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REVIEW

Micronutrients in Preventing Cancer: A Critical Review of Research

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Abstract

About 30–40 percent of all cancers can be prevented by adopting a proper lifestyle and dietary measures. Obesity, sugars and refined flour products that contribute to impaired glucose metabolism (which leads to diabetes), low fiber intake, consumption of red meat, and imbalance of omega 3 and omega 6 fats all contribute to excess cancer risk. However, intake of flaxseed, especially its lignan fraction, and abundant portions of fruits and vegetables will lower cancer risk. Garlic, which contains Allium, cruciferous vegetables, and broccoli sprouts being the richest source of sulforophane, are especially beneficial, for cancer prevention. Protective elements in a cancer prevention diet include all the micronutrients, such as, selenium, folic acid, vitamin B-12, vitamin D, chlorophyll, and antioxidants such as the carotenoids (α-carotene, β-carotene, lycopene, lutein, cryptoxanthin). Further, Ascorbic acid has limited benefits orally, but could be very beneficial intravenously. Supplementary use of oral digestive enzymes and probiotics also has merit as anticancer dietary products. When a diet is compiled according to the proper guidelines, there would be at least a 60–70 percent decrease in breast cancers, colorectal cancers, and prostate cancers, and even a 40–50 percent decrease in lung cancer, along with similar reductions in cancers at other sites. Such a diet would be conducive in preventing cancer and would favor recovery from cancer as well.

Keywords: Nutrition- micronutrients- cancer- epidemiology- prevention- antioxidants- vitamins

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Introduction

Cancer is one of the leading causes of death worldwide. Over the past half century, much progress has been made in improving treatments for patients with cancer. Yet, the mortality rate from cancer remains unacceptably high. A significant percent of all cancers can be prevented by administering appropriate diets, physical activity, and maintenance of physiological body weight [1-3].

However, there is yet to learn how to catalyze effective prevention of cancer globally through diet, and micronutrients. Here we will discuss about: (i) Dietary factors which can increase the risk of cancer; (ii) Dietary factors which are anti-carcinogenic; and (iii) What to eat and what not to eat, when a person already has a cancer.

A. Carcinogenic effects of Foods

Processed Meat: Processed meat contains various preservative to restore color, flavor, etc. Observational studies demonstrated that consuming processed meat are closely associated with an increased risk of cancer, colorectal cancer [4]. However, linking unprocessed red meat to cancer is weak and inconsistent [5].

Overcooked Food: Cooking at high temperatures, like grilling, frying, sautéing, broiling and barbequing, of certain foods can produce harmful heterocyclic amines (HA) and advanced glycation end-products (AGEs). Those in turn may cause the development of cancer and other diseases [6].

Sugar and Refined Carbs: Glucose feeds every cell in our body, including the cancer cells Sugar and it's relationship to higher levels of insulin and insulin-like growth factors (IGFs) influence cancer cell growth and other chronic diseases. Many types of cancer cells have plenty of insulin receptors, making them respond more than the normal cells to insulin and IGFs ability to promote

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cancer cell growth [7-8].

People with diabetes — a condition characterized by high blood glucose and insulin levels — have an increased risk of certain types of cancer, particularly colorectal cancer [9]. Therefore, to protect from cancer, it is better to limit or avoid foods that boost insulin levels, such as foods high in sugar and refined carbs.

B. Overweight or Obese is Linked to Increased Cancer Risk

Obesity is one of the biggest risk factor for cancer worldwide [10]. It increases the risk of 13 different types of cancer, including of the esophagus, colon, pancreas and kidney, as well as breast cancer after menopause. In the US, estimated weight problems account for 14% and 20% of all cancer deaths in men and women, respectively [11]. Obese people tend to have higher levels of inflammatory cytokines in their blood, which causes chronic inflammation and encourages cells to divide [12].

• Fat cells contribute to increased estrogen levels, which increases the risk of breast and ovarian cancer in postmenopausal women [13].

• Several studies have shown that weight loss among overweight and obese people is likely to reduce cancer risk [14].

C. Dairy Products and Cancer

Several observational studies have indicated that high dairy consumption may increase the risk of prostate cancer [15]. One study result with almost 4,000 men showed that high intakes of whole milk increased the risk of prostate cancer progression and death [16]. More research is needed to determine possible cause and effect.

D. Gluten and Risk of Cancer

There is no connection between gluten and risk of most cancers. In fact, numerous observational studies show that the more whole grains a person eats, including the gluten-containing grains (wheat, rye, barley, and triticale), the lower his or her risk of most cancers. This is true for some of the most common types of cancer, such as breast, prostate, and colon cancers, as well as for less common cancers, such as cancer of the pancreas [17].

E. Family history of cancer

Women whose mother, daughter, or sister have ovarian cancer, they have an increased risk of the disease. Also, family history of breast, uterus, colon, or rectum cancer may also indicate an increased risk of ovarian cancer for that woman. Other considering factors are: Ovarian cancer rates increase with age. Most women are over age 55 when diagnosed with ovarian cancer. Elderly women who have never been pregnant have an increased risk of ovarian cancer.

Some studies have suggested that women who take estrogen by itself (estrogen without progesterone) for 10 or more years may have an increased risk of ovarian cancer.

F. Prevention of Cancer

Many prostate cancer specialists believe that the differences in diet are one of the biggest reasons for different numbers of prostate cancer in different parts of the world.

In general, a plant-based diet is associated with lower risk of prostate cancer. A plant-based diet that are minimally processed, and whole plant foods, such as vegetables, fruit, legumes, nuts, seeds, and whole grains should be adopted for preventing cancers. Lean protein from healthful sources, such as fatty fish (salmon, sardines, and others), also can be part of a diet plan designed to reduce prostate cancer risk, or risk of recurrence.

As well, the healthy lifestyle intervention increases relative telomere length, and longer telomeres protect DNA, our genetic material, from damage. This, in turn, may be protective against chronic diseases, including cancer.

G. Anti-carcinogenic effects of Foods

• Cancer Fighting Foods: Many nutrition recommendations for cancer prevention include eating more fruits and vegetables, which are often the best sources of phytochemicals, and reducing in the consumption of red and processed meats. The American Cancer Society offers practical recommendations on Nutrition and Physical Activity for cancer survivors [18-19].

Specifically some of them are:

(i) Beans and Legumes: Beans and legumes are high in fiber, and some studies suggest that higher intake of this nutrient may protect against colorectal cancer. One study with over 3,500 people found that legumes in diet can lower the risk of certain types of cancers by ~50% [20].

(ii) Nuts: Regularly eating nuts may be linked to a lower risk of certain types of cancer. For example, one study in more than 19,000 people found that those who ate more nuts had a reduced risk of dying from cancer [21].

(iii) Olive Oil: Many studies show a link between olive oil and reduced cancer risk. One large review of observational studies found that people who consumed the highest amount of olive oil had a 42% lower risk of cancer, compared to the control group [22].

(iv) Garlic: Allicin, which is present in garlic, has been shown to have cancer-fighting properties in vitro [23]. Other studies have found an association between garlic intake and a lower risk of specific types of cancer, including stomach and prostate cancer [24].

(v) Fish: There is evidence that eating fresh fish can help protect against cancer, possibly due to healthy fats that can reduce inflammation. A large review of 41 studies found that regularly eating fish reduced the risk of colorectal cancer by 12% [25].

(vi) Flaxseeds: Flaxseeds have been associated with protective effects against certain cancers and may even reduce the spread of cancer cells. To understand potential effects of flaxseed and how they may affect breast cancer, it helps to understand what flaxseeds are, and why some consider them a concern for women with a history of breast cancer.

Flaxseed and phytoestrogens: Flaxseed is the richest dietary source of lignans, a type of phytoestrogen [26].

A phytoestrogen is a plant nutrient that is somewhat similar to the female hormone estrogen. Due to this similarity, lignans may have estrogenic and/or anti-estrogenic effects in the body. Lignans are the nutrients that are at the center of the controversy regarding whether it is safe for women with breast cancer to eat flaxseeds [27-28].

Phytoestrogens are found in a variety of foods, including soy, flaxseeds, other nuts and seeds, whole grains, and some vegetables and fruit [29]. Most of the research regarding flaxseed and breast cancer focuses on the lignans found in flaxseeds, and their potential for weak estrogenic or anti-estrogenic effects in a woman's body. Researchers have shown that flaxseed sprouts can increase apoptosis (programmed cell death) [30]. Some cell and animal studies have shown that two specific phytoestrogens found in lignans, named enterolactone and enterodiol, may help suppress breast tumor growth [31-36].

Phytoestrogens and breast cancer treatment:

In animal study it was shown that flaxseed inhibited the growth of human estrogen-dependent breast cancer, and strengthened the tumor-inhibitory effect of tamoxifen. Multiple other studies with mice have shown that dietary flaxseed works with tamoxifen to inhibit breast tumor growth [37-38].

Flaxseeds and prostate cancer: Phytoestrogens, since it resembles resemble our own estrogens, may reduce our risk of hormone-related cancers, including prostate cancer [39].

Studies in Western populations, such as in the United States and Europe, haven't given clear answers on the relationship between phytoestrogens in the diet and prostate cancer risk. Most people in these places don't eat a lot of phytoestrogens, so the question is tough to study there [40]. However, in many Asian countries, where much of the population eats phytoestrogen-rich foods on a regular basis, particularly soy foods, rates of hormone-related cancers are lower. However, it is not clear whether the phytoestrogen-rich foods, such as soy and flaxseeds, may offer prostate cancer-protective effects.

In one study, with the blood samples and prostate tumor tissue samples collected before and after adding flaxseed into the diet, the results have suggested that flaxseed reduces the levels of prostate specific antigen (PSA), level of which should be as low as possible like control subjects [41].

A 2008 study by the same research group also found that adding flaxseeds into the diet reduced tumor proliferation [42]. Combining flaxseeds with a low-fat diet has the added benefit of reducing cholesterol levels as well.

In 2015, a systematic review was published to take another look at past studies which explored potential links between lifestyle factors and the prevention of prostate cancer progression and mortality [43]. This review agrees with the study that showed consuming flaxseed in the diet may result in less tumor proliferation.

Use Caution with flaxseed oil: Some studies have found that a type of fat found in flaxseeds, called alpha-linoleic acid (ALA), actually may make prostate tumors more aggressive. Flaxseed oil doesn't contain lignans, the nutrients that are thought to potentially reduce prostate tumor aggressiveness. It only contains pure fat, and it's a type of fat that may cause more harm than good. Also, some health experts suspect that genetic differences in how men metabolize alpha linoleic acid may contribute to whether or not this fat is harmful in terms of prostate tumor growth.

Therefore, it is better to talk to your dietician / doctor before taking flaxseeds. Further, if you do decide to add flaxseeds into your diet, stick with ground flaxseeds, rather than flax oil. Also, a low-fat diet is another safe option for men with prostate cancer. A dietitian can help you design a healthy, balanced, low-fat diet that meets all of your nutrition needs.

In addition, other benefits of flaxseed include important micronutrients such as magnesisum, manganese, thiamin, and selenium. It is an excellent source of fiber, and also contains protein.

(viii) Vegetables: Observational studies have linked a higher consumption of vegetables with a lower risk of cancer. Many vegetables contain cancer-fighting antioxidants and phytochemicals. [44].

For example, cruciferous vegetables, like broccoli, cauliflower and cabbage, contain sulforaphane, a substance that has been shown to reduce tumor size in mice by more than 50% [45]. Other vegetables, such as tomatoes and carrots, are linked to a decreased risk of prostate, stomach and lung cancer [46].

(ix) Fruits: Similar to vegetables, fruits contain antioxidants and other phytochemicals, which may help prevent cancer [47]. One review found that at least three servings of citrus fruits per week reduced stomach cancer risk by 28% [47].

Lycopene is one of a group of compounds called carotenes, which are known for their antioxidant properties, and which may have cancer preventive properties as well. Cooked tomato products, such as tomato juice and soup, and tomato sauce have the most lycopene. Watermelon and pink grapefruit also contain some lycopene, though not as much as cooked tomatoes. Some studies suggest lycopene may decrease prostate cancer risk. Other research doesn't show a large cancer preventive effect of lycopene. However, given that eating lycopene-rich foods is unlikely to cause harm, it makes sense to include these foods in a healthy diet [49].

(x) Caffeine and Cancer: Coffee and tea contain antioxidants and other nutrients that are linked with better health: (a) Isoflavones: Compounds called isoflavones are found mainly in soybeans, and these nutrients seem to protect against prostate cancer. Good sources of isoflavones include tofu, soymilk, soy nuts, tempeh, and edamame (steamed soybeans). (b) Green tea: Green tea contains compounds called flavonoids, which act as antioxidant and may have anticancer activities. Studies suggest several cups of green tea per day are needed to maximize the potential cancer-preventive effects of the beverage. And early trials have found that green tea

extract may prevent pre-cancerous prostate growths from becoming cancerous tumors [50].

For most types of cancer, coffee appears either to decrease risk of cancer, or to have no effect on cancer risk at all. Even in countries with very high intake of caffeine from coffee, such as Scandinavian countries, research does not support a link between coffee or caffeine and cancer risk [51-57].

The only exception may be lung cancer [58]. For lung cancer, study results are conflicting. Some studies show a decreased risk of lung cancer among heavy coffee drinkers, while other studies show no risk, or a small increased risk with heavy coffee consumption.

(xi) Cancer-Fighting Vitamins and Minerals in Spinach:

Cancer is referred as a "free radical" disease, and free radical damage to cells can accumulate with aging. Spinach is a source of antioxidant vitamins (e.g. vitamins C and E), which can help lower cancer risk by controlling levels of free radicals.

Spinach is a source of folate as well, a nutrient important for cell division. Population studies following large groups of people have found an association between higher dietary folate intake and lower risk of colorectal cancer [59]. However, it's important to note that getting this nutrient through supplements, which is a slightly different version of this nutrient called folic acid, may not protect against colorectal cancer. In fact, some studies have suggested getting too much folic acid from dietary supplements may increase colorectal cancer risk. For this reason, food sources of folic acid are the best option for most people.

Other spinach nutrients, including vitamin A, B6, and folate, promote a healthy immune system, which is essential for disease prevention. And magnesium, found in abundance in spinach, is important to hundreds of vital processes in the body, and helps manage inflammation. Not getting enough magnesium has been associated with inflammatory stress, which may increase risk of chronic diseases including some forms of cancer. Over 40% of Americans do not consume recommended amounts of magnesium, and spinach is one of the best dietary sources available.

Spinach also contains Cancer-Fighting Phytonutrients:

Phytonutrients are bioactive compounds found in fruits, vegetables, whole grains, beans, nuts, seeds, tea, coffee, and even herbs and spices. Phytonutrients infuse vegetables and fruits with many of their cancer-fighting benefits. Researchers agree that as fruit and vegetable intake increases, so does phytonutrient intake [60]. However, randomized, clinical trials do not support a role for dietary supplements of vitamins, minerals, and phytochemicals for cancer prevention. For example, two widely reported intervention studies examining effects of beta-carotene supplements on prostate cancer risk found either no effect or an increased risk of cancer from beta-carotene in supplement form.

Some studies (though not all) have suggested dietary intake of phytonutrients in spinach and other plant foods are linked with lower risk of colon cancer, breast cancer (particularly Estrogen Receptor (ER) negative), advanced prostate cancer, and esophageal adenocarcinoma.

There are three main concerns regarding spinach:

1. Spinach, tea, rhubarb, and parsley are major sources of oxalic acid, and Oxalic acid binds to calcium, iron, and other minerals in food, thus reducing their absorption by the body.

2. Fresh spinach may be contaminated with salmonella and E. coli, and therefore needs irradiation before consumption and /or to monitoring in compliance with established food safety practices.

Discussion

For the cancer survivors, eating a healthy diet, staying physically active, and maintaining a healthy body weight are very important. Eating well can help you regain your strength, rebuild tissue, and make you feel better overall. Research also suggests that proper nutrition, physical activity and weight control may improve survival and may reduce the risk of cancer recurring. Additionally, physical activity and diet quality have been associated with higher quality of life, improved function, and lower risk of other illnesses, such as cardio- vascular disease, osteoporosis or diabetes.

Maintain a Healthy Weight: During cancer treatment, many people lose weight because of treatment- related side effects such as nausea, taste changes and loss of appetite. If you are underweight, you may want to include high calorie, high nutrient foods in your meal plan. If weight regain is challenging and you just cannot seem to eat or drink enough calories to gain weight, work with your health care team, and especially with your dietitian, to discuss other nutrition options.

Other people may gain excess weight from medications, reduced activity, or emotional and stress- related eating. Here are some tips to maintaining a healthy weight after cancer treatment:

Food and Leukopenia: Leukopenia, low white blood cell counts, can occur at certain times throughout chemotherapy of Cancer. Most of the time, blood counts will return to normal before a person starts the next round of chemotherapy, and also after cancer therapy is completed. While no specific foods or diet changes are proven to increase production of white blood cells, if you have low WBC (leukopenia), it is very important to practice good hygiene, hand-washing, and food safety practices. Neutrophils are the cells that fight bacterial infection. Neutropenia, which simply means low levels of neutrophils, occurs when Absolute neutrophil count (ANC) falls below 1500 [61]. When this happens, a person is more susceptible to infections. In case, ANC is low, one can minimize the risk of infection by using an anti- bacterial soap and warm water, and scrubbing your hands for 15-30 seconds several times per day, and every time before you prepare food [62].

If someone have neutropenia, they should avoid raw meat, eggs and fish, moldy or expired food, unwashed or moldy fruit and vegetables, and unpasteurized beverages, including fruit and vegetable juice, beer, milk, as well as

unpasteurized honey. You do not need to avoid fresh fruit and vegetables, because this practice has not been shown to reduce the number of major infections [63]. However, you should wash these foods thoroughly before you eat them.

Is there anything that can be changed in the diet to bring up white blood cell count?

1) Good quality protein is important for cancer patients to include in their diet, because our bodies need the building blocks (amino acids) from the protein we eat to make the new WBCs.

2) Multivitamin and mineral supplement with vitamin B12 and folate. The body needs these two vitamins to make white blood cells [64].

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Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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