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Cancer Chemoprevention - Is It Reality?

Melník M[1*], Tomo M[2], Raganová A[3], Kriška M[3], Kristová V[3] and Bohmer D[2]

[1]*Faculty of Pharmacy, Comenius University Bratislava, Slovakia*
[2]*Department of Biology and Genetics, Faculty of Medicine Comenius University, Bratislava, Slovakia*
[3]*Department of Pharmacology and Toxicology, Faculty of Pharmacy Comenius University, Bratislava, Slovakia*

[*]**Corresponding author:** Melník M, Faculty of Pharmacy, Comenius University Bratislava, Slovakia, E-mail: qmelnik@stuba.sk

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Abstract

Chemoprevention is proposed as a clinical analogue of population prevention, aimed at reducing likelihood of disease progression. It is know, that cardiovascular chemoprevention is successful, but what about chemoprevention of cancer? Many researches pay much attention to the selenium and its derivatives as promising anticancer agents. The improving bioactivity of selenium and its derivatives, some papers deal with a special combination of antioxidants and micronutrients, or with beta glucan and some studied inhibition of selenium nanoparticles on cancer cell or even prevention. The results help to elucidate not only anticancer effects but also chemoprevention of mixture studied, providing further evidence to exploit novel mixture agents for cancer chemoprevention.

Keywords: Selenium; Se Organic Derivatives; Antioxidants; Micronutrients; Glucan; Selenium Nanoparticles; Cancer Chemoprevention

Introduction

One of the most developing areas of pharmaceutical research is medicinal chemistry. One of the fundamental items in medical chemistry is the development of active new cancerostatic drugs. There are many studies which were focused in this area. One of the promising and perspective anticancer agents is selenium and its compounds. Selenium is an essential trace element with an inhibitory effect on many types of human cancer. Research opinion on the relationship between selenium and the risk of cancer has undergone radical change over the years. Much attention, especially for selenium supplement use and multivitamins and after diagnosis, is associated with risk of biochemical recurrence of prostate cancer [1], soft tissues cancer [2]. On the basis of clinical studies, can be proposed that the selenium supplementation - improved the general conditions of the patients with the cancer diseases, their quality of hope and reduced the vide effects of radiotherapy [3].

In general, it's well known, that cancer diseased is most spread in the human population. At the end of life the majority of such patients and their relatives are looking for complementary treatment approaches. Special acceptance is seen in methods of communicative and patient focused medicine. Basal stimulation and aroma therapy are also established components of modern palliative care [4].

In the modern medicine much attention is focused on the chemoprevention. Chemoprevention is proposed as a clinical analogue of population prevention, aimed at reducing likelihood of disease progression. For example, it is known that cardiovascular chemoprevention is successful via control of hyperlipidaemia and hypertension. But what about cancer chemoprevention? The aim of this review article is to show if cancer chemoprevention is real or not.

Cancer chemoprevention

The research studies which handling with the chemoprevention of cancer can be divided into the two groups, one with imaging proposed and another one with reality. The cancer chemoprevention is problematic, there is the evidence of a wide variety of agents and their largely deleterious, sometimes null, and in one case, large beneficial, consequences as a possible chemoprevention. These agents include beta-carotene, folic acid, retinol and retinoid, vitamin E, vitamin C, multivitamin supplements, calcium and selenium, as well as agents targeted at metabolic and hormonal pathways: statin, estrogen and antagonists, 5-alfa-reductase inhibitors [5].

Oral mucositis is a complication of high-dose of chemotherapy followed by haematopoiesis with few effective treatments. Selenium has a cytoprotective role via the glutathione peroxidase enzyme and prevents chemotherapy induced toxicities. Selenium can reduce the duration and severity of oral mucositis after high-dose chemotherapy [6].

The effects of Se-methyl-selenocysteine on the toxicity and antitumor activity of cyclophosphamide, cisplatin, oxaliplatin and irinotecan was studied in animal models. Se-methyl-selenocysteine affects selective protection against organo-specific toxicity induced by clinically active agents and enhances further antitumor activity, resulting in improved therapeutic index [7].

Selenium compounds have a role as a prevention approach to the problem of drug resistance which develops during ovarian cancer platinum chemotherapy (cisplatin, carboplatin). Selenium compounds can prevent the induction of resistance by platinum compounds in human ovarian tumors, and thus may offer an approach to extending the long-term efficacy of platinum chemotherapy [8].

The association between trace elements and efficacy of chemotherapy in patients with hepatocellular carcinoma was studied. In vitro sensitivity of cancer cells to five chemotherapeutic drugs (5-fluorouracil, doxorubicin, cisplatin, carboplatin and mitomycin) was tested using the 3-(4,5-dimethylthiazol -2-yl)-2,5 diphenyltetrazolium bromide assay in cancer cells from patients. Trace elements (zinc, copper, manganese and selenium) levels had the same gradient distribution in different liver tissues. Results suggest that the selenium and manganese content in primary hepatocellular carcinoma tissues could influence the response of the carcinoma cells to carboplatin and doxorubicin [9].

To clarify the effects of selenium level on the risk of gastric cancer and gastric cancer mortality, a meta-analysis was performed. This meta-analysis suggested that selenium might inversely associate with gastric cancer risk and gastric cancer mortality [10]. Quantification of the association between selenium and risk of oesophageal adenocarcinoma is still conflicting. The purpose of meta-analysis was to explore the relationship between selenium levels and oesophageal adenocarcinoma risk. The analysis indicated that a higher selenium level was not significantly associated with the risk of oesophageal adenocarcinoma [11].

Each year 490.000 people in U.S.A. are diagnosed with bladder cancer. Due to the high recurrence rate of the disease, primary prevention is paramount. Meta-analysis on modifiable risk factors of primary bladder cancer was reviewed. Probability of causation was calculated for individual factors and a subset of lifestyle factors was combined. Statistically significant associations were found for smoking, antioxidant supplementation, obesity, high intensity physical activity levels, higher body levels of selenium and vitamin D and higher intakes of processed meat, vitamin A, vitamin E, folate, fruit, vegetables, citrus fruit and cruciferous vegetables. Three occupations with the highest risk were tobacco workers, dye workers and chimney sweeps. The probability of causation for individual factors may range from 4 to 68%. The combined probability of causation was 82% [12].

The main goal of Meplan, *et al.* [13] was to elucidate whether expression of factors crucial for colorectal homoeostasis is affected by physiologic differences in selenium status. Integrating proteomics and transcriptomics datasets revealed reduced inflammatory and immune responses and cytoskeleton remodelling in the suboptimal selenium status group. This study combining omics technologies to describe the impact of differences in selenium status on colon rectal expression patterns, revealing that suboptimal selenium status could alter inflammatory signalling pathways and cytoskeleton in human rectal mucosa and so influence cancer risk.

Eradicating cancer stem-like cells may be essential to fully eradicate cancer. Metabolic changes in the cancer could hold a key to their targeting. There was reported that the dietary micronutrient selenium can trigger apoptosis of the cancer derived from chronic or acute myelogenous leukaemia when administered at supraphysiologic but nontoxic doses [14].

In vitro effects of the selenium compounds, sodium selenite and selenomethionine on cholangiocarcinoma cell growth and migration was examined to determine potential usefulness as anticancer agents. Both selenium compounds increased selenoprotein M in cholangiocarcinoma cells. The selenium may potentially be an alternative anticancer agent that might lead to a better prognosis in patients with cholangiocarcinoma [15].

Organic selenium compound have been documented to play a role cancer prevention in such a way that selenomethionine induces p^{53} activation without genotoxic effects including apoptosis and cell arrest. The mechanism by which organic selenium compounds promote p^{53} - mediated base excision repair activity was investigated. This may provide insight into the development of effective chemopreventive strategies against various oxidative stresses that contribute to a variety of human diseases, particularly cancer [16].

The term “epigenetics” refers to modification in gene expression caused by heritable, but potentially reversible, changes in DNA methylation and chromatin structure [17]. Epigenetic alterations have been identified as promising new targets for cancer prevention strategies as they occur early during carcinogenesis and represent potentially initiating events for cancer development. Over the years, nutri-epigenetics the influence of dietary components on mechanisms influencing the epigenome has emerged as an exciting new field in current epigenetic research. In paper are summarized the potential of natural chemo preventive agents to counteract these cancer-related epigenetic alterations by influencing the activity or expression of DNA methyltransferases and histone modifying enzymes [17]. The results demonstrate the functional relevance of epigenetic mechanism for health promoting or cancer preventive efficacy of natural products.

There are several studies used a nanomics approach combing bioinformatics and systematically investigate the Nano-bio interaction of selenium nanoparticles in cancer cells. From these studies, they conclude that selenium-nanoparticles could be used as potential candidates for cancer chemoprevention [18-21].

It is known, that the beta glucans are well established immunomodulatory agents with strong effects resulting in slowing or even inhibiting cancer growth. Recent studies have repeatedly suggested that the biological activities of beta glucan can be potentiated by the addition of other bioactive agents [22]. There was a study focused on the anticancer effects of a combination of yeast-derived beta glucan and a selenium linked pseudodisaccharide. Using three different models of murine cancer. Study showed that this combination strongly suppressed growth of all three types of cancers, most probably via stimulation of immunity, as well as via the interaction with natural anticancer antibodies [23].

There are several studies in which main goal being treated many patients for cancer use micronutrient supplements with the intention to complement the cancer treatment or help them cope with the therapy and dose-associated side effects [24-27]. There are many concerns that antioxidants might decrease the effectiveness of chemotherapy but increasing evidence suggests a benefit when antioxidants and other micronutrients, such as selenium, L-carnitine and vitamins are added to conventional cytotoxic therapies. Observational studies have suggested that antioxidant nutrients may reduce cancer and overall mortality risks. However, most randomized trials have failed to show survival benefits. Examining nonlinear associations between antioxidant levels and health outcomes may help to explain these discrepant findings [28].

Detail aspects of the treatment as well as chemoprevention's are discussed in the respective manuscripts, therefore will be not repeat in the review article.

Conclusions

Chemoprevention is proposed as a clinical analogue of population, aimed of reducing likelihood of disease progression. It is know, that cardiovascular chemoprevention is successful, but what about chemoprevention of cancer? This review brings brief view of such problem. The last decades researches pay a lot attention to the selenium and its compounds therefore that have been documented that they to play a role in cancer prevention. Selenium ions play an important role in biological systems, and without their catalytic presence in trace or ultra-trace amounts many essential co-factors for many biochemical reactions would not take place.

Improving activity of organic selenium derivatives, some authors used a combination of antioxidants with micronutrients, another one a special combination of beta glucan with organic selenium derivatives and some studied inhibition of selenium nanoparticles on cancer cells or even prevention.

So far, data are still mainly derived from in vitro investigations, and results of animal or human intervention studies are limited that demonstrate the functional relevance of epigenetic mechanism for health promising of cancer preventive efficacy of natural products. Epigenetic alterations have been identified as promising new targets for cancer prevention strategies as they occur early during carcinogenesis and represent potentially initiating events for cancer development. Over the past years nutri epigenetics - the influence of dietary components on mechanisms influencing the epigenome-has emerged as a screw field in current epigenetic research.

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