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Review

Mechanisms of mammary cancer chemoprevention by organoselenium compounds

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Abstract

Searching for optimal diets and for naturally occurring agents in routinely consumed foods that may inhibit cancer development, although challenging, constitutes a valuable and plausible approach to finding ways to control and prevent cancer. To date, the use of the micronutrient selenium in human clinical trials is limited but the outcome of these investigations indicates that selenium is one of the most promising agents. Data presented in this mini-review indicate that the dose and the form (structure) in which selenium is used are the most critical determinants of success in future clinical trials. The focus of this mini-review is on the mechanisms of mammary cancer chemoprevention by organoselenium compounds. Among the naturally occurring organoselenium compounds, Se-Methylselenocysteine is more efficacious than the most extensively studied forms, such as selenomethionine. However, we showed that synthetic organoselenium compounds can be tailored to achieve greater chemopreventive efficacy with minimal side effects by structural modifications; it is evident that synthetic agents are superior to the inorganic selenite, naturally occurring selenium compounds and their sulfur-containing analogs. We have demonstrated that 1,4-phenylenebis (methylene) selenocyanate (*p*-XSC) and its putative metabolite glutathione conjugate (*p*-XSeSG) are highly promising agents in the chemoprevention of mammary carcinogenesis in the 7,12-dimethylbenz[*a*]anthracene (DMBA)-rat mammary tumor model system. Both compounds inhibit the initiation phase of carcinogenesis by inhibiting DMBA–DNA adduct formation in the target organ in vivo. cDNA microarray analysis indicates that both selenium compounds alter genes in a manner that leads to inhibition of cell proliferation and induction of apoptosis; modulation of apoptosis and cell proliferation can account for chemoprevention during the post-initiation phase of mammary carcinogenesis. Using a rat mammary cancer cell line, we compared *p*-XSC and *p*-XSeSG as inhibitors of cell proliferation; depending on the selenium dose and time point selected, *p*-XSC was comparable to or better than *p*-XSeSG. Collectively, the results described here, suggest that the molecular targets modulated by organoselenium compounds are highly useful indicators of success in clinical cancer chemoprevention trials.

Keywords: Selenium; Mammary cancer

Abbreviations: BSC, benzylselenocyanate; BTC, benzylthiocyanate; DMBA, 7,12-dimethylbenz[*a*]anthracene; *p*-XSC, 1,4-phenylenebis(methylene)selenocyanate; *p*-XSeSG, glutathione conjugate of *p*-XSC; *p*-XSeH, aromatic selenol moiety of *p*-XSeSG

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