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Review Article

Dietary Carcinogens and Anticancer Effect of Bioactive Food Components

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Abstract

Nutrition plays a crucial role in the prevention of chronic diseases, as most of them can be related to diet. Diet is an important factor in determining cancer incidence in many countries and regions. Diet can have both positive and negative effects on carcinogenesis. Dietary carcinogens represent 30 to 35% of cancer causes. Several substances in diet such as mycotoxins, heterocyclic amines, polycyclic aromatic hydrocarbons, N-nitroso compounds and acrylamide have been associated with increased risk of cancer. Diet also contains bioactive food components (BFC) which prevent cancer development. Their beneficial effects could be either maintenance or promotion of a state of well being or health and/or a reduction of cancer risk. Research on BFC continues to evolve albeit with shared challenges among scientists in the field of cancer treatment and prevention. Certain compounds such as phytochemicals and probiotics have cancer preventing properties. Awareness of the importance of consumption of functional foods or BFC as well as the importance of the whole diet rather than the isolated compounds as a cancer-preventive strategy for the general public should be promoted.

Key words: dietary carcinogens, bioactive food components (BFC), cancer prevention.

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Cancer is caused by changes in a cell's DNA – its genetic "blueprint." Only 5-10 % of these changes may be inherited, while 90-95% may be caused by outside exposures, which are often referred to as environmental factors and also by life-style factors, including diet (30-35%), tobacco smoking (25-30%) and alcohol (4-6%).[(1)] Several lines of evidence indicate that diet and nutrition can contribute to human cancer risk. Foods and dietary behaviors are thought to increase cancer risk, which is partly due to the consumption of food mutagens. These mutagens contribute to cancer along the route of exposure (oral cavity, esophagus, gastrointestinal tract) and in organs that are distant to the route of exposure (e.g., liver).[(2)] Advances in analytic technology, especially the Ames test have disclosed that in experimental systems an astonishing variety of compounds occurring naturally in the diet are carcinogenic or mutagenic. Ames concluded, "Nature is not benign; no human diet can be entirely free from mutagens and carcinogens."[(3)]

1-Carcinogenesis

1.1- Carcinogens and mutagens

Substances and exposures that can lead to cancer are called carcinogens. In genetics, a mutagen is a physical or chemical agent that changes the genetic material, usually the DNA of an organism and thus increases the frequency of mutations above the natural background level. As many mutations can cause cancer, mutagens are therefore also likely to be carcinogens. Some carcinogens do not affect the DNA directly, but lead to cancer in other ways. For example, they may cause cells to divide at a faster than normal rate, which could increase the chances that DNA changes will occur. Carcinogens do not cause cancer in every case, all the time. Substances labeled as carcinogens may have different levels of cancer-causing potential. Some may cause cancer only after prolonged and/or high levels of exposure. For any particular person, the risk of developing cancer depends on many factors, including how they are exposed to a carcinogen, the length and intensity of

the exposure, and the person's genetic makeup.[4]

1.2- Classification of carcinogens

Several national and international agencies are responsible for determining the cancer causing potential of different substances. Among these are the International Agency for Research on Cancer (IARC) and the US National Toxicology Program (NTP).[5]

The International Agency for Research on Cancer is part of the World Health Organization (WHO). Its major goal is to identify the causes of cancer. The most widely used system for classifying carcinogens comes from the IARC. In the past 30 years, the IARC has evaluated the cancer-causing potential of more than 900 likely candidates, placing them into one of the following groups:

Group 1: Carcinogenic to humans.
Group 2A: Probably carcinogenic to humans.
Group 2B: Possibly carcinogenic to humans.
Group 3: Unclassifiable as to carcinogenicity in humans.
Group 4: Probably not carcinogenic to humans.

Based on how hard it can be to test these candidate carcinogens, most are listed as being of probable, possible, or unknown risk. Only a little over 100 are classified as "carcinogenic to humans."

National Toxicology Program [6]

The Report on Carcinogens identifies 2 groups of agents:

Group 1: Known to be human carcinogens.
Group 2: Reasonably anticipated to be human carcinogens.

1.3- Carcinogen in preserved food

1.3.1-Mycotoxins

Mycotoxins are the most important carcinogen in preserved food. A mycotoxin means "fungus poison," and is a metabolite from fungal metabolism. The term is typically reserved for toxins produced by fungi that colonize crops. Mycotoxins are not necessary for fungal growth or reproduction; it is speculated that they are produced in order to weaken the host. Some mycotoxins, such as the well-known penicillin, are toxic to other fungi or bacteria. They are not broken down by heat or time, but are stored in animal tissue, and thus concentrated as we move up the food chain. There are six major types of mycotoxins: aflatoxins, fusarium toxins, patulin, ergot alkaloids, citrinin, and ochratoxin. Aflatoxins and ocratoxin A are the most potent carcinogens.[5]

1.1.1-Aflatoxins

Aflatoxins are produced by Aspergillus, and refer to 4 different subtypes: B1, B2, G1, and G2. Aflatoxins are mutagenic, carcinogenic, hepatotoxic, and immunosuppressive. They negatively affect DNA synthesis, DNA repair, RNA synthesis, and protein synthesis.[4] In one study, rats exposed to B1, the most common aflatoxin, grew hepatic tumors. Twenty percent also had colon tumors, and a small number had cancer of the kidney, oral cavity, and hematopoietic system.[7] In another study looking at the synergy between hepatitis B and liver cancer, the authors concluded that exposure to aflatoxin greatly magnifies the chance of liver cancer in individuals infected with both the hepatitis B and C viruses. They stated that "reducing aflatoxin exposure to non-detectable levels could reduce hepatitis cases in high-risk areas by about 23%."[8]

In an experimental study, bronchial epithelial hyperplasia, alveolar hyperplasia, and adenocarcinoma of lung were observed in mice receiving AFG1 treatment. The incidences of bronchial epithelial hyperplasia, alveolar hyperplasia, and adenocarcinoma of lung were 6.0%, 10.0%, and 30.0% respectively for mice receiving 3 microgram/kg AFG1 and 28.6%, 35.7%, 42.9% for mice receiving 30 microgram/kg of the toxin respectively.[9]

Aflatoxins are detoxified through the cytochrome p450 pathway, specifically the CYP3A4 pathway. This detoxification pathway creates high levels of oxidative stress in the body. It was reported that antioxidants such as vitamins A, C, and E were shown to reduce oxidation from aflatoxin processing in the liver.[10] Lactic-acid producing bacteria have been reported to remove mycotoxins from aqueous solution through binding properties. In a study, researchers used lactobacillus casei and lactobacillus reuteri in mice exposed to aflatoxin. They measured many parameters and noted that aflatoxins decreased food intake and body weight, increased serum alkaline phosphatase, cholesterol, triglycerides, uric acid, creatinine, and lipid peroxidation in the liver, and decreased antioxidant status. Both strains of lactobacillus were effective in improving all biochemical parameters.[11]

1.3.1.2-Ochratoxin

Ochratoxin is produced by penicillium and aspergillus species. Ochratoxin A is the most prevalent and relevant fungal toxin of this group, while hratoxins B and C are of lesser importance. Ochratoxin A is known to occur in commodities such as cereals, coffee, dried fruit, and red wine. It is possibly a human carcinogen and is of special interest as it can be accumulated in the meat of animals. Thus, meat and meat products can be contaminated with this toxin.[4] Exposure to ochratoxins through diet can cause acute toxicity in mammalian kidneys. Ochratoxin has been found to increase CRP (C-reactive protein) levels in those with higher serum ochratoxin levels.[12] In vitro, ochratoxin induced kidney cell apoptosis.[13]

1.4- Carcinogens in prepared food

1.4.1- Heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs)

Heterocyclic amines and PAHs are chemicals formed when muscle meat including beef, pork, fish, or poultry is cooked using high temperature methods, such as pan frying or grilling directly over an open flame.[14] In laboratory experiments, HCAs and PAHs have been found to be mutagenic. They cause changes in DNA that may increase the risk of cancer. HCAs are formed when amino acids, sugars, and creatine react at high temperatures. PAHs are formed when fat and juices from meat grilled directly over an open fire drip onto the fire, causing flames. These flames contain PAHs that then adhere to the surface of the meat. PAHs can also be formed during other food preparation processes, such as smoking of meats.[14]

The formation of HCAs and PAHs varies by meat type, cooking method, and "doneness" level (rare, medium, or well done). Whatever the type of meat, however, meats cooked at high temperatures, especially above 300ºF (as in grilling or pan frying), or that are cooked for a long time tend to form more HCAs. For example, well done, grilled or barbecued chicken and steak all have high concentrations of HCAs. Cooking methods that expose meat to smoke or charring contribute to PAH formation.[15] HCAs and PAHs become capable of damaging DNA only after they are metabolized by specific enzymes in the body, a process called "bioactivation." Studies have found that the activity of these enzymes, which can differ among people, may be relevant to cancer risks associated with exposure to these compounds.[16-18]

1.4.2- N-nitroso compounds

Other dietary carcinogens include N-nitroso compounds that are formed in smoked, salted, and pickled foods cured with nitrate or nitrite. Sodium and potassium nitrates are present in a variety of foods, and they give hot dogs and luncheon meats their pink color. Nitrates can be readily reduced to nitrite, which in turn can interact with dietary substrates such as amines and amides to produce NOCs (e.g., N-nitroso compounds or nitrosamines and nitrosamides). This conversion, known as i/-nitrosation, has been demonstrated to occur in saliva, as well as in the stomach, colon, and bladder. Nitrosamines are also present in tobacco and tobacco smoke. Diets with high amounts of fruits and vegetables that contain vitamin C and phytochemicals can retard the conversion of nitrites to nitrosamines.[19]

1.4.3- Acrylamide

A group of Swedish scientists reported finding acrylamide, in carbohydrate-rich foods such as potatoes and baked goods that had been cooked at high temperatures.[20] Acrylamide is a by-product that is formed during frying, roasting, and baking. Studies in rodent models have found that acrylamide exposure poses a risk for several types of cancer.[21-23] However, the evidence from human studies is still incomplete. The NTP and the IARC consider acrylamide to be a "probable human carcinogen," based on studies done in laboratory animals given acrylamide in drinking water. However, toxicology studies have shown differences in acrylamide absorption rates between humans and rodents.[24]

A series of case-control studies have investigated the relationship between dietary intake of acrylamide and the risk of developing cancers of the oral cavity, pharynx, esophagus, larynx, large bowel, kidney, breast, and ovary. These studies generally found no excess of tumors associated with acrylamide intake.[25-29] To accurately determining acrylamide exposure, biomarkers of exposure were recently used in a Danish cohort study designed to evaluate the subsequent risk of breast cancer in postmenopausal women.[30] Among women with higher levels of acrylamide bound to the hemoglobin in their blood, there was a statistically significant increase in risk of estrogen receptor-positive breast cancer. This finding suggests an endocrine hormone-related effect, which would be consistent with the results of a questionnaire based cohort study in the Netherlands that found an excess of endometrial and ovarian cancer -but not of postmenopausal breast cancer -associated with higher levels of acrylamide exposure.[31] Another cohort study from the Netherlands suggested a positive association between dietary acrylamide and the risk of renal cell cancer, but not of prostate or bladder cancer.[32]

2. Mechanisms of diet induced carcinogenesis

Food mutagens absorbed orally pass through the liver and are distributed in the body. Those carcinogenic compounds are classified as direct (act directly on DNA) but most require enzymatic conversion and are thus labeled as indirect or pro-carcinogens. Metabolic activation of procarcinogen is controlled by phase I reactions while phase II reactions protect the body through the transformation of activated compounds into inert products, which are easily eliminated from the body. Metabolic activation occurs predominantly in the liver at the endoplasmic reticulum where the cytochrome P450 (an important enzyme in phase I reactions) is more abundant. The results are a powerful electrophilic product capable of establishing interaction with the nucleophilic component (DNA, ribonucleic acid RNA and proteins), altering the structural integrity and forming covalent bounding, called adduct. If the adduct being produced by metabolic activation is not

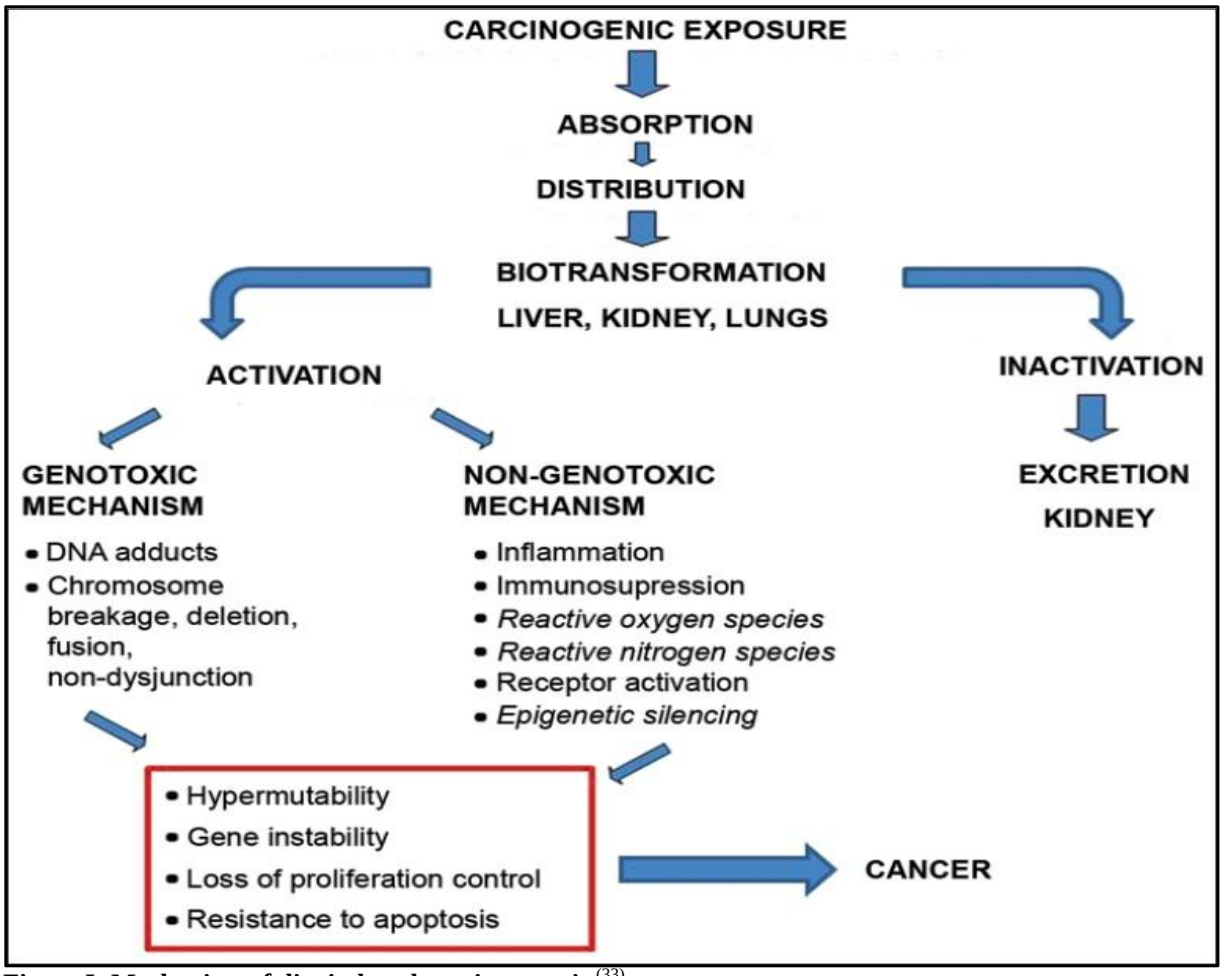

Figure I: Mechanism of diet induced carcinogenesis [33]

able to be repaired by DNA repair before the replication process, then a mutation in proto-oncogene and tumor suppressor gene will occur which is a very important step in carcinogenesis initiation. On the contrary, non-genotoxic carcinogens do not need metabolic activation, do not react directly with DNA and do not raise adducts; they act as promoters and modulate cell growth and cell death and are potential to have the effect of genotoxic carcinogens.[2]

3. **Functional Foods**

The tenet "Let food be the medicine and medicine be the food," espoused by Hippocrates nearly 2,500 years ago, is receiving renewed interest. In particular, there has been an explosion of consumer interest in the health enhancing role of specific foods or bioactive food components. Clearly, all foods are functional, as they provide taste, aroma, or nutritive value. Bioactive food components are chemicals that give plant foods their color, taste and smell. By eating these compounds in relatively low amounts they are very good at keeping person's health as they have a range of interesting biological activities. Within the last two decades, however, the term functional has been applied to foods that are providing an additional physiological benefit beyond meeting basic nutritional needs.[34]

4. Mechanism of action of functional foods and bioactive food components in cancer prevention

The process of carcinogenesis consists of three major steps: initiation, where an irreversible change is affected in the cellular genes; promotion, where the initiated cells expand by self-proliferation leading to abnormal growth and further mutations and progression, where the cells detach from the primary tumor and invade other organs and tissues forming metastatic growths. Angiogenesis is the physiological process through which new blood vessels form from pre-existing vessels. Angiogenesis plays an important role in the tumor metastasis. Different types of cancer genes - oncogenes and anti-oncogenes (tumor

suppressor genes) are involved in cancer development. Gain of function mutations in the oncogenes, leads to abnormal cell proliferation and loss of function mutations in the anti-oncogenes leads to suppression of cell differentiation and apoptosis. These are the major events leading to cancer development.[35] There is now considerable evidence that the chemopreventive properties of plant-based food are related to their ability to block the progression of latent micro-tumors. These properties arise from the high content of phytochemicals, molecules that target several key events in the development of cancer. Intensive research conducted over the last few years has shown that phytochemicals derived from the diet interfere with tumor progression by acting directly on tumor cells as well as by modifying the tumor's microenvironment (stroma) and creating physiologic conditions that are hostile to tumor growth.[35]

Several classifications of the mechanisms of anti-cancer agents have been proposed by a number of investigators. Wattenberg (1985) subdivided anticarcinogens into two major categories; blocking agents and suppressing agents on the basis by which they exert a protective effect at specific stages of multi-step carcinogenesis. Blocking agents are substances that can inhibit initiation either by inhibiting the formation of carcinogens from pre-cursor molecules or reactive intermediates from the parent carcinogens or by preventing the ultimate electrophilic species from interacting with macromolecules such as DNA, RNA and proteins. Suppressing gents act at the promotion or the progression stage by preventing the malignant expression of initiated cells.[36]

4.1- Direct inhibitory actions on tumor cells

4.1.1-Reduction of damage to DNA

Phytochemicals elicit their anti-cancer effects by modulating the enzymatic systems responsible for neutralizing these carcinogens, either by reducing their carcinogenic potential or by increasing their excretion.[37-39]

4.1.2- Cytotoxicity against tumor cells

Several phytochemicals also inhibit tumor growth by directly inducing cancer cell death by apoptosis. Overall, the cytotoxic properties of diet-derived phytochemicals contribute to the chemopreventive effects associated with intake of plant-derived foods and could play an essential role in preventing the growth of cells that have already acquired an initiated phenotype (precancerous cells).[40-42]

4.1.3- Anti-proliferative activity

Recent researches have shown that various phytochemicals reduce the tumor cell proliferation by causing cell cycle arrest and inducing apoptosis. Their actions are exerted at various stages of cell cycle. Certain phytochemicals act at mitochondrial and nuclear level to inhibit cell division.[43]

4.2- Effects on tumor microenvironment

4.2.1- Antiangiogenic properties

Angiogenesis is the process by which tumor cells stimulate the formation of new blood vessel networks that sustain the development of cancer by providing oxygen and nutrients to tumor cells. Work has shown that several phytochemicals possess strong antiangiogenic activity and that this effect likely plays a significant role in their chemopreventive properties.[41,44]

4.2.2- Anti-inflammatory effects

It is becoming increasingly clear that inflammatory stimuli participate in the progression of several cancers, including those of the colorectum, breast and lung.[45] In addition to the important role of dietary Polyunsaturated fatty acids **(**PUFAs**),** there is also growing evidence that several phytochemicals from dietary sources reduce inflammatory processes and that this anti-inflammatory effect contributes to their anti-cancer properties.[46]

5. Main categories of functional foods involved in cancer prevention

5.1- **Phytochemicals**

Phytochemicals are naturally occurring, biologically active chemical compounds in plants. The prefix "phyto" is from a Greek word meaning plant. In plants, phytochemicals act as a natural defense system for host plants and provide color, aroma and flavor. More than 4000 of these compounds have been discovered to date. Phytochemicals are rich sources of vitamins and antioxidants, which are thought to have anti-cancer properties. They are divided into flavonoids, carotenoids, indoles, isothiocyanates, polyphenols, capsaicin, phytoestrogens, phytosterols, protease inhibitors, saponins, sufides, tannins and terpenes.[47-51] The anti-cancer activity of phytochemicals is summarized in table 1.

Examples of phytochemicals containing foods involved in cancer prevention:

5.1.1- Cruciferous vegetables which are part of the *Brassica* genus of plants. Cruciferous vegetables are rich in nutrients, including several carotenoids (beta-carotene, lutein, zeaxanthin); vitamins C, E, and K; folate; and minerals. They also are a good fiber source. In addition, cruciferous vegetables contain a group of substances known as glucosinolates, which are sulfur-containing chemicals. These chemicals are responsible for the pungent aroma and bitter flavor of cruciferous vegetables. During food preparation, chewing, and digestion, the glucosinolates in cruciferous vegetables

are broken down to form biologically active compounds such as indoles, nitriles, thiocyanates, and isothiocyanates. Indole-3-carbinol (an indole) and sulforaphane (an isothiocyanate) have been most frequently examined for their anticancer effects.[52] Indoles and isothiocyanates have been found to inhibit the development of cancer in several organs in rats and mice, including the bladder, breast, colon, liver, lung, and stomach.[53,54] In vitro studies have identified several potential ways in which these compounds may help prevent cancer:

- They help protect cells from DNA damage.
- They help inactivate carcinogens.
- They have antiviral and antibacterial effects.
- They have anti-inflammatory effects.
- They induce cell death (apoptosis).
- They inhibit angiogenesis and tumor cell migration (needed for metastasis).

Researchers have investigated possible associations between intake of cruciferous vegetables and the risk of cancer. The evidence has been reviewed by various experts. Key studies regarding four common forms of cancer are described briefly below.

Table 1: The anti-cancer activity of phytochemicals [47]

Phytochemical	Action	Dietary sources
Capsaicin	Antioxidant; prevents carcinogens from binding to DNA	Chillies, hot pepper
Carotinoids		
• Alpha carotene • Beta carotene • Lutein	Antioxidant; inhibits cell proliferation Antioxidant; pre-cursor to vitamin A; helps in differentiation of normal epithelial cells; inhibits cell proliferation Antioxidant	Yellow and orange vegetables and fruits, green leafy vegetables
• Lycopene	Antioxidant	Tomatoes, water melons
Flavanoids • Kaempferol • Nobiletin • Rutin • Tangeretin • Quercetin	Antioxidant; may reduce cell proliferation; extends action of vitamin C; inhibits blood clot formation; antinflammatory action	Tea, peppermint, most of the fruits and vegetables
• Resveritrol	Antioxidant; protects against heart disease	Red wine, berries, grapes
Glucosinolates/indoles • Dithiolthiones • Indoles	Increases activity of enzymes involved in detoxication of carcinogens and other foreign compounds Protects against estrogen-promoted cancers, induces protective enzymes	Broccoli, cabbage, cauliflower and other cruciferous vegetables
Isothiocyanates • Sulphorophane	Exceptionally potent inducer of detoxification enzyme	Cruciferous vegetables
Phytoestrogens	Antioxidant; inhibits growth of cancer cells; lowers blood cholesterol level and platelet aggregation	Nuts and oil seeds, soy products, legumes, soyabean, tofu
Phytosterols	Protects against hormone-dependent cancers; slows colon cancer and growth	Nuts, cereals, berries
Protease inhibitors	Anticancer agent; suppresses enzyme action of cancer cells	Soy products, legumes
Saponins	Anticancer activity; possibly by preventing tumor cell division; binds bile acid and cholesterol to help reduce cholesterol level	Soyabeans, maize, alfalfa
Sulfides (*Allium*)	Stimulates anticancer enzymes, detoxifies carcinogens	Garlic, onion
Tannins	Prevents carcinogens from binding to target sites	Tea, wine, berries
Terpenes	Increases activity of glutathione transferase, a detoxification enzyme	Citrus fruits
Vallinoids curcumin		Turmeric, ginger, mustard

DNA: Deoxyribonucleic acid

Prostate cancer: Case control studies have found that people who ate greater amounts of cruciferous vegetables had a lower risk of prostate cancer.[55,56] However, Cohort studies in the Netherlands,[57] United States,[58] and Europe.[59] have examined a wide range of daily cruciferous vegetable intakes and found little or no association with prostate cancer risk.

Colorectal cancer: Cohort studies in the United States and the Netherlands have generally found no association between cruciferous vegetable intake and colorectal cancer risk.[60-62] The exception is one study in the Netherlands - the Netherlands Cohort Study on Diet and Cancer - in which women (but not men) who had a high intake of cruciferous vegetables had a reduced risk of colon (but not rectal) cancer.[63]

Lung cancer: Cohort studies in Europe, the Netherlands, and the United States have had varying results.[64-66] Most studies have reported little association, but one US follow up study using data from the Nurses' Health Study and the Health Professionals' showed that women who ate more than 5 servings of cruciferous vegetables per week had a lower risk of lung cancer.[67]

Breast cancer: One case control study found that women who ate greater amounts of cruciferous vegetables had a lower risk of breast cancer.[68] An additional cohort study of women in the United States

similarly showed only a weak association with breast cancer risk.[69] A meta-analysis of studies conducted in the United States, Canada, Sweden, and the Netherlands found no association between cruciferous vegetable intake and breast cancer risk.[70]

Few studies had shown that the bioactive components of cruciferous vegetables can have beneficial effects on biomarkers of cancer-related processes in people. For example, one study found that indole-3-carbinol was more effective than a placebo in reducing the growth of abnormal cells on the surface of the cervix.[71]

5.1.2-Flaxseed

Whole grain flaxseed contains bioactive fatty acids and lignans among other nutrients. The major lignan in flaxseed is called secoisolariciresinol diglucoside (SDG). It should be noted that SDG is also present in wheat and other grains, but flaxseed contains the highest level. Many reports have indicated potential ability of this compound to inhibit tumor development in animal disease models.

Bioavailability of SDG is very poor with reported ranges of a few nanomoles to a few micromoles per liter of human plasma or urine. Thus, the anti-cancer effect of SDG is believed to be mediated through its two main metabolites, enterolactone and enterodiol, that are formed via anaerobic fermentation of SDG by colon bacteria.

Apart from anticancer effects of the metabolites, SDG in its native form can inhibit colon cancer cell growth through induction of S-phase cell cycle arrest, an effect that is similar to those of the metabolites. When tested in a cell culture system, SDG was more stable than its metabolites, which suggests that SDG may be more effective in providing longer-lasting effects. Flaxseed was found to affect prostate and breast cancers.

A small study of 15 men found that a low-fat diet supplemented with flaxseed lowered their blood prostate specific antigen (PSA) levels and slowed the growth of benign prostate cells.[72] Another study of 25 men with prostate cancer found that a low-fat diet along with ground flaxseed reduced serum testosterone, slowed the growth rate of cancer cells, and increased the death rate of cancer cells.[73]

In 2008, a study looked at men with prostate cancer who were scheduled for surgery. Researchers gave some men flaxseed while others ate their usual diets; some were put on low fat diets. The men who got the flaxseed had slower cancer growth than those who did not, regardless of total fat intake. This was a fairly small study that did not look at survival or relapse rates.[74] In 2011, a study that compared flaxseed and low fat diets in men with prostate cancer found that a low fat diet, but not flaxseed, helped lower certain factors in the blood that are linked to prostate cancer growth.[75]

5.1.3- Tea

Tea is made from the leaf of the plant *Camellia sinensis*. Shortly after harvesting, tea leaves begin to wilt and oxidize. During oxidation, chemicals in the leaves are broken down by enzymes, resulting in darkening of the leaves and the well-recognized aroma of tea. This oxidation process can be stopped by heating, which inactivates the enzymes. The amount of oxidation and other aspects of processing determine a tea's type. Black tea is produced when tea leaves are wilted, bruised, rolled, and fully oxidized. In contrast, green tea is made from unwilted leaves that are not oxidized. Tea is composed of polyphenols, alkaloids (caffeine, theophylline, and theobromine), amino acids, carbohydrates, proteins, chlorophyll, volatile organic compounds (chemicals that readily produce vapors and contribute to the odor of tea), fluoride, aluminum, minerals, and trace elements.[76]

The polyphenols, a large group of plant chemicals that includes the catechins,[77] are thought to be responsible for the health benefits that have traditionally been attributed to tea, especially green tea. The most active and abundant catechin in green tea is epigallocatechin-3-gallate (EGCG). The active catechins and their respective concentrations in green tea infusions are listed in the table 2.

Black tea contains much lower concentrations of these catechins than green tea.[78]

The polyphenol concentration of any particular tea beverage depends on the type of tea, the amount used, the brew time, and the temperature.[75]

Table 2: Catechin concentrations of green tea infusions [78]

Catechin in green tea infusion	Catechin concentration (mg/L)*	Catechin concentration (mg/8 fl oz)*
Epigallocatechin-3-gallate (EGCG)	117–442	25–106
Epigallocatechin (EGC)	203–471	49–113
Epicatechin-3-gallate (ECG)	17–150	4–36
Epicatechin (EC)	25–81	6–19

*mg = milligram; L = liter; fl oz = fluid ounce.

Decaffeination reduces the catechin content of tea.[79] Among their many biological activities, the predominant polyphenols in green tea—EGCG, EGC, ECG, and EC—and the aflavins and arubigins in black

tea have antioxidant activity.[80] Several clinical trials have investigated the role of tea and tea polyphenols in cancer prevention.[81] These chemicals, especially EGCG and ECG, have substantial free radical scavenging activity and may protect cells from DNA damage caused by reactive oxygen species.[80] Tea polyphenols have also been shown to inhibit tumor cell proliferation and induce apoptosis in laboratory and animal studies.[82] In other laboratory and animal studies, tea catechins have been shown to inhibit angiogenesis and tumor cell invasiveness.[83] In addition, tea polyphenols may protect against damage caused by ultraviolet (UV) B radiation,[82,84] and they may modulate immune system function.[85]

5.2-Probiotics

The bacteria that reside in the intestinal tract generally have a symbiotic relationship with their host. Beneficial bacteria produce natural antibiotics to keep pathogenic bugs in check (preventing diarrhea and infections) and produce some B vitamins in the small intestine where they can be utilized. There is a solid theoretical basis for why probiotics should help prevent cancer, especially colon cancer and even reverse cancer. Probiotics produce short chain fatty acids in the colon, which acidify the environment. Lower colon pH is associated with a lower incidence of colon cancer. Probiotic bacteria reduce the level of procarcinogenic enzymes such as beta-glucuronidase, nitroreductase and azoreductase.[83-85]

6- Dietary Guidelines for cancer prevention

The American Institute for cancer research stated ten recommendations for Cancer Prevention (October 2012). These recommendations are drawn from the World Cancer Research Fund/American Institute for Cancer Research WCRF/AICR Second Expert Report.[86]

1. Be as lean as possible without becoming underweight.
2. Be physically active for at least 30 minutes every day.
3. Avoid sugary drinks. Limit consumption of energy-dense foods.
4. Eat more of a variety of vegetables, fruits, whole grains and legumes such as beans.
5. Limit consumption of red meats (such as beef, pork and lamb) and avoid processed meats.
6. If consumed at all, limit alcoholic drinks to 2 for men and 1 for women a day.
7. Limit consumption of salty foods and foods processed with salt (sodium).
8. Don't use supplements to protect against cancer.
9. It is best for mothers to breastfeed exclusively for up to 6 months and then add other liquids and foods.
10. After treatment, cancer survivors should follow the recommendations for cancer prevention.

CONCLUSION AND RECOMMENDATIONS

Diet and nutritional factors are one of the major causes of carcinogenesis. Functional foods or bioactive food components are considered to be an inexpensive, readily applicable, acceptable and accessible approach for cancer control and prevention. With health-care costs being a key issue today, it would be cost-effective and highly recommended to promote awareness of the best methods of food preparation and storage to avoid or minimize the exposure to dietary carcinogens. Awareness of the importance of consumption of functional foods or bioactive food components as well as the importance of the whole diet rather than the isolated compounds as a cancer-preventive strategy for the general public should be promoted.

Conflict of interest: none to declare

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