to be due to sulforaphane, an isothiocyanate metabolite produced from glucoraphanin by myrosinase. Here we show, in rat liver, that while glucoraphanin slightly induces Phase-II enzymes, it powerfully boosts Phase-I enzymes, including activators of polycyclic aromatic hydrocarbons (PAHs), nitrosamines and olefins. Induction of the cytochrome P450 (CYP) isoforms CYP1A1/2, CYP3A1/2 and CYP2E1 was confirmed by Western immunoblotting. CYP induction was paralleled by an increase in the corresponding mRNA levels. Concomitant with this Phase-I induction, we also found that glucoraphanin generated large amount of various reactive radical species, as determined by electron paramagnetic resonance (EPR) spectrometry coupled to a radical-probe technique. This suggests that long-term uncontrolled administration of glucoraphanin could actually pose a potential health hazard.