

THE IMPORTANCE OF PHYTOCHEMICALS IN HUMAN CANCER AND TYPE II DIABETES.

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Abstract-

Important phytochemicals for the health supplement industry can only be identified at the junction of the pharmaceutical and food industries. These phytochemicals are bioactive substances that either maintain or improve a person's health. These materials may include genetically engineered designer foods, herbal goods, processed foods and beverages, isolated nutrients, and specialized diets. In addition, they might take the shape of particular diets. Dietary supplements are another potential method of administration. Common names for phytochemicals include phytoestrogens, terpenoids, carotenoids, limonoids, phytosterols, glucosinolates, polyphenols, flavonoids, isoflavonoids, and anthocyanidins. All of these are subclasses of flavonoids. There are several types of phytoestrogens, which include phytoestrogens. They have a significant impact on healthcare, particularly on cancer and diabetes, and can provide several benefits to medical health, such as the prevention and/or treatment of diseases and irregularities in physiological function. Whole grains, legumes, fruits, vegetables, and herbs are just a few examples of foods that are rich in phytochemicals that are of interest to the field of nutraceutical research. These phytochemicals are present in berries, fruits, vegetables, and herbs, among other foods. In isolation or in combination, these phytochemicals have considerable lot of therapeutic promise for the treatment of a wide variety of illnesses. Regarding health claims, functional foods, and the presence of certain phytochemicals, the pertinent health benefits are founded on science and ethics. They are anti-inflammatory, anti-allergic, antioxidants, antibacterial, antifungal, antispasmodic, chemopreventive, hepatoprotective, hypolipidemic, neuroprotective, hypotensive, antiaging, diabetes, osteoporosis, DNA damage, cancer, and heart diseases; they induce apoptosis; they are diuretics; they stimulate the central nervous system; they analgesic; and they induce apoptosis

Keywords: *Phytochemicals; Nutraceuticals, Phytochemical Research, Cancer and Type 2 Diabetes*

Introduction:

The old adage "eat your fruits and veggies" was probably initially meant to urge individuals to consume meals that would supply all of their nutritional needs. The discovery of phytochemicals by the science of nutrition confirms the wisdom of the recommendation. Phytochemicals, which are found in fruits and vegetables and other whole foods like nuts, legumes, and whole grains, can affect bodily processes and provide protection

against cardiovascular disease, cancer, and a host of other chronic illnesses. To put it more simply, phytochemical refers to chemicals found in plants. Indeed, the Greek word meaning "plant" is the etymological root of the word "phyto." Plant meals include organic compounds called phytochemicals that have little nutritional value. Although these nutrients are not required for survival, they may increase longevity due to their positive effects on health.

Protecting plants and people

Phytochemicals are produced by plants as a defensive strategy. They safeguard young plants from pests and pollution. Consuming plant-based foods supply us with these antioxidant compounds. It is believed that phytochemicals in food have a role in our preferences for (or aversions to) specific foods. Due to their distinct chemical components, all foods have distinctive looks, tastes, and scents. They contribute to the flavor of habaneros, the perfume of garlic, the crunch of broccoli, and the brilliant orange color of carrots. Carotenoids, for example, are responsible for the red, orange, and yellow colors of several foods, and anthocyanins are responsible for the red, purple, and blue hues of numerous others. Flavonoids are responsible for the many additional hues of yellow, orange, and red are seen in foods. Isothiocyanates and indoles are the chemical compounds in cabbage responsible for its infamous cooking odor. Capsaicin gives chili peppers their heat.

How phytochemicals help the body

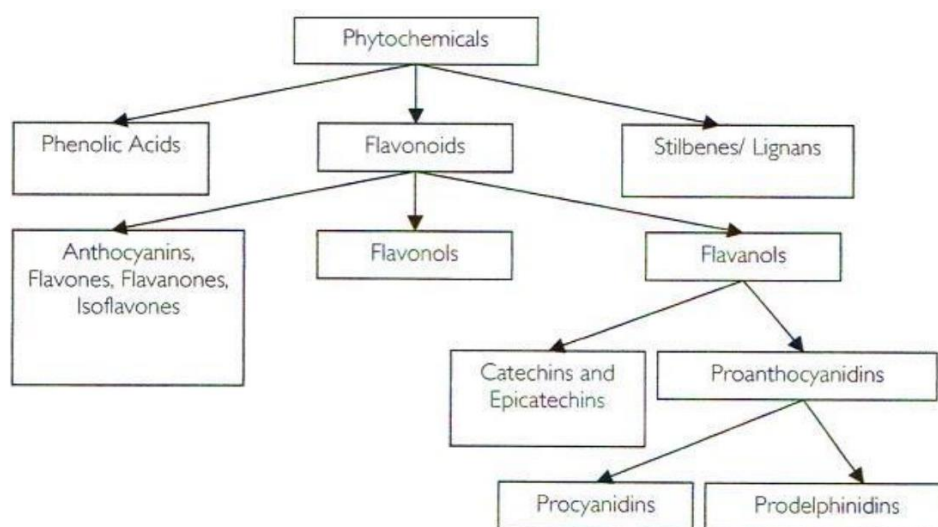
The physiological effects of phytochemicals appear to be considered in the body. They appear to work to prevent the beginnings of illnesses such as cancer and heart disease by acting as antioxidants, imitating hormones, activating enzymes, interfering with DNA replication, eliminating germs, or attaching to cell walls. Some phytochemicals appear to act alone, whereas others appear to work in concert with other elements in the diet, such as vitamins. The more vibrantly colored the meal, the more phytochemicals it contains, perhaps making it more healthful. However, less colorful fruits and vegetables, such as onions and maize, are high in phytochemicals as well. The best approach to reap all of the potential advantages of phytochemicals is to consume a wide range of fruits and vegetables.

There are about 1,000 known phytochemicals, with much more likely to be discovered. The table below lists many kinds of phytochemicals, their potential benefits, and food sources for each. A recent study on phytochemicals' possible health benefits has shown a plethora of possibilities. Anthocyanins and other flavonoids appear to be beneficial to eye health. Resveratrol is being researched for its potential role in the prevention of prostate cancer. Soybean isoflavones may lower inflammation and the risk of heart disease. Lignans have shown promise in slowing the growth of malignant tumors, especially those in the breast and prostate. Cranberries have complex phytochemical content, and research suggests that they may assist to minimize cancer and other aging illnesses. Apple phytochemicals have been demonstrated to lower cardiac risk factors in obese rats with metabolic syndrome. Whole-grain diets include a wide range of unique phytochemicals, which are considered to be responsible for the health advantages associated with whole-grain eating.

Phytochemicals Defined

Phytochemicals, which are also known as phytonutrients, may be discovered in foods such as fruits, vegetables, whole grains, legumes, beans, herbs, spices, nuts, and seeds. These compounds are organized into categories based on their chemical structures and the functions they perform in the body. It is easy to become confused by the various terms that are used to refer to phytochemicals, such as flavonoids, flavonols, flavanols, proanthocyanidins, and procyanidins. Compounds such as salicylates, phytosterols, saponins, glucosinolates, polyphenols, protease inhibitors, monoterpenes, phytoestrogens, sulfides terpenes, and lectins are examples of the types of substances that fall under the category of phytochemicals. The Phytochemical Family Tree organises the various types of phytochemicals that may be found in food into their respective categories.

Phytochemical Family Tree



Thousands of phytochemicals have been found, and experts believe there are many more that have yet to be discovered in the foods we eat. Though the broadest phytochemical groups, such as flavonoids, isoflavones, or anthocyanidins, are frequently referred to as a homogeneous group, the individual compounds within each group have different chemical structures, are metabolised differently by the body, and may have different health effects. Erdman and colleagues (2005) 10 Flavonoids are the most numerous, diverse, and a well-studied class of phytochemicals. In fact, over 6,000 flavonoids included in plant diets have been identified. (Arts and Hollman, 2005) Plants normally create a number of phytochemicals that operate as a defence mechanism against environmental stressors; the more environmental stresses a plant encounters, the more phytochemicals it produces. (1999, Chalker-Scott). As a result, phytochemical concentration varies depending on growth circumstances. There is limited data on the average phytochemical consumption of Americans. However, it is not unexpected that persons who consume the required amounts of fruits and vegetables have a greater intake of phytochemicals. Murphy and colleagues (2012) Despite advice to consume a variety of fruits, vegetables, and whole grains, single meals frequently account for the bulk of overall phytochemical consumption. ((Murphy *et.al* 2012). (Murphy *et.al* 2012).

Phytochemical Research

As it was mentioned, research on particular phytochemicals in foods and their effects on disease risk is limited; however, there is sufficient evidence, most of which comes from looking at the association between foods rich in phytochemicals and disease risk, to strongly suggest that consuming foods and beverages rich in these compounds may help prevent disease. This evidence comes primarily from looking at the association between foods rich in phytochemicals and disease risk. However, it is not known whether the health benefits are the result of individual phytochemicals, the interaction of various phytochemicals, the fibre content of plant foods, or the interaction of phytochemicals and the vitamins and minerals found in the same foods. This is because it is not known which of these factors is responsible for the health benefits.

Cardiovascular Disease There is some evidence to suggest that decreasing one's risk of developing cardiovascular disease can be accomplished by eating foods that are high in phytochemicals. (Dauche *et.al.*, 2003). According to the findings of one meta-analysis, a 17% reduction in risk was related to increasing daily fruit and vegetable consumption from fewer than three servings to more than five servings per day. According to the findings of yet another meta-analysis, the consumption of an additional serving of fruits and vegetables each day was associated with a 4% reduction in the risk of coronary heart disease. The outcomes of research that sought to determine a link between certain fruit polyphenols and the risk of cardiovascular disease have been limited; nonetheless, there is support for the existing recommendations that individuals consume a range of fruits and vegetables on a daily basis. (Murphy *et.al* 2012). However, the majority of research that has been conducted on cardiovascular disease has focused on the consumption of soy (which is high in isoflavones) and/or cocoa (rich in polyphenols). Consumption of soy, cocoa, as well as black and green teas, has been shown in several studies to be connected with a lower risk of developing cardiovascular disease. The phytochemical content of these foods and beverages is associated with a wide variety of health benefits, some of which include lowering blood pressure, reducing inflammation, increasing HDL cholesterol while decreasing LDL oxidation, increasing blood vessel dilation, and reducing the tendency of the blood to clot. (Andujar 2012). It was discovered that cocoa might increase endothelium function through the dilatation of blood arteries; the effect was shown to be most prominent in those over the age of 50. 18 Consuming an average of 2.5 to five servings of whole grains per day was associated with a 21% lower risk of cardiovascular disease compared with consuming fewer than 0.2 servings per day, according to the findings of a meta-analysis and a systematic examination of prospective cohort studies and randomized controlled trials. These findings were found through a systematic examination of prospective cohort studies and randomized controlled trials. It is thought that the presence of a wide variety of phytochemicals, such as anthocyanins, phytosterols, phenolic acids, lignans, and carotenoids, in grains like wheat, rye, oats, and rice, contributes to the cardioprotective benefits of these foods. (Fardet 2010). Consuming whole grains that are high in phytochemicals is also linked to having lower blood pressure, which is beneficial for the prevention of cardiovascular disease. There is a correlation between eating at least four servings of whole grains on a daily basis and a reduced chance of developing high blood pressure by 23 percent. The eating of whole grains has been shown to be associated with a general reduction in blood pressure. (Wang *et.al.*, 2007). Although the results have been mixed, intervention studies have also discovered a favorable link between the consumption of whole grains and blood pressure. (Tighe and colleagues, 2010).

Cancer

The intake of fruits, vegetables, and whole grains, as well as dietary patterns such as the Mediterranean diet that highlight these items, have been related to a decreased risk of multiple different forms of cancer, including breast cancer, lung cancer, and colon cancer. (Hui et.al., 2015). An increase of three servings per day of whole grains was related to a 17% decreased risk of colorectal cancer, according to the findings of a comprehensive analysis of prospective studies carried out by Hui et al. in 2015. (Aune *et.al.*, 2011). However, the reduction in risk associated with eating fruits, vegetables, and grains that are whole has not been documented in every study on the topic. (McCullough *et al.*, 2011). Researchers have also investigated the relationship between the consumption of certain phytochemicals and a lower risk of developing cancer. (Romagnolo *et.al.*, 2013). According to the findings of one piece of research, a reduced risk of breast cancer was exclusively connected with certain subgroups of flavonoids. According to the findings of other researchers, the decreased risk of cancer was not as significant for individual phytochemicals as it was for diets rich in phytochemicals. (Romagnolo *et.al.*, 2013). Consuming cruciferous vegetables on a regular basis, such as broccoli, cabbage, and cauliflower has been shown to be connected with a lower risk of developing prostate, lung, breast, and colon cancers. (Juge *et.al.*, 2007) It is thought that the isothiocyanate phytochemicals present in cruciferous vegetables, particularly the sulforaphane found in broccoli, which has been the subject of a significant amount of research, may give some degree of protection against the disease. Both the prevention and treatment of cancer may benefit from the use of food-based therapeutic combinations that are high in phytochemicals that have not yet been characterized. There is also evidence that different phytochemicals may have different impacts in relation to the risk of developing cancer, depending on the age of the person and the individual's genetic makeup. Isoflavones, for instance, have estrogenic effects and, depending on a person's genetic makeup and whether or not they have gone through menopause, may either raise or lower the risk of breast cancer. Resveratrol, sulforaphane, curcumin, quercetin, and genistein are a few examples of phytochemicals that have the potential to boost the efficacy of chemotherapeutic agents, which are drugs used to treat cancer.

However, it is still too soon to prescribe phytochemicals or certain meal combinations as a method to prevent cancer or to boost the efficacy of chemotherapy. Tea polyphenols have been shown to reduce the risk of developing cancer in a number of different organs and tissues, including the skin, lung, oral cavity, esophagus, stomach, liver, pancreas, small intestine, colon, bladder, prostate, mammary glands, according to a substantial amount of research conducted in laboratories and on animals. It has been demonstrated that the polyphenols included in tea can influence gene regulation as well as tumor suppression and the replication of cancer cells. 38 These benefits are typically related to the catechin polyphenols that are found in tea. However, investigations conducted on people have not been able to clearly show a relationship. There may not be a consistent effect in humans because they do not consume the larger doses that are typically used in animal studies; it may also be because it is difficult to obtain accurate measurements of tea intake among human subjects; genetic diversity is more prevalent in the human population than it is in research animals. All of these factors may contribute to the lack of a consistent effect. Research conducted in laboratories has demonstrated that the polyphenols found in cocoa can suppress the growth of cancer cells at all phases of the disease, beginning with the disease's onset and continuing through its progression. Even while chocolate, especially dark chocolate, has a high level of these

polyphenols, it is not known whether or not these polyphenols would have the same cancer-preventing advantages in the body, nor is it known how much of these polyphenols would be necessary to be effective.

Type 2 Diabetes:

Eating foods that are high in phytochemicals may lower the risk of developing type 2 diabetes in two different ways, namely, directly, by reducing inflammation and increasing insulin sensitivity, and indirectly, by preventing weight gain, which is the single most important risk factor for developing the disease. Research has shown that this may be the case. In both laboratory and animal experiments, the consumption of polyphenols was found to particularly produce positive effects on the levels of glucose in the blood while fasting as well as the sensitivity of the body to insulin. Dietary polyphenols have the potential to inhibit carbohydrate digestion and glucose absorption in the intestine, stimulate insulin secretion from the pancreas, modulate glucose release from the liver, activate insulin receptors and glucose uptake in insulin-sensitive tissue, and modulate intracellular signaling pathways and gene expression. Dietary polyphenols can be found in a variety of plant-based foods and beverages.

According to the findings of a number of studies, the greatest reduction in risk was shown with an increase in the consumption of green leafy vegetables, which are abundant in phytochemicals. Higher intakes of anthocyanins and fruits rich in anthocyanins were connected with a decreased risk of developing type 2 diabetes in three separate studies conducted on nurses: the Nurses' Health Studies I and II, as well as the Health Professionals Follow-Up Study. However, the Women's Health Study did not uncover the same association, but the researchers speculated that eating apples and drinking tea could have a little protective impact against breast cancer. There is some evidence that the polyphenols found in cocoa and tea may help increase insulin sensitivity and reduce the chance of developing type 2 diabetes. Drinking tea was shown to be related to a considerably reduced risk of acquiring type 2 diabetes in a large population research that included participants from eight countries in Europe. To be more specific, people who drank more than four cups of tea each day had a 16% decreased chance of developing the disease when compared to people who didn't consume tea. Patients diagnosed with diabetes who participated in a study that was controlled by a placebo and in which patients were given flavonoid-rich chocolate and supplemental isoflavones for a period of one year experienced significantly decreased insulin levels, improved insulin sensitivity, and decreased total cholesterol, HDL ratio, and LDL cholesterol. When compared with individuals who never or rarely consumed whole grains, those who consumed up to 80 grams of whole grains on a daily basis (three to five servings) had a 26% lower risk of developing type 2 diabetes. This finding was discovered through a systematic review of 45 prospective cohort studies. A study that looked at the prospective Nurses' Health Studies I and II, which included almost 162,000 women from the United States who did not have a history of diabetes, found that those who had the highest intake of whole grains had a 37% lower risk of developing type 2 diabetes compared to those who had the lowest intake of whole grains. This was found in comparison to those who had the lowest intake of whole grains. The committee that developed the 2010 Dietary Guidelines for Americans came to the conclusion that there is insufficient evidence to support the hypothesis that eating whole grains lowers one's chance of developing type

2 diabetes. On the other hand, the German Nutrition Society came to the conclusion that there is plausible data suggesting that it lowers the risk of developing type 2 diabetes.

Neurodegeneration There is some evidence that phytochemicals can offer some protection against neurodegenerative illnesses like Parkinson's and Alzheimer's. Research has shown that certain phytochemicals, such as capsaicin (which can be found in red pepper), curcumin (which can be found in the spice turmeric), epigallocatechin gallate (which is catechin in tea known as EGCG), and resveratrol (which can be found in grapes, wine, and peanuts), may have neuroprotective effects. It is believed that flavonoids, in general, can help reverse the age-related declines in cognitive function by increasing the number of connections between neurons. This, in turn, protects vulnerable neurons and enhances the functioning of existing neurons. Flavonoids can also help improve blood flow to the brain, which also protects vulnerable neurons. Consuming foods rich in flavonoids throughout life, such as cocoa and berries, may have the ability to reduce, halt, or reverse the normal or pathological decline in cognitive function that is associated with aging in the brain. A decreased chance of getting Parkinson's disease or postponing the illness's beginning by many years has been found to be associated with drinking tea, according to the findings of multiple studies. Flavonoids in general, and berries in particular, have been linked to a reduced risk of Parkinson's disease. It has been suggested that the association is due to its caffeine content, which is also a naturally occurring phytochemical. However, flavonoid intake in general has also been linked to a reduced risk of Parkinson's disease. It is possible that combining specific dietary flavonoids that are well absorbed and can penetrate the blood-brain barrier (which exists to prevent many substances in the blood from reaching the brain), and thus preventing or slowing the production of damaging free radicals in the body, could help prevent and treat a variety of neurodegenerative disorders. These disorders include Alzheimer's disease, Parkinson's disease, and vascular dementia. However, this particular phytochemical cocktail has not yet been characterized in terms of its potent effectiveness. Consuming cocoa that is high in flavanols has been shown to increase cerebral blood flow, which is essential for maintaining peak brain function and reduces the risk of developing Alzheimer's disease and dementia. It has been hypothesized that maintaining a diet high in flavonoids throughout life with foods such as cocoa and berries may help prevent cognitive decline and restrict the progression of neurodegeneration. There is some evidence that phytoestrogens, which are compounds contained in foods like soy and whole grains that have estrogen-like action, might help avoid the cognitive deterioration that can occur after menopause.

Factors that Affect Metabolism

The number of phytochemicals that are bioavailable to the body can range from less than 0.03% of what is ingested (in the case of some flavonols) to as much as 50%. (isoflavones). Research indicates that there are no long-term reserves of polyphenols in the body, despite the fact that there is only a limited amount of knowledge regarding how phytochemicals are kept. In addition to the intrinsic variances in the bioavailability of these chemicals, absorption is also impacted by the microbiota of the stomach and the genetic makeup of the individual, both of which can be quite different from one person to the next. In addition, the final food product may include lower concentrations of some phytochemicals if it has been subjected to processing methods such as boiling, steaming, drying, or freezing.

Unidentified Therapeutic Intakes:

Despite the fact that many phytochemicals are thought to have disease-preventing abilities, the Institute of Medicine has been unable to establish a Dietary Reference Intake (DRI) for any of them due to the lack of information on food composition and the incomplete knowledge of their absorption, metabolism, and interaction. In addition, unlike vitamins and minerals, these substances aren't regarded as nutrients because they aren't necessary. The benefits of eating foods high in phytochemicals may be more advantageous for persons who have more severe metabolic abnormalities, such as higher blood lipids, type 2 diabetes, or obesity, and may not be as noticeable in otherwise healthy populations, which complicates studies on phytochemicals. Specific phytochemical recommendations cannot yet be made due to the complexity of the phytochemical family, their potential interactions, and the potential differences in quantities found in any one diet. Furthermore, people consume a variety of foods and nutrients on a daily basis, and each combination has the potential to have different interactive effects. For these reasons, it is very challenging to correlate a particular food, nutrient, or phytochemical with a particular outcome in terms of health or disease. Before nutritional suggestions may be provided, further data is required. A DRI should be created for one or more of the classes of flavonoids, according to experts, once there is enough evidence available.

Potential dangers Although phytochemicals are commonly present in the food supply, it is still challenging to estimate consumption since there isn't a reliable, complete database. This impairs the capacity of researchers to establish the ideal amount of phytochemical consumption or the level of intake that may potentially constitute a health concern. The role of phytochemicals as antioxidants is one of their primary activities. But just like other antioxidant substances, after they have served their intended purpose, they turn into oxidising substances. Large quantities of antioxidants in the form of supplements have the potential to be hazardous, despite the fact that it would be challenging to consume an excessive quantity of antioxidant phytochemicals through food. Supplements are not advised because it is unknown what huge doses of phytochemicals will do to your health over the long run. The risks of consuming high intakes aren't well understood due to the sheer volume of these compounds found in foods, the lack of accurate information regarding dietary intake, and the lack of studies evaluating their safety, even though taking large amounts of phytochemicals as supplements could theoretically pose a risk.

Guidelines for Practice Although there are numerous, significant connections with a diet high in fruits, vegetables, tea, whole grains, and other plant foods, they do not clearly show a cause-and-effect connection. However, authorities like the American Institute for Cancer Research³ and the 2010 Dietary Guidelines for Americans Committee¹ concur that eating a range of plant-based meals is crucial for health. According to research, those who consume the recommended amounts of fruits and vegetables have significantly greater levels of phytochemical intake. The best recommendation for clients and patients is to eat a wide variety of plant-based foods, following the MyPlate guidelines, which call for consuming three to five servings of fruits and vegetables daily, at least three servings of whole grains, and adding beans, legumes, roasted soybeans (1 /4 cup cooked), nuts or seeds (1 /2 oz), as well as other lean proteins like eggs, fish, and poultry. Although there are no recommended daily intakes for coffee, tea, or cocoa, moderate use of all three may have extra health

advantages provided that it is taken into account when calculating daily caloric intake. Keep in mind that white, green, oolong and black tea all contain varying levels and types of phytochemicals that may have varying health advantages. Dark chocolate is also higher in phytochemicals than milk chocolate.

References:

- Andujar I, Recio MC, Giner RM, Rios JL. Cocoa polyphenols and their potential benefits for human health. *Oxid Med Cell Longev*. 2012; 2012:906252
- Arts IC, Hollman PC. Polyphenols and disease risk in epidemiologic studies. *Am J Clin Nutr*. 2005;81(1 Suppl):317S-325S.
- Aune D, Chan DS, Lau R, et al. Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. *BMJ*. 2011;343:d6617
- Chalker-Scott L. Environmental significance of anthocyanins in plant stress responses. *Photochem Photobiol*. 1999;70(1):1-9.
- Dauchet L, Amouyel P, Hercberg S, Dallongeville J. Fruits and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies. *J Nutr*. 2006;136(10):2588-2593.
- Erdman JW Jr, Balentine D, Arab L, et al. Flavonoids and heart health: Proceedings of the ILSI North America Flavonoids Workshop, May 31-June 1, 2005, Washington, DC. *J Nutr*. 2007;137(3 Suppl 1):718S-737S.
- Fardet A. New hypotheses for the health-protective mechanism of whole-grain cereals: what is beyond fibre? *Nutr Res Rev*. 2010;23(1):65-134.
- Hui C, Qi X, Qianrong Z, Xiaoli P, Jundong Z, Mantian M. Flavonoids, flavonoid subclasses and breast cancer risk: a meta-analysis of epidemiologic studies. *PLoS One*. 2013;8(1):e54318.
- Juge N, Mithen RF, Traka M. Molecular basis for chemoprevention by sulforaphane: a comprehensive review. *Cell Mol Life Sci*. 2007;64(9):1105-1127
- McCullough ML, Robertson AS, Chao A, et al. A prospective study of whole grains, fruits, vegetables and colon cancer risk. *Cancer Causes Control*. 2003;14(10):959-970.
- Murphy MM, Barraj LM, Herman D, Bi X, Cheatham R, Randolph RK. Phytonutrient intake by adults in the United States in relation to fruit and vegetable consumption. *J Acad Nutr Diet*. 2012;112(2):222-229
- Romagnolo DF, Selmin OI. Flavonoids and cancer prevention: a review of the evidence. *J Nutr Gerontol Geriatr*. 2012;31(3):206-238.
- Tighe P, Duthie G, Vaughan N, et al. Effect of increased consumption of whole-grain foods on blood pressure and other cardiovascular risk markers in healthy middle-aged persons: a randomized controlled trial. *Am J Clin Nutr*. 2010;92(4):733-740.
- Wang L, Gaziano JM, Liu S, Manson JE, Buring JE, Sesso HD. Whole- and refined-grain intakes and the risk of hypertension in women. *Am J Clin Nutr*. 2007;86(2):472-479.