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The process of cancer. Part II. Selected plant compounds in cancer. Chemoprevention

Sylwia Jopkiewicz

Orcid: <http://orcid.org/0000-0001-5453-4751>

PhD student in the field of health sciences, Jan Kochanowski University,
Faculty of Medicine and Health Sciences, ul. Ages IX Kielce 19, 25-317 Kielce.

Address for correspondence: Sylwia Jopkiewicz, Jan Kochanowski University,
Faculty of Medicine and Health Sciences, ul. IX Wieków Kielc 19, 25-317 Kielce; tel.
797 186-370, e-mail: Sylwia.Jopkiewicz@wp.pl.

Summary:

Introduction and objective: Constantly increasing number of cancers, as well as too low efficiency of the treatment of advanced stages of the disease implies the search for effective action both in terms of primary prevention and secondary. The article comp is only an outline of selected compounds share vegetable chemoprevention of cancer. Its aim is to introduce the concept of chemoprevention and discussion of selected plant compounds and their impact on the process of carcinogenesis.

Description of knowledge: Method of connecting primary and secondary prevention is cancer chemoprevention. It uses natural and synthetic compounds to inhibit, delay or reverse the neoplastic process.

Glucosinolates found in cruciferous vegetables have potent biological properties applicable to the prevention of the carcinogenesis process. The best-known glucosinolates are sulforaphane and indole -3-carbinol. Curcumin is a natural agent having a broad antitumor effect. It is among the blocking and suppressive chemopreventive agents. Inhibits activation of cancer gene, tumor growth, cell proliferation and angiogenesis. Resveratrol shows efficacy in blocking all stages of carcinogenesis, while lycopene is a powerful antioxidant, which inactivates free radicals thereby reducing the DNA damage of the cell.

Conclusions: Chemoprevention is a method which may intervene in all stages of carcinogenesis, and the largest of its efficacy is observed in the initiation and promotion of cancer lesions. Some food ingredients have both a anticarcinogenic and cytostatic effects on cancer cells.

Key words: Chemoprevention, glucosinolates, curcumin, resveratrol, lycopene

Introduction

Tumor diseases hardly develop as a result of inheritance of certain predispositions. About 70% of human cancer arises from genetic defects and disorders of epigenetic. They are usually the result of long-term occupational or environmental exposure to various harmful external factors. They also stem from conducting unhealthy lifestyle [1,2].

Prevention of oncological traditionally divided into primary prevention and secondary. In the first pass all actions to be aimed at promoting awareness of tumors, and the factors which directly or indirectly contribute to both increase and reduce the risk of developing the disease [3]. While secondary prevention focuses on finding and treating asymptomatic individuals whoin the body appeared preneoplastic lesion or tumor cells [4].

Chemoprevention is focused on the use of non-toxic synthetic and natural bioactive substances in order to stop, slow down the process of tumorigenesis, and

reverting the changes already established tumors. It is based on the concept of multi-level ground and on wieloetapowości the carcinogenesis process [5,6].

Chemopreventive agents can be divided into two main groups, blocking agents, and tumor suppressor. The main task of blocking agents is to prevent direct interaction of carcinogens to DNA, RNA and cellular proteins, the inhibition of the metabolic activation of carcinogenesis and prevent the harmful factors to reach destinations. Suppressor factors act on the stage of the initiation or progression of tumors by inhibition of neoplastic transformation of cells [7,8]. The purpose of the cell cycle is the creation of two daughter cells containing the same genetic information as the original parent. The cell cycle consists of two phases: an interphase (the period of time between cell divisions) and mitosis (division). The so-called interphase stands out. G1, S and G2. At this stage of the synthesis of DNA. It is also a period of time, wherein it is possible to repair DNA damage in order to avoid mitosis to produce cells "error" caused by the interaction of various carcinogens. In all phases are called. checkpoints (called. check points). Their aim is to control the proper conduct of the cycle. When need be, these points lead to a temporary stop cycle that could lead to attempts to repair damage to the cells or to direct the path of apoptotic death. In many cancer cells checkpoints are inactive, which contributes to the perpetuation of damage caused, and thus the proliferation of diseased cells. Apoptosis is therefore one of the main defense mechanisms against cancer [9]. in order to avoid mitosis to produce cells "error" caused by the interaction of various carcinogens. In all phases are called. checkpoints (called. check points). Their aim is to control the proper conduct of the cycle. When need be, these points lead to a temporary stop cycle that could lead to attempts to repair damage to the cells or to direct the path of apoptotic death. In many cancer cells checkpoints are inactive, which contributes to the perpetuation of damage caused, and thus the proliferation of diseased cells. Apoptosis is therefore one of the main defense mechanisms against cancer [9]. in order to avoid mitosis to produce cells "error" caused by the interaction of various carcinogens. In all phases are called. checkpoints (called. check points). Their aim is to control the proper conduct of the cycle. When need be, these points lead to a temporary stop cycle that could lead to attempts to repair damage to the cells or to direct the path of apoptotic death. In many cancer cells checkpoints are inactive, which contributes to the perpetuation of damage caused, and thus the proliferation of diseased cells. Apoptosis is therefore one of the main defense mechanisms against cancer [9]. these points lead to a temporary stop cycle that could

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Most cancers is the result of long-term accumulation of DNA damage. Many of them work in parallel, mutually enhancing its influence on the process of carcinogenesis. For this reason, it is considered reasonable approximation issues chemoprevention and selected chemopreventive agents to be used both to reduce the risk of neoplastic process as well as the inhibition of progression of malignancies.

Antitumor properties of glucosinolates

Research shows that natural factors are chemoprewencyjnymi cruciferous vegetables (various kinds of cabbage, broccoli, radishes, cauliflower, Brussels sprouts) due to the presence of the so-called. glucosinolates. These compounds are secondary metabolites cruciferous. By contact with myrosinase enzyme, also present in the vegetables to form derivatives with potent biological properties applicable to the prevention of the carcinogenesis process. Currently we identified about 300 compounds belonging to the group of glucosinolates [10,11].

Glucosinolates are of utmost importance in primary chemoprevention. Healthy people, who in their diet include eating more cruciferous vegetables reduce the risk of cancerous changes. This is due to the fact that glucosinolates inactivate the free radicals scavenge reactive oxygen species, DNA repair processes running, and reduce the activity of these enzymes that activate carcinogens. Glucosinolates can also be used for chemoprevention secondary, consisting in reversing established cancer lesions and in assisting the cancer therapy, but these stages substances delivered through the plant body to have a limited effect [12,13]. Glucosinolates support the inhibition of angiogenesis, inflammatory processes, and allow degradation of malignant cells [14].

Sulforaphane (SFN) is a biologically active isothiocyanate, the largest amount found in broccoli sprouts and their. It is important in the process to block the action of carcinogens. supports metabolism and a process of removing mutagens and genotoxic

insults thereby reducing the risk of structural changes in DNA. Sulforaphane stage tumor promotion can prevent the expression of cells in which genetic changes have occurred, and reduce the formation of malignancies. These objectives at this stage are achieved thanks to the properties of SFN interference among others in proliferation, apoptosis or cell cycle [15,16,17]. They include SFN ability to inhibit the enzyme histone deacetylase (HDAC) inhibitor can block the cell cycle, differentiation, and stimulation of tumor cell death. It should be noted that the formation of disturbances in the mechanisms responsible for the control of these areas is caused by excessive activity of this enzyme in the cell [16,18].

Indole-3-carbinol (I3C), together with their derivatives exhibit a strong action in the area of prevention of cancer because it stimulates the detoxification of carcinogens by inducing factors, enzymes I and Phase II detoxification. The carcinogen activation of enzymes involved in phase I, and in the process of neutralization by enzymes phase II. I3C compound arrests the cell cycle, induce apoptosis, promotes DNA repair processes and inhibits proliferation of tumor cells [19]. Scientific studies have shown I3C efficacy in preventing cervical cancer, breast and endometrium, by the antagonistic actions to estrogen and inhibition of the transcription of genes that are responsible for coding the estrogen receptors [20]. Furthermore, after oral administration of I3C regression was observed endothelial neoplasia in the case of cervical cancer [21].

The highest concentrations of glucosinolates found in fresh vegetables that are not subjected to any heat treatment, since the greatest loss of these substances takes place during the cooking process. This is due to the fact that the glucosinolates are very soluble in water [23]. In order to reduce the loss of the concentration of these compounds in the process of their preparation for use it is recommended to add powdered mustard, which retains an adequate level of glucosinolates in the product [13].

Curcumin and its role in cancer chemoprevention

Curcumin is a polyphenol, which is present in the rhizomes turmeric (*Curcuma longa*). Is used as a natural flavoring and coloring of food products, for example. Margarine [24]. Because of the broad spectrum of action, it includes both blocking and suppressive chemopreventive agents. At the stage of initiation has the ability to inhibit carcinogen activation and tumor growth, whereas at later stages

inhibits malignant cell proliferation and angiogenesis [25]. It also contributes to preventing metastasis and apoptosis. The process of metastasis (metastatic) is associated with the growth and activity of metalloproteinases (MMP) secreted by tumor cells. MMP-2 (gelatinase A) and MMP-9 (gelatinase B), cause the destruction of collagen IV, which is the basement membrane of the tumor. As a result, the tumor cells moving through the vascular system have the ability to populate the other organs. Animal studies have shown that curcumin is an inhibitor of metalloproteinases these two. It inhibits the growth and results in a decrease of MMP-2 and MMP-9. In addition, curcumin also inhibits synthesis of nuclear transcription factor NF- κ B (ang. Nuclear factor kappa B), and vascular endothelial growth factor, which stimulates angiogenesis required for tumor growth [26,27]. The expression of NF- κ B may occur in the course of inflammation and is one of the indicators of activity neoplastic tissue. The best known is the factor NF- κ B p65 / p50, which is composed of two proteins. It is present in every cell functioning properly. Consequently, this is one of the causes of tumor development through the increase in cell proliferation, angiogenesis and inhibition of apoptosis. Research shows that in the process of carcinogenesis and tumor aggressiveness level plays a significant role abnormal transcriptional regulation NF- κ B p65 / p50 [28,29,30,31].

Resveratrol and its antitumor activity

resveratrol (trans-3,5,4'-trihydroxystilben) polyphenol is classified as a group of phytoalexins produced in response to attacks on the plant variety of pathogens (viruses, fungi, insects) and due to a strong stressor (e.g. UV radiation). It is, among others, in peanuts variables red dry wine, grapefruit, grapes, fruit mulberry [32,33]. Is a compound which exhibits efficacy in blocking all stages of carcinogenesis. It is involved in the metabolism of detoxification of carcinogenic agents (activated enzyme Phase II detoxification) and contributes to the removal of reactive oxygen species (ROS) [34,35]. Resveratrol plays a key role in reducing the activity of compounds belonging to the cytochrome P450 (CYP). Scientific studies have shown that by reducing effect of resveratrol on the expression and activity of these compounds, the cells of the body are protected from various carcinogens include polycyclic aromatic hydrocarbons. It should be noted that cytochromes are those compounds that contribute to the generation of ROS and participate in increasing the activity of carcinogenic agents [35,36]. Resveratrol is inhibitory to the DNA polymerase and

ribonucleotide reductase, thereby limiting Filmaster cancer [36]. Chemopreventive activity of resveratrol is also connected to its antiangiogenic action. It affects the reduction of the production of mediators of angiogenesis, especially vascular endothelial growth factor (VEGF), which in turn reduces the vascularization of the tumor. It therefore reduces the possibility of the appearance of metastasis and invasion of cancer [37,38]. In addition, resveratrol increases the effectiveness of chemotherapy through the inactivation of NF-kB protein. The result is a slowing down tumor cell proliferation and a decrease in their resistance to this form of therapy [39]. Research shows that it reduces the risk of, among others, breast, prostate and colon. Inhibits the proliferation of androgen-dependent and androgen-independent prostate tumor cells because it blocks the function of the androgen receptor. Exhibits an antiproliferative and pro-apoptotic tumor cells in the large intestine [40,41]. The result is a slowing down tumor cell proliferation and a decrease in their resistance to this form of therapy [39]. Research shows that it reduces the risk of, among others, breast, prostate and colon. Inhibits the proliferation of androgen-dependent and androgen-independent prostate tumor cells because it blocks the function of the androgen receptor. Exhibits an antiproliferative and pro-apoptotic tumor cells in the large intestine [40,41]. The result is a slowing down tumor cell proliferation and a decrease in their resistance to this form of therapy [39]. Research shows that it reduces the risk of, among others, breast, prostate and colon. Inhibits the proliferation of androgen-dependent and androgen-independent prostate tumor cells because it blocks the function of the androgen receptor. Exhibits an antiproliferative and pro-apoptotic tumor cells in the large intestine [40,41].

Lycopene

Lycopene is a carotenoid, which is soluble dye plant fat. It does not have the properties of provitamin A. The highest concentrations occur among in tomatoes, red peppers, pink and red grapefruit and watermelon. It should be noted, however, that this compound is better absorbed from processed tomatoes than raw tomatoes [42].

Lycopene has strong antioxidant properties. This ability is related to its construction. The structure is lipoken 11 conjugated double bonds, allowing it to a chemical reaction of molecules containing unpaired electrons. In addition, open ring carotenoid lycopene, decides that he is definitely a better antioxidant than β - carotene and α - tocopherol [43,44]. Two times more efficiently than β - carotene and ten times

the α -tocopherol "sweeps" singlet oxygen [45]. The reactive oxygen species formed by reaction of hypochlorous acid (HOCl) from hydrogen peroxide. HOCl is a powerful oxidant and precursor to chloramines [46]. Increased capacity of antitumor lycopene is also connected with the fact that the compound in the serum binds to PDGF-BB (ang. platelet-derived growth factor). PDGF-BB is a platelet derived growth factor BB, which has a pro-angiogenic. It affects the invasiveness, frequency division and metastasis of cancer cells. Lycopene also inhibits the activity of MMP-2 and MMP-9 [47]. It also causes cell cycle arrest in the G1 phase, in which the entry cell in the next stage of replication and initiation of DNA synthesis. Inhibits the expression of cyclin D and E [48]. Cyclins are proteins whose concentration depends on the phase of the cell cycle. These decision-makers whether a cell can enter the next stage of life. The correct expression of cyclins is essential for normal cell proliferation while the problems in this area can cause malignant transformation [49].

Lycopene inactivates insulin growth factor (IGF-1), which is important in the control of growth, survival, metabolism, and proliferation. High levels of free and bioactive IGF-1 enhances the development of a tumor [50].

Lycopene reduces the risk of cancers of digestive tract, lung, breast, liver, ovarian and leukemia [44]. In addition this compound in most accumulates in the cells of the prostate, and therefore prevents the development of breast cancer [51]. Research shows that the food from 2 to 4 servings per week raw tomatoes reduces the risk of this type of tumor. This risk can be even further reduced by consuming these vegetables in a processed form (eg. Ketchup, sauces, tomato soup, tomato paste) [52].

Summary:

Chemoprevention is the first method that can interfere in all stages of carcinogenesis, and the greatest efficiency is observed in the initiation and promotion of cancer lesions. It may be an alternative to the still ineffective anticancer therapy.

2. Some food ingredients have anticarcinogenic effects both as and cytostatic to tumor cells. The appropriate choice in their daily diet can help to reduce the risk of cancer progression of the disease, or even a reversal.
3. The biologically active food ingredients, among others, destroy free radicals and various factors that cause DNA damage, stimulates repair processes in the cells, inhibit cell proliferation, angiogenesis, metastasis. They also have a pro-apoptotic activity.

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