

THE RELATIONSHIP BETWEEN FLAVONOIDS AND CANCER

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Abstract: Flavonoids are the effective ingredients of the compounds found in grains, vegetables, fruits, seeds and some drinks that have medicinal, free radical reducing and anti-cancer functions. In plants, flavonoids play an important role in multiple functions including color formation, growth, and protection against damage and microorganisms. Articles have stated that the molecular functions of flavonoids may improve health and reduce disease symptoms, reduce antibiotic resistance and reduce inflammation in humans. One of the features of such research is the potential effect of flavonoids on cancer risk. Chemically, flavonoids have an overall 15-carbon skeletal structure consisting of two phenyl rings and one heterocyclic ring. This carbon structure can be abbreviated as C6-C3-C6. Flavonoids are the effective ingredients of the compounds found in grains, vegetables, fruits, seeds and some drinks that have medicinal, free radical reducing and anti-cancer functions. In plants, flavonoids play an important role in multiple functions including color formation, growth, and protection against damage and microorganisms. Articles have stated that the molecular functions of flavonoids may improve health and reduce disease symptoms, reduce antibiotic resistance and reduce inflammation in humans. One of the features of such research is the potential effect of flavonoids on cancer risk.

Keywords: Flavonoid, Cancer, Antioxidant



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Annotation

Flavonoids are rich in antioxidant activity and can help your body rid itself of daily toxins. Including more flavonoids in your diet is a great way to help keep your body healthy and reduce your risk of certain chronic diseases. When they were first extracted from oranges by scientists in the 1930s, they were thought to be a new type of vitamin and were therefore called vitamin P. This name is no longer used because flavonoids are not vitamins. More than 8000 compounds with flavonoid structure have been identified. Together with carotenoids, they are responsible for the vibrant colors

in fruits and vegetables. Flavonoids are considered as health-promoting and disease-preventing food supplements. Epidemiological, clinical, and animal studies suggest that flavonoids may have protective effects against various diseases, including cardiovascular disease and cancer. Flavonoids are rich in antioxidant activity and can help your body rid itself of daily toxins. Including more flavonoids in your diet is a great way to help keep your body healthy and reduce your risk of certain chronic diseases. This name is no longer used because flavonoids are not vitamins. More than 8000 compounds with flavonoid structure have been identified. Together with carotenoids, they are responsible for the vibrant colors in fruits and vegetables. Flavonoids are considered as health-promoting and disease-preventing food supplements. Epidemiological, clinical, and animal studies suggest that flavonoids may have protective effects against various diseases, including cardiovascular disease and cancer. Flavonoids are rich in antioxidant activity and can help your body rid itself of daily toxins. Including more flavonoids in your diet is a great way to help keep your body healthy and reduce your risk of certain chronic diseases. This name is no longer used because flavonoids are not vitamins. More than 8000 compounds with flavonoid structure have been identified. Together with carotenoids, they are responsible for the vibrant colors in fruits and vegetables. Flavonoids are considered as health-promoting and disease-preventing food supplements. Epidemiological, clinical, and animal studies suggest that flavonoids may have protective effects against various diseases, including cardiovascular disease and cancer. There are several mechanisms by which flavonoids may help prevent the growth of cancer cells, including that these compounds can stimulate the process of apoptosis (programmed cell death), inhibit the growth of tumors, and prevent the formation of new blood vessels in Prevent tumors (a process called angiogenesis) which is necessary for their growth. However, more studies are needed to fully understand the exact role and effectiveness of flavonoids in cancer prevention and treatment. So far, research has shown that moderate consumption of foods rich in flavonoids, such as fruits and vegetables, may help reduce the risk of some types of cancer (1).

These chemical compounds have a wide range of proven health-promoting effects, including antioxidant, anti-inflammatory, anti-mutagenic and anti-cancer properties. The family of flavonoids includes more than 6000 phenolic compounds of flavan derivatives. The main subgroups are flavon, isoflavone, flavonol, flavanone and dihydroflavonol, flavan-3-l and anthocyanin. Flavan nucleus is identified in every flavonoid structure, which consists of 15 carbon atoms and consists of two aromatic rings A and B, which are connected by a three-carbon chain. The C-linked carbon chain is part of a central heterocyclic ring and plays a decisive role in the naming of different flavonoid groups .(2)

Flavonoids help regulate cellular activity and fight free radicals that cause oxidative stress in your body. Simply put, they help your body function more efficiently while protecting it from toxins and stressors. Flavonoids are also powerful antioxidant agents. Antioxidants help your body fight off potentially harmful molecules that can be introduced into the body. Your body produces antioxidants naturally, but they are also found in dark chocolate, legumes, and many fruits and vegetables. Inflammation is one of your body's immune responses. Allergens, germs, toxins, and other irritants can cause inflammation that leads to uncomfortable symptoms. Flavonoids may help your body suppress this inflammatory response to reduce these symptoms .(3)

Flavonoids are powerful antioxidants with anti-inflammatory, antibacterial, antiviral and immune system benefits. Diets rich in flavonoid-containing foods are sometimes associated with cancer, neurodegeneration, and prevention of cardiovascular disease. Population studies have shown that consumption of flavonoids is inversely related to mortality from cardiovascular diseases. Flavonoids have been reported to have a beneficial effect on atherosclerosis-related parameters, including lipoprotein oxidation, blood platelet aggregation, and vascular reactivity. Antioxidant, anti-thrombotic, anti-inflammatory and lipid-lowering properties play an important role in reducing cardiovascular mortality observed with higher consumption of flavonoids. Therefore, recently, flavonoids are the focus of much current nutritional and therapeutic interest. The anti-inflammatory and antioxidant effects of flavonoids have also encouraged research to study their potential as anticancer drugs. Research has shown that certain flavonoids may help prevent cancer cells from

multiplying. Including foods containing flavonoids and maintaining a healthy diet may reduce the risk of certain cancers (4).

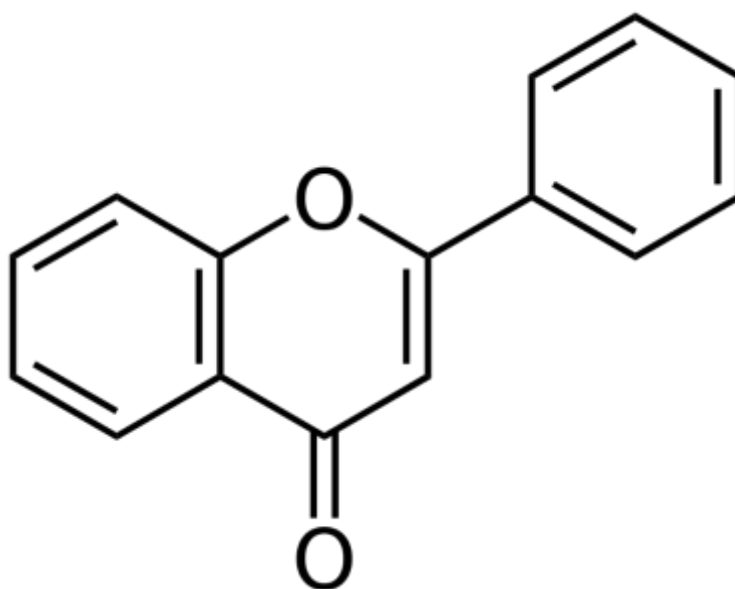
Antioxidants are substances that can prevent damage to body cells caused by the attack of free radicals or slow down the process of damage to cells. The main sources of antioxidants are found in two natural and synthetic forms. On the other hand, the human body always produces a type of antioxidant known as endogenous antioxidant. Antioxidants that are supplied from outside the body are also called exogenous antioxidants. Cells produce free radicals in response to waste materials in the body. One of the functions of the immune system is to process and eliminate free radicals. If for any reason the body cannot process and eliminate these free radicals effectively, oxidative stress occurs. Creating this stress can cause serious damage to the body's cells and functions. Factors that increase the production of free radicals in the body include internal factors and external factors. Internal factors such as body inflammations and others such as: air pollution, exposure to cigarette smoke and ultraviolet rays are among external factors. Oxidative stress has been linked to heart disease, cancer, arthritis, stroke, respiratory disease, immunodeficiency, emphysema, Parkinson's disease, and other inflammatory or ischemia (lack of oxygen) conditions (5).

Types of flavonoids

Flavonoids can be divided into different subgroups depending on the carbon of the C ring to which the B ring is attached and the degree of unsaturation and oxidation of the C ring. Flavonoids in which the B ring is connected at the 3 position of the C ring are called isoflavones. Those in which the B ring is attached at the 4 position are called neoflavonoids, while those in which the B ring is attached at the 2 position can be divided into several subgroups based on the structural features of the C ring.

Flavones

Flavones are a group of flavonoids based on the main nucleus of 2-phenylchromone-4-one (2-phenyl-1-benzopyran-4-one), which is shown in the first picture of this article. Flavones are found in some foods, including spices and some yellow or orange fruits and vegetables are available. Common flavones include apigenin (7,5,4-trihydroxyflavone), luteolin (3,7,5,4-tetrahydroxyflavone), tangerine (8,7,6 5,4-pentamethoxyflavone), chrysin (7,5-dihydroxyflavone) and 6-hydroxyflavone .(6)



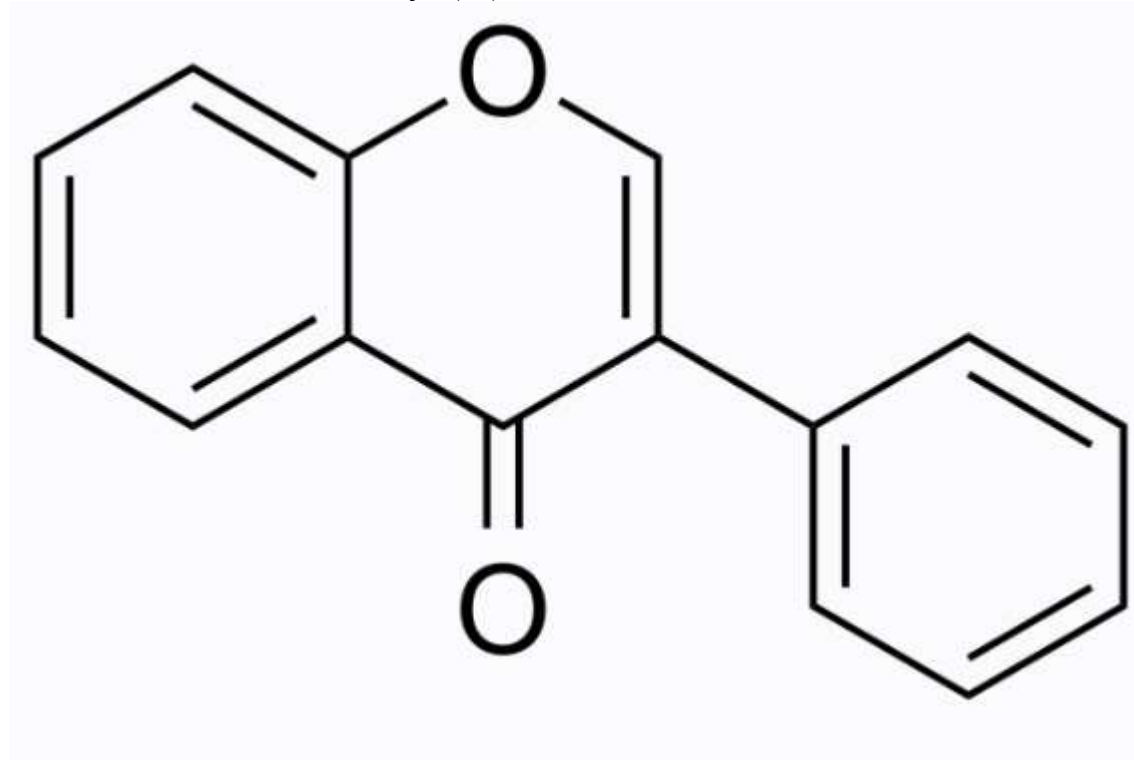
(7) Figure 1. Flavones

Preliminary research has shown that regular consumption of food sources rich in flavones can help preserve memory and cognitive abilities and reduce the risk of chronic neurological diseases such as Alzheimer's. Despite all the above-mentioned benefits, it is important to consume flavones in a balanced way and in the context of a varied and nutritious diet. More research is needed to fully understand the full effects and exact mechanisms of action of these amazing compounds in the human body. Flavones work through several mechanisms, including boosting the immune system, preventing the formation of blood vessels that tumors need to grow (inhibition of neoangiogenesis), and inducing the death of cancer cells (apoptosis). Although evidence suggests that flavones may be useful in preventing some types of cancer, more research is needed to fully understand their role and optimal intake to obtain maximum benefits. For this reason, doctors and researchers often recommend consuming a varied diet rich in flavone-rich foods as part of a healthy lifestyle .(8)

This recommendation is based on the fact that a diverse combination of flavones in a diet can provide complementary protective effects .(9)

Isoflavone

This subgroup includes genistein, glycinin and daidzein. Isoflavones are highly concentrated in soybeans and soybean products, as well as legumes. They are phytoestrogens, meaning they are chemicals that act like the hormone estrogen. Scientists suspect that they may be useful in reducing the risk of hormonal cancers, such as breast, endometrial and prostate cancer, although study results are currently mixed. In various studies, isoflavones have sometimes acted as antioxidants and sometimes as oxidants, so their effects on cancer are unclear. They are also being studied as a way to treat menopausal symptoms. By reducing the risk of breast cancer, endometriosis, prostate cancer, and regulating the menstrual cycle, isoflavones play an important role in maintaining the hormonal balance of the body. Chemical structure similar to estrogens in the human body, they can bind to estrogen receptors. This feature allows isoflavones to play a role in regulating physiological processes and mimic hormonal effects in the body .(10)



(11) Figure 2. Isoflavone

Some research has shown that regular consumption of isoflavones can help lower blood

pressure, improve vascular function, and lower cholesterol, all of which reduce heart disease risk factors. Extensive research has been conducted on the role of isoflavones in the prevention and treatment of cancer, but the results are still mixed. Some studies suggest that isoflavones may reduce the risk of certain types of cancer, especially breast and prostate cancer. This protective effect is probably due to the ability of isoflavones to regulate the activity of hormones, their antioxidant properties and their anti-inflammatory effects. However, some other research points to challenges and limitations that include individual differences in the metabolism of isoflavones and their different effects on individuals with different hormonal levels. Also, some animal studies have shown that high isoflavone consumption can have negative effects on certain tissues, although these findings do not necessarily generalize to humans .(12)

And while animal studies show the potential for negative effects of high consumption of isoflavones on some tissues, human studies are usually limited to investigating the effects of moderate consumption within the context of a balanced diet. In this context, moderate consumption of isoflavones through natural food sources is generally considered safe and beneficial for health. In particular, consumption of soy and its derived products, which are rich sources of isoflavones, has been associated in many societies with lower rates of lifestyle-related diseases, including some types of cancer and heart disease .(13)

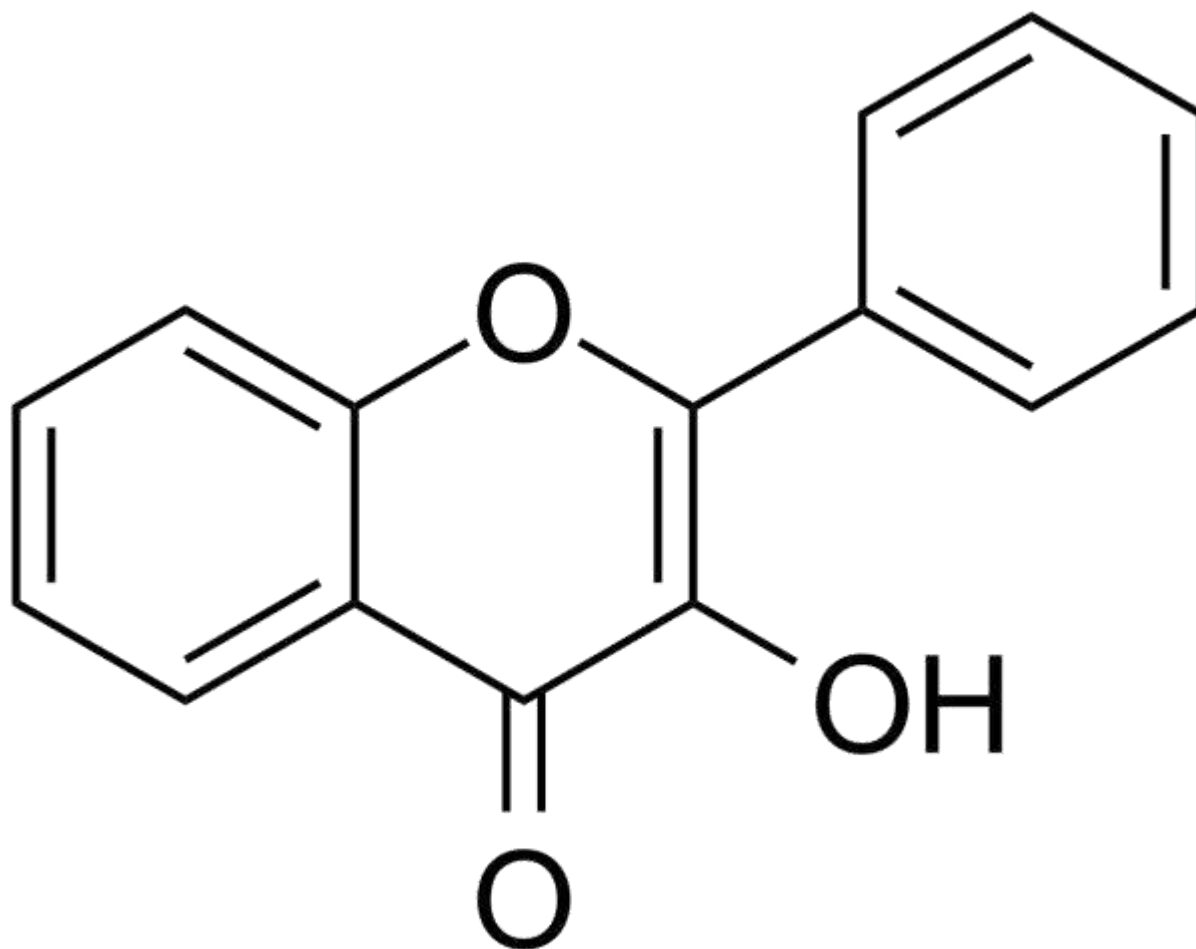
Isoflavones and cancer prevention

- Mechanism of action: Isoflavones can bind to estrogen receptors, but less strongly than natural estrogen. It can reduce the effect of estrogen in the body, which in turn can slow the growth of estrogen-dependent cancer cells.
- Antioxidant effects: Isoflavones also have antioxidant properties that can help reduce oxidative stress and prevent DNA damage, both of which are important factors in the development of cancer.

Effect on estrogen metabolism: Isoflavones may direct estrogen metabolism to less carcinogenic pathways .(14)

Flavonol

Flavonols are a group of phenolic compounds found naturally in many plants and known for their antioxidant, anti-inflammatory, and anticarcinogenic properties. These compounds, which form an important part of the human diet, are mainly found in fruits, vegetables, chocolate, tea and red wine. This widely distributed subgroup of flavonoids includes quercetin and kaempferol. They are found in onions, leeks, Brussels sprouts, kale, broccoli, tea, berries, beans, olive oil, tomatoes, onions and apples. Quercetin is an antihistamine that helps relieve hay fever and hives. It is also known for its anti-inflammatory benefits. Kaempferol and other flavonols are associated with strong anti-inflammatory and antioxidant activities that lead to the prevention of chronic diseases. However, although evidence suggests that flavonols can provide many benefits as part of a healthy diet, more research is still needed to fully understand their exact mechanisms of action and how they can best be used to prevent and treat disease (15)



(16) Figure 3. Flavonol

These phenolic compounds, which are abundant in fruits, vegetables, chocolate, tea, and red wine, can be effective in combating the development and progression of cancer in several ways.

Antioxidant properties: Having strong antioxidant properties, flavonols can protect cells from damage caused by free radicals. Free radicals are molecules that can damage cellular DNA, which can lead to genetic changes and pave the way for the development of cancer.

Anti-inflammatory properties: Inflammation is one of the factors that can play a role in the development and progression of cancer. Having anti-inflammatory properties, flavonols can help reduce inflammatory reactions in the body, thereby preventing the development of cancer (17).

Flavan-3-ols

Flavan-3-ol are a group of flavans in which the structure of 2-phenyl-3,4-dihydro-2H-chromen-3-ol is repeated in common .(18)

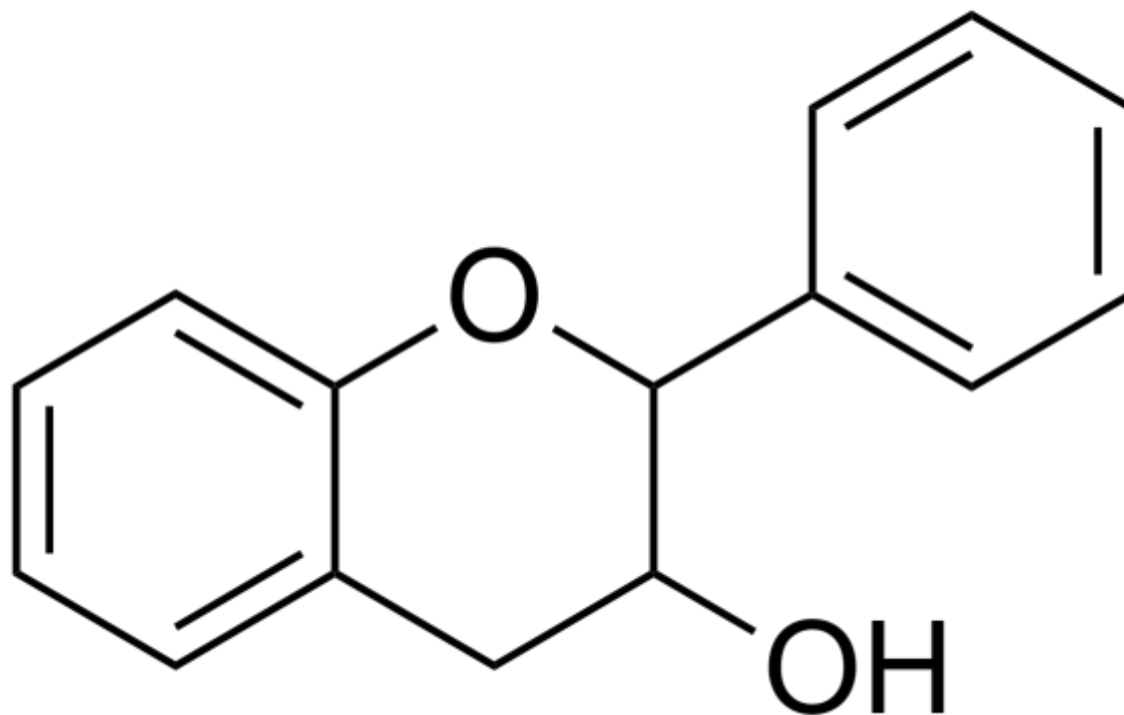


Figure 4. Flavan-3-ols (19)

In addition, flavan-3-ols may reduce the risk of cancer by reducing oxidative stress and protecting DNA from damage that can lead to cancerous mutations. However, despite promising results from laboratory and animal studies, we still need more research to fully understand the effect of flavan-3-ols on cancer in humans. These studies should include extensive clinical trials to definitively confirm the effectiveness and safety of these compounds in the prevention and treatment of cancer .(20)

Flavan-3-ols, which are a type of flavonoid and are found in abundance in fruits, vegetables, red wine, and tea, studies have shown that these compounds can play an important role in supporting the body's health and preventing diseases, especially cancer. Due to their strong antioxidant abilities, flavan-3-ols can be effective in dealing with oxidative stress and preventing cell damage that can lead to the formation of cancer cells. In addition, there are other mechanisms through which flavan-3-ols may help fight cancer, including regulating signaling pathways related to cell growth and apoptosis, as well as inhibiting metastasis and proliferation of cancer cells. Nevertheless, it is important to emphasize that although preliminary research has shown positive results, to generalize these results to the human population and confirm the benefits of flavan-3-ols in the prevention and treatment of cancer, we need more evidence from clinical trials that can To evaluate the long-term effects and safety of using these compounds in humans .(21)

Flavanone

Flavanones are a group of chemical compounds belonging to the larger family of flavonoids, which itself is a broader subset of phenols. These compounds are found naturally in many plants and are part of the protective factors of plants against pests and diseases. Flavanones are found in many fruits, vegetables, and even teas, and are known for their antioxidant, anti-inflammatory properties, and their ability to improve cardiovascular function.(22)

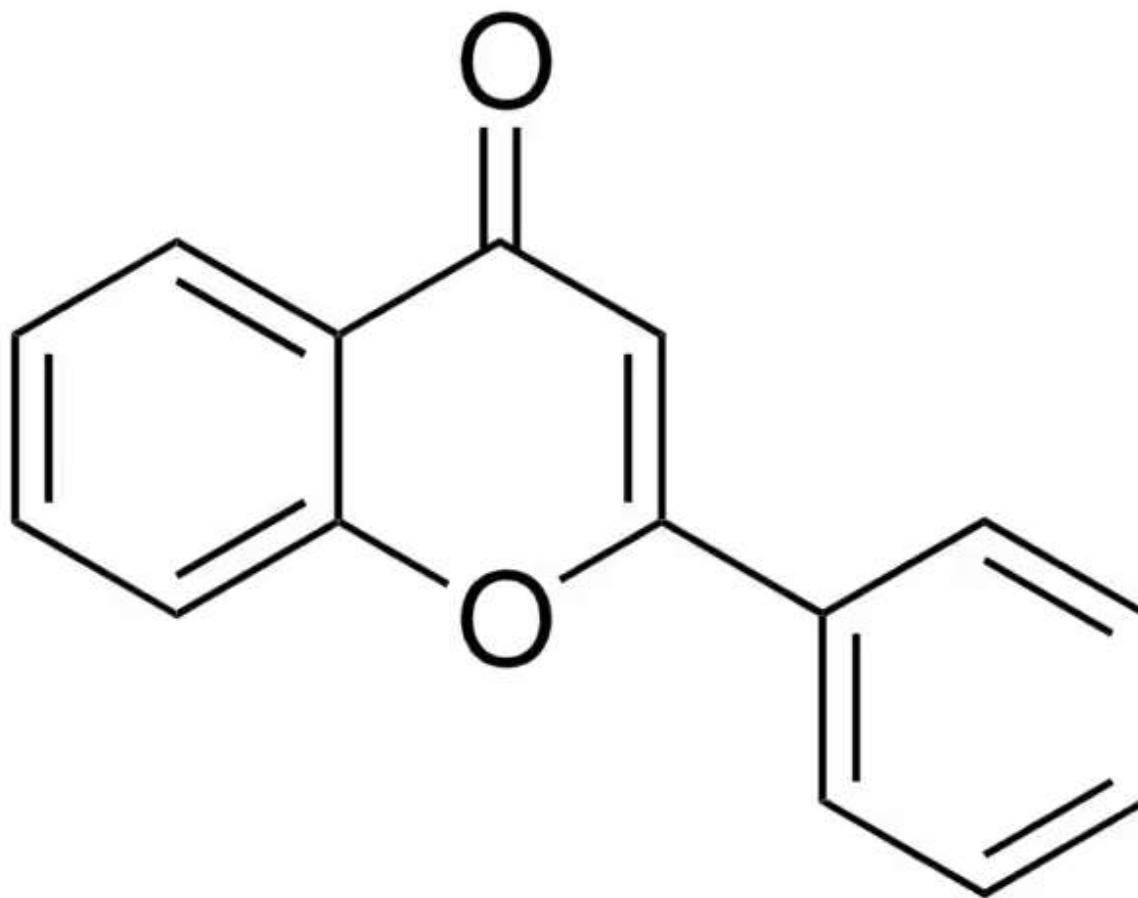


Figure 5. Flavanone (23, 24)

Anthocyanins

These diverse compounds play an important role in the biological processes of plants, including attracting insects for pollination and protecting against environmental stresses such as intense sunlight and low temperatures. Anthocyanins are also known as powerful antioxidants that can protect the human body from damage caused by free radicals and thus help prevent various diseases including heart disease and some types of cancer. Studies have shown that consuming foods rich in anthocyanins can help improve brain function and reduce the risk of cognitive disorders in the elderly. Considering these impressive benefits, paying attention to the regular consumption of anthocyanin-rich fruits and vegetables is very important to maintain health and prevent diseases .(22)

Anthocyanin Among the most important natural pigments obtained from plants are anthocyanins. After chlorophyll, these pigments are the most abundant types of natural food pigments. These pigments are actually glycosylated 3, 5, 7, and 3 tetrahydroxy flavylum derivatives. They are among the important pigments in nature. Anthocyanins are polyphenolic compounds that are a subset of flavonoids. They cause blue, red and purple colors in most fruits and flowers. The main sources of this pigment are berries, grapes, eggplant, blueberries and cherries. One of the characteristics of anthocyanins is their non-toxicity. These pigments are soluble in water and are found in the cellular fluid of vascular plants. They are widely used in the food industry. To date, about 540 types of anthocyanin pigments have been identified in plants and different compounds. This group also changes the type of sugar depending on the replacement of sugar in carbon number 5 and 3. Among the most common of these types, the following can be mentioned: Polarogonidin Delphinidin Petunidine Malobedin cyanidin These pigments are unstable compounds and their stability depends on the following factors: temperature, oxygen, light, enzymes and pH. Anthocyanins have a

glycosidic structure. That is, they consist of a sugar part and a non-sugar part. The sugar part can include rhamnose, galactose or glucose, and the non-sugar part includes anthocyanidin or aglycone. The most sugar in the structure of anthocyanins is glucose. This sugar part is usually connected to the hydroxyl group of carbon number 3. In most plants, these pigments are located in cells near the surface. To extract this group, the use of acidic solvents causes damage to the cell wall of the plant and as a result, the pigments dissolve. The common method for extracting anthocyanins is the classical method. Methanol and ethanol can be mentioned among the solvents used in the classical method. Then the extract is concentrated for use in the next steps. To separate the solvent from the pigment, the process is carried out under vacuum and low temperature conditions. It should be noted that ethanol is less toxic than methanol. Therefore, it is more used in anthocyanin extraction processes. To date, many researches have been conducted on the effect of anthocyanin pigment on human health. According to this research, this pigment has the ability to absorb free radicals. Considering that free radicals are carcinogenic compounds, this action of anthocyanins creates anti-cancer and antioxidant properties. It also destroys free radicals and reduces arteriosclerosis. Anthocyanins also reduce the level of triglycerides and free fatty acids. They increase vision, have a selective inhibitory effect on the growth of cancer cells, reduce some types of cancer, and improve diabetes and liver damage.

Anthocyanins have an important link with cancer because they act as powerful antioxidants and can play a role in fighting oxidative stress and cellular damage that can lead to cancer development. Oxidative stress occurs when the production of free radicals and other reactive molecules in the body upsets the balance with antioxidant defense systems. As a result, this process can lead to DNA damage, which is one of the main mechanisms in causing cancerous changes. Several studies have shown that anthocyanins may play a role in preventing and fighting cancer through several mechanisms. Some research has shown that anthocyanins can inhibit the growth and proliferation of cancer cells. They can stop or slow down the cell cycle, which prevents cancer cells from multiplying too much. Anthocyanins can stimulate activities that lead to the death of cancer cells without negatively affecting healthy cells. This feature makes them a valuable factor in cancer treatment. Chronic inflammation can increase the risk of developing cancer. Anthocyanins have strong anti-inflammatory properties that can help reduce inflammatory reactions in the body, thereby reducing the risk of cancer. Some studies have shown that anthocyanins can reduce the ability of cancer cells to invade and metastasize (spread to other parts of the body). This effect occurs by inhibiting the molecular activities that cancer cells need to move and establish in new tissues. Additionally, anthocyanins may help boost the immune system, which in turn can help the body fight cancer cells. Due to the strong antioxidant properties of anthocyanins, these compounds can help protect cells from damage caused by free radicals, which can reduce the risk of cancer .(25)

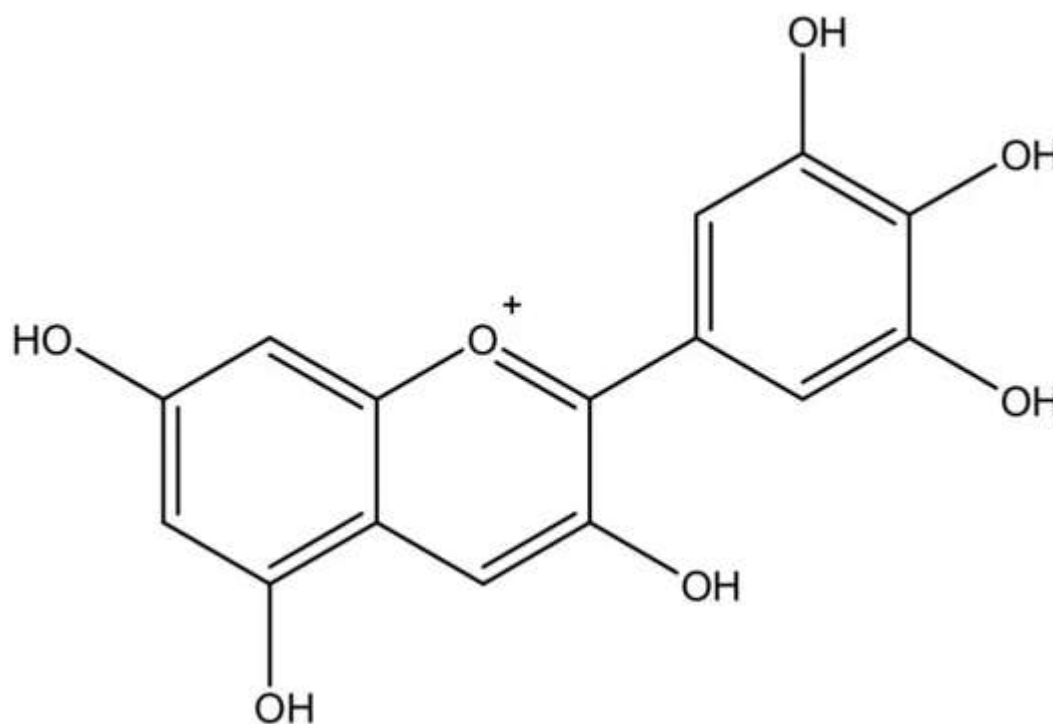


Figure 6. Anthocyanins (26)

Cancer prevention with flavonoids

Research in this field has brought different results. According to the Linus Pauling Institute, animal studies have shown positive results in lung, mouth, stomach, colon, skin and other cancers, but human studies have yet to show similar results. More research is needed. The most promising studies to date are related to breast and stomach cancer. A large study published in 2003 in the British Journal of Cancer found that women who consumed higher levels of flavones had a lower risk of breast cancer, while a study in Cancer Causes & Control found that There is a connection between kaempferol and reduced risk of stomach cancer. . On the other hand, another study published in the same journal did not associate a reduced risk of stomach cancer with kaempferol but flavonones. Although flavonoids exhibit powerful antioxidant activity, compared to antioxidants such as vitamin C and vitamin E, they have a relatively low concentration in the bloodstream when compared to the world's healthiest foods. This may reduce their overall antioxidant power, thereby reducing their cancer-fighting effects.(27)

Flavonoids as a class of useful compounds are known as "nature's biological response modifiers" due to their ability to change the body's reactions to other compounds such as allergens, viruses and carcinogenic properties. In addition, flavonoids as powerful antioxidants protect the body against oxidative damage and free radicals. Flavonoids have antioxidant activity against free radicals, and epidemiological studies on them show that the consumption of these compounds is associated with a reduction in the risk of cancer and cardiovascular diseases. Many medicines that are prepared from foods, juices, plants and bee pollen directly contain flavonoids. Most flavonoids have antioxidant properties and some of them also have anti-inflammatory properties.(28)

Isoflavones are highly concentrated in soy products as well as legumes. They are phytoestrogens. This means that they have chemicals that act like the hormone estrogen. Scientists believe that this substance may be useful in reducing the risk of developing hormonal cancers, such as breast, endometrial and prostate cancer. In various studies, it has been determined that some isoflavones act as antioxidants and some act as oxidants. Therefore, their effect on cancer is not known. They have also been studied as a way to treat menopausal symptoms .(29)

Flavonoids have been studied a lot in recent years and it has been found that foods containing

these compounds are associated with better human health. A meta-analysis of 12 studies published in the journal PLOS One found that the risk of breast cancer was significantly lower in women with a high dietary flavonoid intake(30)(31). Another study published in the Journal of Translational Medicine found that people who got more flavonoids in their diet had a lower risk of heart disease, nonfatal heart problems, and death from heart disease(32)(33)

Conclusion

The Research conducted in this field, including laboratory investigations and clinical studies on humans, show that flavonoids can help fight cancer through various mechanisms such as antioxidant, anti-inflammatory properties, inhibition of tumor growth, stimulation of apoptosis, and inhibition of metastasis. . However, it should be emphasized that while the initial results are promising, more research is still needed to fully understand the effect of flavonoids on cancer and to determine the exact doses and methods of their administration to achieve the greatest degree of efficacy and safety. In particular, more and more detailed clinical studies on humans are necessary to confirm the obtained results definitively and to consider these compounds as part of standard treatment strategies for cancer. In any case, moderate and regular consumption of foods rich in flavonoids, including fruits, vegetables, tea, and wine (in moderation), can be an important part of a healthy, balanced diet that improves overall health and reduces the risk of disease. It helps chronically.

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