

## Impact of diet on the risk of breast cancer

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### Abstract

This work concerns the issue of women nutrition in the prevention of breast cancer, which is the most common malignant tumour and the second death related cancer of the females. The aim of the work is to present types of diets, the use of which can reduce the risk of breast cancer. The article refers the chemo preventive action of substances naturally present in foods such as plant polyphenols, dietary fibre and polyunsaturated omega-3 fatty acids. The presented review confirms that they are able to reverse, inhibit or delay the process of carcinogenesis, as a result of the apoptosis initiation, anti-inflammatory and antioxidant effects and by inhibition of angiogenesis and proliferation. The described compounds may also reduce estrogen concentration and prevent the development of obesity. Most of the experiments carried out so far prove that overweight and obesity, excessive consumption of products with a high glycaemic index, alcohol and red meat are factors contributing to the

occurrence of breast cancer. However, not all epidemiological data are unambiguous in this matter. Mediterranean, vegetarian, Asian and low glycaemic index diets, through the synergistic interaction of nutrients contained in them, most effectively reduce the risk of breast cancer.

**Keywords:** breast cancer, chemoprevention, antineoplastic diets

## **Introduction**

Breast cancer is the most common malignant tumour in women and the second most common cause of cancer deaths in female. Therefore, chemoprevention becomes more and more important - a strategy that is based on the use of bioactive substances naturally present in foods to inhibit, slow down or reverse the process of carcinogenesis. It is rational to look for a nutrition model with high anticancer potential, consisting of biologically active food ingredients such as carotenoids, dietary fibre, polyunsaturated omega-3 fatty acids, vitamins and minerals, and plant polyphenols. Mediterranean, vegetarian, traditional Asian and low glycaemic index diets are sources of compounds with antioxidant, anti-angiogenic, anti-mutagenic and anti-inflammatory properties thus they can have beneficial effects in preventing breast cancer [1].

## **Purpose of work**

The aim of the work is to present the types of diets which use has an inhibitory effect on the development of mammary gland cancer, presentation of food components that prevent and promote the process of carcinogenesis.

## **Mediterranean diet**

The Mediterranean diet is characterized by a balanced composition of food products, including in the first place whole-grain cereal products, followed by a large amount of fruits, vegetables, nuts, seeds and legumes. It also has a favourable ratio of omega-6 to omega-3 fatty acids, which is about 2:1. The main source of fat in this nutrition model is olive oil, added to various dishes. Dairy products are mainly consumed in the form of yoghurts and cheeses, while fish and poultry are consumed in moderate amounts. An inseparable element of a daily menu is garlic, onion and other spices such as basil, oregano, rosemary, thyme or

cumin. In the smallest amounts, red meat, eggs and sugar are eaten. The diet typical of Mediterranean inhabitants contains very low level of substances adversely affecting health, such as saturated fatty acids, trans fatty acids or cholesterol. It consists of many components that are necessary for the proper functioning of the human body: unsaturated fatty acids, antioxidant vitamins and minerals. It is also rich in carotenoids, phytoestrogens, polyphenols and dietary fibre, which play an important role in cancer prevention [2, 3]. One of the studies confirming the relationship between the Mediterranean diet and the reduced risk of breast cancer is a study conducted in Spain. Qualified women aged 60-80 were randomly assigned to three groups, each of which used a different diet - Mediterranean with the addition of olive oil, Mediterranean with added nuts or a control diet (with a reduction in the supply of fats). After an observation lasting about 5 years, 35 cases of mammary gland cancer were identified. Participants assigned to the group using the Mediterranean diet with additional supplementation of olive oil were 62% less likely to develop breast cancer, and women receiving an additional 30 g of nuts by 38% compared to those assigned to the control group [4]. As part of the EPIC research program, the compliance of the diet used by Greek women with the traditional Mediterranean diet was assessed using a 9-point scale, where 0 meant minimum compliance with this diet model, and 9 maximum compliance. The increase in compliance of the diet by 2 points reduced the possibility of breast cancer by 22% in women after menopause. In the entire study population, 10% of the disease could be prevented if all participants changed their diet to a more similar to the Mediterranean, i.e. a score was changed to 6 points or higher [5]. Bosetti et al. confirmed that the use of this model of nutrition reduces the probability of the breast cancer development by 15% [6].

### **Olive oil**

Olive oil contains many nutrients with health-promoting effects such as: monounsaturated fatty acids (including oleic acid), phenolic compounds, vitamin E, squalene, lignans, carotenoids (lutein,  $\beta$ -carotene, xanthophylls, chlorophylls). These antioxidants neutralizes reactive oxygen species (ROS) which, by damage to the genetic material of cells, can initiate the process of carcinogenesis. Studies have shown that polyunsaturated fatty acids from the omega-3 family are also present in olive oil [7].

### **Alcohol**

Regular, excessive alcohol consumption leads to a deficiency in the body of antioxidants (zinc, folic acid) and can raise the level of estrogen in the blood serum. Estrogens and their metabolites are compounds that affect the process of carcinogenesis in estrogen-dependent tissues. After penetrating the interior of the cell and activating intracellular nuclear receptors,

they enter to the cell where they bind to DNA and affect many genes. Through this mechanism they can contribute to the transformation of proto-oncogenes into oncogenes, inhibit apoptosis in the epithelium of the mamma and stimulate cell proliferation [8, 9]. Reichman et al. [10] investigating women aged 21-40 showed that consumption of 30 g ethanol daily for 3 menstrual cycles increases plasma estrone concentration by 21.2% and estradiol by 27.5%. Contrary results were obtained by Dorgan et al. stating that alcohol consumption is not related to the concentration of estrogens in the blood at any stage of the menstrual cycle [11]. Narod proved that women who drank  $\geq 2$  portions of alcohol a day had a 1.5 times higher risk of breast cancer compared to abstinent women (one portion means 10 g of pure ethanol) [12]. The liver participates in the neutralization of toxins and the breakdown of estrogens. Alcohol abuse can damage hepatocytes and lead to disturbed metabolism of female sex hormones and stimulation of androgen conversion to estrogens. This leads to an increase level of estrogens in the blood, which increases the probability of the mammary gland cancer development [13]. However, in the Mediterranean diet, alcohol (mainly wine) is only served with meals and has no significant impact on the overall risk of breast cancer. Wine is a rich source of polyphenols. One of them is resveratrol, which limits inflammatory processes, initiates apoptosis, inhibits tumour cell proliferation and angiogenesis [14]. There is necessary to limit alcoholic beverages and not exceed the recommended doses - 2 drinks a day for men and 1 drink for women. This supply of alcohol is in line with the principles of the Mediterranean diet [8].

### **Diet with a low glycaemic index**

Hyperinsulinemia and insulin resistance are of great importance in the pathogenesis of breast cancer. The high glycaemic index of the diet contributes to the development of insulin resistance. Food with a high glycaemic index (sweets, cakes, tropical fruit, white bread, pasta and rice) quickly and significantly raises the level of glucose in the blood, which in turn stimulates the secretion of insulin and IGF-1. These products also quickly (after 1-2 hours of their consumption) cause a reduction in the level of glucose, often to values lower than those observed on an empty stomach. This condition is called hypoglycaemia and is manifested by a feeling of hunger, which induces the desire to eat another meal, which will cause an even greater increase in glycaemia [15]. Hyperglycemia is the cause of oxidative stress. Oxidative stress is an imbalance between ROS activity and the ability to detoxify and repair caused by antioxidant systems. This results the damage of proteins, sugars, lipids and genetic material, which can lead to mutations in DNA. Mutations in suppressor genes (p53, BRCA-1) and proto-oncogenes that control the growth and differentiation of cells contribute to the

development of cancer [16, 17]. Hyperinsulinemia reduces synthesis in the liver and levels of SHBG (sex hormone binding globulin) circulating in the blood and increases the concentration of IGF-1, which interacts with estrogen on mammary epithelial cells stimulating angiogenesis. In addition, insulin secretion stimulates the storage of glucose and triglycerides through adipose tissue, which contributes to weight gain, whilst overweight and obesity are risk factors for breast cancer [18, 19]. According to the results obtained by Neuhouser et al. [20], women with BMI  $\geq 35$  kg / m<sup>2</sup> in the postmenopausal age had a higher probability of breast cancer by 58%, compared to participants with normal body weight. This is because in overweight and obese people the conversion of androgens (including testosterone) to estrogens (including estrone and estradiol) is increased by the action of aromatase - an enzyme produced by adipose tissue. Adipose tissue is also an organ that secretes insulin into the blood and insulin-like growth factor (IGF-1) [18, 19]. Barclay et al. [21] noted in a meta-analysis that foods with high glycaemic index (GI) and glycaemic load (GL) increase the risk of breast cancer. Pre-menopausal women with the highest IG ( $> 57.5$ ) and GL ( $> 133.7$ ) of the whole day diet had a higher risk of cancer in comparison with the participants with the lowest IG ( $<53.5$ ) and LG ( $<103.2$ ). A study by Cho et al. [22] proved that in participants with overweight or obesity, whose diet was characterized by the highest glycaemic load, the risk of development mammary gland tumour was 1.6 times higher than in women who consumed lower GL foods.

### **Vegetarian diet**

The classic vegetarian diet consists of nutrition exclusively with plant-derived products, such as grain, oily, root and leguminous plants, fruits, vegetables, nuts and mushrooms. However, existing mild varieties of vegetarianism allow the consumption of fish, poultry, eggs and dairy products. The most commonly practiced and the best known is lacto-ovo-vegetarianism, which in addition to plant products allows the consumption of eggs and dairy products [2]. Lanou and Severson [23] in their review, assessed that this diet, due to the supply of anti-carcinogenic nutrients and the abandonment of red meat consumption, reduces the risk of cancer by 10-12%. Red meat contains a lot of saturated fatty acids increasing cholesterol concentration. Cholesterol is the precursor of estrogen. Thus the more cholesterol production in the body causes the higher concentration of estrogen in the blood [24]. Cho and al. [25] demonstrated that pre-menopausal women, who daily consumed about 90 grams of red meat, had twice higher risk of breast cancer comparing to those who consumed red meat no more than 180 grams weekly. Vegetarian diet consists of products from plant origin, which are a rich source of vitamins A, E, C, dietary fibre and polyphenols having a chemo preventive

effect. In people using this model of nutrition there is a low concentration of insulin, growth factors (IGF-1) and estrogen, which can initiate the process of carcinogenesis. The risk of cancer is higher in obese people, and the vegetarian diet allows to maintain proper body weight and promotes a slim figure [2]. Lanou and Severson showing EPIC study, according to which, after approximately 12 years of observation of 61 566 Britons, cancers were detected in 2 204 participants eating meat, 829 vegetarians and 317 people eating fish. Vegetarians had a lower risk of cancer by 12%, while those surveyed consuming fish by 18% compared to the group consuming meat. In addition, it was observed that vegetarians had a lower weight than those who eat all food ingredients by 3-20% and a lower risk of obesity. [23].

### **Fruits and vegetables**

Fruit and vegetables, which are the basis of a vegetarian diet, are a source of vitamins, polyphenols and carotenoids that neutralize free oxygen species. The aforementioned ellagic acid present in raspberries, strawberries, cranberries, grapes and strawberries, inactivates carcinogenic compounds, inhibits aromatase activity and has antioxidant activity. In turn, anthocyanins, responsible for the intense colour of plant products, can stop the process of angiogenesis [26]. Ellagic acid has anti-inflammatory and antioxidant properties. Adams et al. [27] found that the metabolite of ellagic acid - urolithin B, which arises under the influence of bacterial flora in the human gastrointestinal tract, inhibits aromatase activity. Thus, it reduces the level of female sex hormones in the blood. A study conducted by J. Kruk [28] on a group of 257 women with histologically confirmed breast cancer showed that in the study subjects who were low and moderately physically active in their free time consuming fruits and vegetables, the risk of mammary gland cancer was 80% lower compared to those eating rarely these products. Increased consumption of fruit and vegetables did not reduce this probability in women with high physical activity. Fruits and vegetables are a source of dietary fibre. Fibre removes heavy metals and toxins from the gastrointestinal tract, reduces postprandial blood glucose concentration, increases the time of satiety and limits the amount of meals consumed during the day, prevents excessive body weight and hyperinsulinaemia [29]. A prospective American study lasting 7 years, carried out on 185 598 women in the postmenopausal age in the average age of 62 years old, showed that the participants taking with the diet the largest amounts of fiber (26g/d) had a reduced probability of breast cancer by 13% compared to those who consumed it in the amount of 11g/d [30]. The anti-cancer effect of fiber results from its ability to reduce the concentration of estrogens in the blood, by inhibiting their reabsorption in the large intestine and increasing the removal of their excess with the stool [31].

### **Traditional Asian diet**

The traditional Asian diet is derived from southern and eastern Asia, and more specifically from such countries as India, Japan, China and Korea. It is characterized by low energy density of consumed food products and a small amount of saturated fatty acids, and a high content of dietary fibre, vitamins and minerals. It is dominated by vegetable products - rice, soy, cruciferous vegetables, dark green leafy vegetables, nuts, seeds, fruits and various herbs and spices, such as ginger and garlic. Meals abound with fish and seafood. Meat, poultry and dairy products are consumed in small quantities and rarely. Asians often drink green tea, and the main source of fats in their diet are oils containing polyunsaturated fatty acids [2].

### **Polyunsaturated omega-3 fatty acids**

The essential unsaturated fatty acids include fatty acids from the omega-3 family. This family represents  $\alpha$ -linolenic acid (ALA), a precursor of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). EFAs are not synthesized in the human body, therefore they must be supplied with food. They occur in foods such as fish (herring, mackerel, tuna, trout), seafood (mussels, oysters, shrimps), vegetable oils (linseed oil and rapeseed oil) [32]. A study conducted by Kim et al [33] on 358 Korean patients diagnosed with breast cancer and 360 healthy women in the postmenopausal period showed that participants whose diet delivered more than 0.101g/d of EPA and above 0.213g/d of DHA had a reduced incidence of breast cancer by 62% and 68%, respectively, compared to those consuming 0.014g of EPA and 0.037g of DHA during the day. The chemo preventive action of omega-3 acids is probably due to their ability to inhibit tumour cell proliferation, angiogenesis and lipogenesis, induce programmed cell death and enhance the immune response [34].

### **Soy**

Soy is a source of folic acid, calcium, lignans, dietary fibre and isoflavones (genistein, daidzein). Isoflavones are classified as phytoestrogens. They are characterized by similarity in terms of chemical structure to female sex hormones and affinity to estrogen receptors, thus they can compete with estrogens for access to them. By taking their place, they block the development of hormone-dependent breast cancers [35]. A meta-analysis of studies conducted in Asian women confirmed that moderate consumption of soy, amounting to about 10 mg of isoflavones daily, reduces the likelihood of the development of breast cancer by 12% compared to the lowest level of their consumption ( $\leq 5$ mg/d). Participants receiving the largest amounts of isoflavones ( $\geq 20$ mg/d) with food had a 29% reduction [36]. Tofu is obtained from soya milk. Hirose et al. [37] showed that a diet rich in tofu and isoflavones has a protective effect on breast cancer development. Women taking the highest amounts of tofu

(31.3g/1000 kcal) and isoflavones (18.47mg/1000 kcal) had a reduced probability of this type cancer development by 51% and 56% respectively, compared with those who consumed the smallest amounts, i.e. 8.9g/1000 kcal tofu and 7.61mg/1000 kcal isoflavones. Study conducted in China confirmed high consumption of soy ( $\geq 10.6$  mg isoflavones / 1000 kcal daily) reduces the risk of breast cancer by 26% in postmenopausal women. In the group of participants with BMI  $\leq 24$  kg/m<sup>2</sup>, the probability was 17% lower, and those with BMI  $> 24$ kg/m<sup>2</sup> were 33% lower compared to those who were taking isoflavones at  $<10.6$  mg / 1000 kcal [38 ]. The relationship between soybean consumption during childhood and the possibility of mammary gland tumours development was demonstrated by Korde et al. [39]. Women eating soybeans from 1 to 1.5 times a week and 1.5 times weekly or more at the age of 5-11 years old, had a lower risk of breast cancer by 57% and 60% respectively compared to those who consumed soy in their childhood less than once weekly.

### **Green tea**

An infusion of green tea - a pale yellow drink, with a tart and bitter taste, is obtained from the leaves of a tea bush not fermented. To produce green tea, fresh leaves are scalded or dried at high temperature immediately after collection, resulting in minimal oxidation of the catechins present in them. Catechins can block the damage of genetic material by limiting the formation of ROS or more efficiently through the neutralization by phase II enzymes. Thus, they can be used to inhibit, reverse or delay the process of carcinogenesis at the initiation and promotion stages. They are also responsible for the differentiation and proliferation of adipocytes, preventing the onset of obesity, which is one of the risk factors for breast cancer. Catechins include epigallocatechin-3-gallate (EGCG), constituting 50-80% of this group [40]. Examples properties of EGCG are: induction of apoptosis, anti-inflammatory and antioxidant features, inhibition of carcinogenesis at the initiation stage, ability to arrest the cell cycle and angiogenesis. It is 25-100 times more effective antioxidant than vitamin C or vitamin E [2]. Numerous studies have confirmed that regular consumption of green tea increases the activity of antioxidant enzymes in the body (superoxide dismutase, catalase, S-transferase, reductase and glutathione peroxidase and quinone reductase) [40]. A meta-analysis of epidemiological studies by Sun et al. [41] showed that consumption of  $\geq 3$  cups of green tea daily reduces the probability of breast cancer by 20%. In turn, during a study conducted in Shanghai by Shrubsole et al. [42], it was noted that regular consumption of this type of tea reduces the risk of breast cancer by 12%. The result was similar in both women before and after menopause.



## **Conclusion**

Breast cancer is classified as diet-dependent cancers, so one of the factors responsible for its occurrence is incorrect nutrition, which is the cause of about 25% of all cases. Mediterranean, vegetarian, Asian or low glycaemic index diets contain many valuable components (carotenoids, polyphenols, vitamins, dietary fibre, omega-3 polyunsaturated fatty acids), which due to their synergistic effects can have anticancer effects. The products that are the basis of these diets are a source of antioxidants, reduce estrogen level and help maintain proper body weight. In addition, they protect against the occurrence of hyperinsulinemia, which increases the concentration of IGF-1, and reduces SHBG in the blood serum, consequently increasing the risk of developing breast cancer. Only the use of a diet containing all valuable ingredients in the right proportions, is able to keep the human body in proper health condition and prevent breast cancer.

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