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Selenium and anticarcinogenesis: underlying mechanisms

Matthew I. Jackson and Gerald F. Combs Jr

Grand Forks Human Nutrition Research Center, USDA-ARS, Grand Forks, North Dakota, USA

Correspondence to Dr Gerald F. Combs, Jr. Center Director, Grand Forks Human Nutrition Research Center, USDA-ARS, 2420 2nd Avenue North, STOP 9034, Grand Forks, ND 58202-9034, USA
Tel: +1 701 795 8456; fax: +1 701 795 8230; e-mail: gerald.combs@ars.usda.gov

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Purpose of review

To discuss recent research related to anticarcinogenic mechanisms of selenium action in light of the underlying chemical/biochemical functions of the selenium species, likely to be executors of those effects.

Recent findings

Recent studies in a variety of model systems have increased the understanding of the anticarcinogenic mechanisms of selenium compounds. These include effects on gene expression, DNA damage and repair, signaling pathways, regulation of cell cycle and apoptosis, metastasis and angiogenesis. These effects would appear to be related to the production of reactive oxygen species produced by the redox cycling, modification of protein-thiols and methionine mimicry. Three principle selenium metabolites appear to execute these effects: hydrogen selenide, methylselenol and selenomethionine. The fact that various selenium compounds can be metabolized to one or more of these species but differ in anticarcinogenic activity indicates competing pathways of their metabolic and chemical/biochemical disposition. Increasing knowledge of selenoprotein polymorphisms has shown that at least some are related to cancer risk and may affect carcinogenesis indirectly by influencing selenium metabolism.

Summary

The anticarcinogenic effects of selenium compounds constitute intermediate mechanisms with several underlying chemical/biochemical mechanisms such as redox cycling, alteration of protein-thiol redox status and methionine mimicry.

Keywords

anticarcinogenesis, cancer prevention, carcinogenesis, protein-thiol, redox cycling, selenium

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Introduction

Selenium (Se) is a constituent of some 25 selenoproteins [1], occurring uniquely as selenocysteine. These proteins appear to discharge the nutritional functions of Se, that is, prevent dysfunction associated with deficient Se intakes. Maximal selenoprotein expression appears to require dietary levels of 0.1–0.2 mg/kg for animals and daily intakes no more than 55 μg for humans [2].

The fact that Se can also be anticarcinogenic was suggested in the 1960s based on an inverse relationship of US cancer mortality rates and crop Se contents [3]. Subsequent studies [4–7] found blood Se levels inversely associated with the prevalence of several types of cancer. Animal studies [6] have shown anticarcinogenic effects for both inorganic and organic Se compounds at doses more than is needed for maximal selenoprotein expression. The Nutritional Prevention of Cancer Trial [8] showed that supplemental Se (200 μg Se/day as high-Se yeast) reduced the risks of total cancers and prostate and colorectal carcinomas. Although only a few other clinical trials have addressed this issue, most have indicated reduced cancer risk associated with Se treatment [5–7]; however, a recent one [9] found self-reported Se supplement use to be unrelated to prostate cancer risk.

Evidence indicates several mechanisms for Se anticarcinogenesis: altered carcinogen metabolism, cell cycle regulation, immune surveillance, cell death programming, cancer cell migration and angiogenesis [4–7]. As these effects occur at Se doses higher than those commonly encountered in diets (supranutritional), their molecular basis would appear to involve Se metabolite(s) increased under such conditions [4,6]. Studies [10,11] point to hydrogen selenide (H_2Se) and its methylated metabolite methylselenol (MeSeH) as active species, but selenomethionine (SeMet) may also have a role. Selenoproteins may also be involved, as differential cancer risk has been associated with allelic variants of some.

The efficacious use of Se for reducing cancer risk will demand knowing who can benefit from increased Se intake and what forms/levels are necessary. Answers will

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