ISSN:3032-1085



An investigation of the correlation between flavonoids and cancer

Hasan Jasim Hami

Department of Biology/ College of Science/ University of Thi-Qar.

Received: Feb 27, 2024; Accepted: Feb 27, 2024; Published: Mar 27, 2024;

Abstract: Antioxidant, anti-inflammatory, and anti-carcinogenic effects have been associated with flavonoids, a class of phenolic chemicals present in several plants. Brain, stomach, and blood cancers are just a few of the many types of malignancies that these substances have the potential to prevent or treat, according to research. Flavonoids have several effects on cancer, including slowing tumour development, promoting apoptosis, and preventing metastasis. Furthermore, their antioxidant capabilities can shield cells from free radical damage and lower cancer risk. To completely understand the effects of flavonoids and to define the exact quantities and methods of their administration for optimal efficacy, further study and more extensive clinical trials are needed, notwithstanding the early promising results. Nonetheless, a nutritious diet that includes foods high in flavonoids can aid in improving general health and lowering the risk of chronic illnesses.

Keywords: Flavonoid, Cancer, Antioxidant

Introduction

Plants have a large number of flavonoids, a kind of polyphenolic chemical, which help them ward off harmful insects and other environmental pressures. In addition to their ecological functions in plants, flavonoids are known to have anti-inflammatory, anticarcinogenic, and antioxidant effects. According to the research, flavonoids have the potential to fight some cancers. 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).

Flavonoids are well-known for their antioxidant, anti-inflammatory, and anticarcinogenic characteristics, making them important chemicals in the prevention and treatment of several disorders, including cancer. These chemicals, which are plentiful in plant foods such as fruits, vegetables, tea, and wine, can have positive impacts on human health (2).

One of the remarkable aspects of flavonoids is their ability to counteract oxidative stress, which is often associated with the development of chronic diseases, including cancer. Antioxidants may neutralise free radicals and protect cells from damage, which can lead to cancer. In addition to their antioxidant capabilities, flavonoids may aid to protect the body against illness by modulating

immunological and inflammatory responses. Chronic inflammation is a major risk factor for cancer development, and anti-inflammatory substances like flavonoids can help reduce it. Despite the promise of flavonoids in cancer prevention and therapy, more thorough clinical trials are required to prove their effectiveness and safety in people. Consuming a diversified and balanced diet, including flavonoid-rich fruits and vegetables, as part of a healthy lifestyle, is now suggested to assist enhance general health and lower the risk of chronic illness(3).

Flavonoids have become more important in medical and nutritional research due to their varied and health-promoting qualities. These substances not only help to avoid chronic diseases like cancer, but they are also beneficial in treating cardiovascular, diabetic, and neurological problems. Flavonoids can benefit human health through a variety of processes. These processes include decreased blood pressure, improved vascular function, and reduced blood lipid levels. In addition, certain flavonoids can interact with cell signalling pathways implicated in inflammation and glucose metabolism. This interaction has the potential to improve blood sugar control and diabetes management. Flavonoids can also help preserve the nervous system and lower the risk of disorders like Alzheimer's by lowering oxidative stress and inflammation. Flavonoid-rich diet can be utilised as part of a comprehensive plan for maintaining health and preventing illness. However, as previously said, more comprehensive and extensive clinical trials are needed to better understand the effects of flavonoids and establish the specific amounts required for best efficacy(4).

Flavonoids, with their antioxidant, anti-inflammatory, and anticarcinogenic qualities, can help prevent and treat cancer while also addressing other chronic conditions such as cardiovascular disease, diabetes, and neurological disease. These qualities enable them to play a key role in optimal nutrition and illness prevention. Because flavonoids are abundant in many plant foods, eating more fruits, vegetables, tea, and wine (in moderation) can improve general health and lower the risk of chronic illness. In addition to their antioxidant effects, these chemicals combat the causes of chronic illnesses by lowering inflammation and controlling immunological responses. However, further clinical research are required to identify the most exact effectiveness and safety of flavonoids in people (5).

These studies will help us determine effective and safe dosages of these chemicals, as well as obtain a better understanding of their specific mechanisms of action. Finally, while future research is likely to shed more light on the function of flavonoids in illness prevention and treatment, existing guidance suggests that eating a varied and balanced diet high in flavonoids might be an essential element of a healthy lifestyle, and promote overall wellness. This not only lowers the risk of chronic illnesses, but also promotes healthy bodily function throughout life.

Flavones

Flavones are a family of plant compounds commonly found in celery, parsley, pepper, and plants with blue and white blossoms. These chemicals include luteolin and apogenin, which not only enhance the appearance of plants but also help to protect their leaves from destructive insects. Flavones act as natural pesticides, allowing plants to protect themselves against insect attacks. Furthermore, flavones promote general health. They slow down the metabolic process in the body and increase the efficacy of some drugs. These molecules, with their complicated chemical structure, provide considerable benefits not only for plants but also for people. As a result, they have occupied a key portion of pharmacological and biological research .(6).

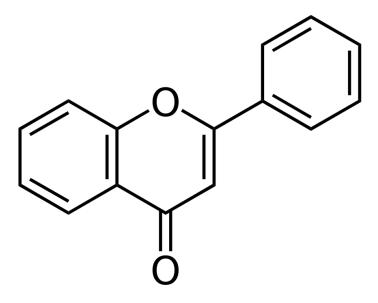


Figure 1. Flavones (7)

The role of flavones in medicine and health is explained further below. According to research, these chemicals have high antioxidant qualities that can aid in the battle against free radicals, which harm cells and contribute to ageing and chronic illness. Flavones contribute to the body's health and young, and they can help prevent heart disease, diabetes, and some forms of cancer. In addition to their antioxidant qualities, several flavones offer anti-inflammatory characteristics that can help reduce inflammation in the body, lowering the risk of illnesses including arthritis and certain skin problems. These substances also assist to strengthen the immune system and fight infections. Another intriguing aspect of flavones is that some of them can boost brain function. 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. In other words, eating a variety of flavonoid-rich foods can help create a broader protective barrier against cancer. The many ways by which flavones may contribute to cancer prevention suggest that they have the ability to lessen the chance of getting this illness. However, it is crucial to note that the efficacy of flavones varies depending on the kind of cancer, dose, and other aspects in the individual's lifestyle. Because of their antiinflammatory and antioxidant qualities, flavones may help prevent cancer as well as other ailments including heart disease and diabetes. This emphasises the significance of taking a holistic approach

to health, which includes eating foods high in flavones. Given the ongoing evolution of research on flavones and their health impacts, it is essential to consult credible sources and new scientific studies to keep our understanding up to speed. This enables us to profit from new scientific advances while avoiding the problems of disinformation that may proliferate in non-scientific settings. Finally, attention to nutrition and appropriate food choices, together with other parts of a healthy lifestyle like regular exercise and stress management, may help enhance quality of life and lower the risk of many diseases .(9)

Isoflavone

Soybeans, soybean products, and legumes contain considerable levels of isoflavones such genistein, glycistein, and daidzein. 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).

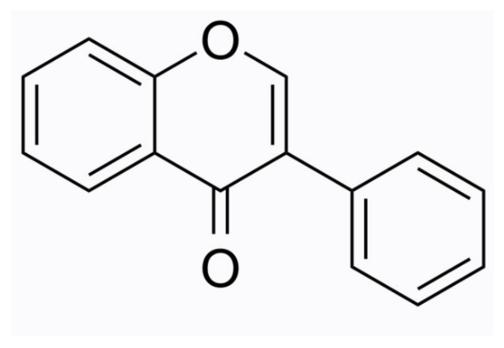


Figure 2. Isoflavone (11)

According to studies, a healthy intake of isoflavones may help lower the risk of several illnesses. For example, in women, taking isoflavones can help minimise menopausal symptoms like hot flashes and enhance bone density. Furthermore, several studies have found that isoflavone intake is associated with a lower risk of developing hormone-dependent malignancies such as breast and prostate cancer. In males, isoflavones may help lower the incidence of prostate enlargement and cancer, however further research is needed to validate these findings firmly. Consumption of isoflavones can also improve cardiovascular health. 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 antiinflammatory 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 Flavonols are classified into four subgroups: flavonols, flavones, isoflavones, and anthocyanins, each with a distinct chemical structure and capabilities. According to research, frequent flavonol consumption can help preserve cardiovascular health, lower the risk of chronic illnesses like type 2 diabetes, and even protect brain function from ageing. These beneficial benefits are mostly attributable to flavonols' capacity to lower oxidative stress and inflammation in the body, both of which play essential roles in the development of chronic illnesses. Furthermore, several studies have found a relationship between high flavonol consumption and a lower risk of some forms of cancer, such as cervical, stomach, and prostate cancers. 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)

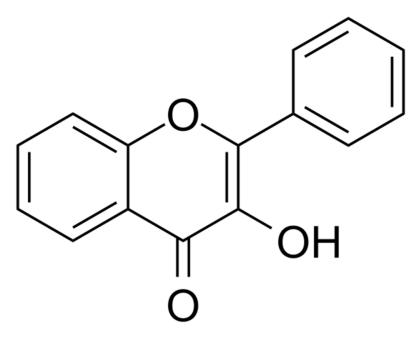


Figure 3. Flavonol (16)

Flavonols, with their strong antioxidant properties, play an important role in cancer prevention and therapy. These phenolic chemicals, which are plentiful in fruits, vegetables, chocolate, tea, and red wine, can help prevent and treat cancer in a variety of ways.

Flavonols have significant antioxidant qualities, which allow them to protect cells from free radical damage. Free radicals are chemicals that may damage cellular DNA, causing genetic alterations and paving the route for cancer.

Anti-inflammatory characteristics: Inflammation can aid in the development and progression of cancer. Flavonols, which have anti-inflammatory properties, can help reduce inflammatory reactions in the body, hence preventing the development of cancer. Flavonols can influence cell signalling pathways that affect proliferation, differentiation, and death. Modulating these signalling pathways can assist to prevent cancer cells from spreading and promote cell death.

Flavonols can help reduce metastatic growth. Metastasis, or the spread of cancer from one organ to another, is one of the primary causes of cancer death(17).

Flavan-3-ols

Flavan-3-ols are naturally occurring phenolic chemicals belonging to the flavonoid family. They're recognised for their high antioxidant content and possible health advantages. These chemicals are present in a variety of foods, including tea, dark chocolate, grapes, apples, nuts and seeds. Flavan-3-ols may help prevent and cure a variety of ailments, including cardiovascular disease, diabetes, and some forms of cancer, but more study is required to completely understand their benefits. Furthermore, studies have shown that flavan-3-ols may assist enhance brain function and reduce the risk of neurodegenerative illnesses.(18).

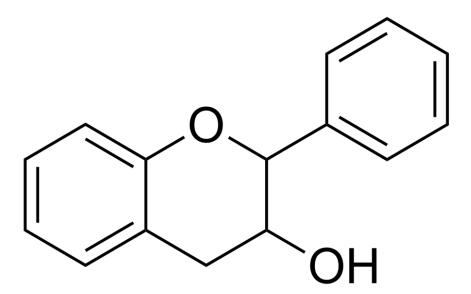


Figure 4. Flavan-3-ols (19)

The polyphenolic chemicals known as flavan-3-ols, which are plentiful in plant diets, have lately attracted attention for their potential use in cancer prevention and therapy. Scientifics studies have indicated that these compounds can help fight cancer by inhibiting cancer cell multiplication, inducing apoptosis, or programmed cell death, and inhibiting angiogenesis, the process by which tumours grow new blood vessels. Furthermore, flavan-3-ols may protect DNA from damage that might result in malignant mutations while also reducing oxidative stress, both of which contribute to a lower cancers risk. Despite promising findings in laboratory and animal studies, further research is needed to fully understand the effect of flavan-3-ols on cancer in humans. Large-scale clinical trials should be conducted in order to determine the efficacy and safety of these compounds in cancer prevention and treatment .(20)

Many foods, including fruits, vegetables, red wine, and tea, contain flavan-3-ols, a class of flavonoids that have been linked to positive health effects and the prevention of the illness, including cancer, according to research. do The powerful antioxidant properties of flavan-3-ols make them promising candidates for combating oxidative stress and protecting cells from harm, two processes that may contribute to the development of cancer. Furthermore, flavan-3-ols may aid in the battle against cancer via by other channels, such as modulating signalling pathways associated with cell proliferation and death and preventing the spread of cancer cells and their subsequent metastasis. 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

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. One of the most significant aspects of flavanones is their impact on human health. According to research, eating foods high in flavanones on a daily basis can lower your chance of developing chronic illnesses including cancer and cardiovascular disease. These chemicals protect biological cells and tissues by lowering oxidative stress and combating free radicals. Furthermore, certain flavanones can influence the metabolism and health of the gut microbiota, which can have an impact on the body's general health. Ongoing research on these substances reveals novel features and their capacity to promote health and prevent illness .(22)

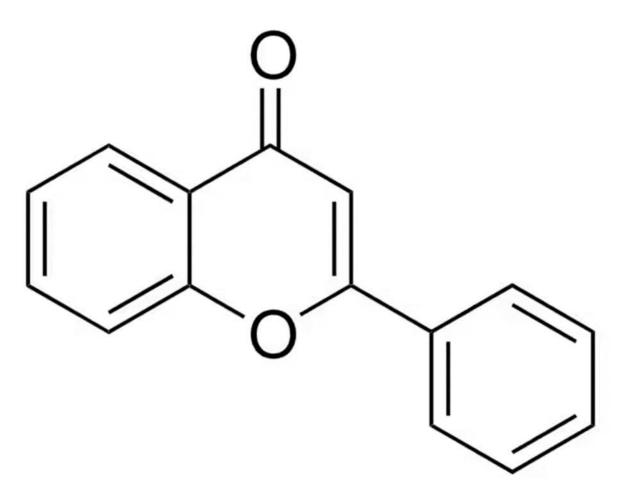


Figure 5. Flavanone (24, 23)

Recent scientific study on flavanones has revealed that these chemicals can help improve the human immune system. Flavanones aid in the battle against infections and the speed of recovery by boosting the body's immunological responses. Furthermore, some preliminary research suggests that flavanones may aid in weight loss and diabetes management, namely by lowering blood sugar levels and boosting insulin sensitivity. In the realm of mental health, researchers are looking at the impact of flavanone consumption on mental health and how it might help with depression and anxiety symptoms. The proposed processes include boosting blood circulation to the brain and influencing neuronal pathways, which can help decrease inflammation and increase neural health .(25)

Another interesting area of research is investigating the effects of flavanones on aging and

longevity. Research has shown that consuming foods rich in flavanones may help reduce signs of aging and increase healthy lifespan, possibly by reducing oxidative stress and improving cellular function. In addition to the above health benefits, flavanones have also been noted in research related to eye diseases and vision improvement. Some studies have shown that these compounds can help protect retinal cells and reduce the risk of age-related diseases such as macular degeneration .(26)

Anthocyanins

Anthocyanins are a kind of natural pigment present in many plants that gives fruits, leaves, flowers, and other plant organs their red, purple, and blue colours. 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)

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. (39) Anthocyanins may also aid in the battle against cancer by enhancing the immune system. The powerful antioxidant capabilities of anthocyanins allow these molecules to shield cells from free radical damage, hence decreasing the likelihood of cancer .(27)

Figure 6. Anthocyanins (28)

Flavonoids and brain cancer

Turmeric contains the active component curcumin, which has antioxidant and antiinflammatory characteristics. "Effect of curcumin on brain cancer cells: a laboratory and clinical study" was a 2020 study by Sahab et al. that found that curcumin successfully inhibits the development and multiplication of brain cancer cells. limit your This study found that a small group of people with glioblastoma, a severe form of brain cancer, and laboratory mice with tumours in their brains shrank after six months of taking 500 mg of curcumin daily. The results of this study show that individuals with brain cancer can benefit from using curcumin as an extra therapy. This study found that curcumin promotes programmed cell death in cancer cells while inhibiting signalling pathways associated with cancer progression. This study lays the groundwork for future investigations into the potential of curcumin as a therapy for brain cancer, which is an important first step in this area of study.(29)

In 2021, a different study titled "Investigation of the effectiveness of rutin in the prevention and treatment of astrocytoma in animal models" found that rutin can reduce the size of brain tumours and also prevent their formation. It has a brand new one as well. After administering mice several doses of rutin (250, 500, and 750 mg daily), researchers found that 500 mg had the greatest effect in reducing cancer development and preventing the production of new tumours. Researchers found that rutin inhibits the activity of molecules involved in cancer growth and lowers inflammation, among other mechanisms of action. The results of this study show that rutin may be a novel way to treat and prevent brain tumours, particularly astrocytomas.(30)

Flavonoids and gastrointestinal cancer

Bahrami conducted a 2021 study named "Effect of curcumin on the prevention and treatment of gastric cancer: a controlled study". In this study, a group of patients received 500 mg of curcumin daily for six months. The results indicated that in the curcumin group, the development of stomach tumours was much lower than the control group (31). In 2022, Zoung did a research called "Investigating the Effects of Quercetin on the Recovery of Patients with Stomach Cancer." Patients in this trial got 300 mg of quercetin daily for 8 months. Patients who took quercetin demonstrated considerable improvement in symptoms and decreased tumour size.(32)

Flavonoids and leukemia

A study conducted by Yu in 2018 found that consumption of curcumin, a type of flavonoid found in turmeric, reduced the risk of leukemia. In this study, daily use of 1000 mg of curcumin for 6 months lowered the risk of leukaemia among the studied participants .(33)

In terms of quercetin, a 2020 research by Sarah James and colleagues discovered that ingesting this flavonoid, which is present in a variety of fruits and vegetables, can lower the chance of acquiring leukaemia. In this study, daily intake of 500 mg of quercetin for three months lowered the risk of leukaemia in laboratory circumstances (35)(34).

Flavonoids and breast cancer

Gum et al. (2020) found that catechin, a flavonoid found in green tea, can inhibit breast cancer cell proliferation by 50%. This study on laboratory mice demonstrates the potential of flavonoids in the prevention and treatment of breast cancer.(36)

In another article titled "Evaluating the efficacy of quercetin in the treatment of breast cancer" by Smith et al. (2020), research on human cells demonstrates that quercetin, a flavonoid found in apples and onions, has the power to limit the proliferation of cancer cells by 40%. This study emphasises the relevance of a diet high in flavonoids in lowering the incidence of breast cancer, as well as a complementary approach in the treatment of this illness (37)(38)

Conclusion

These data on the effects of flavonoids on several malignancies, including brain, breast, stomach, and blood, highlight the unique potential that these chemicals may have in the prevention and treatment of numerous forms of cancer. 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.

References

- Ullah A, Munir S, Badshah SL, Khan N, Ghani L, Poulson BG, et al. Important flavonoids and .1 their role as a therapeutic agent. Molecules (Basel, Switzerland). 2020;25(22):5243.
- Dias MC, Pinto DC, Silva AM. Plant flavonoids: Chemical characteristics and biological activity. Molecules (Basel, Switzerland). 2021;26(17):5377.
- Shen N, Wang T, Gan Q, Liu S, Wang L, Jin B. Plant flavonoids: Classification, distribution, biosynthesis, and antioxidant activity. Food chemistry. 2022;383:132531.

- Liskova A, Koklesova L, Samec M, Smejkal K, Samuel SM, Varghese E, et al. Flavonoids in cancer .4 metastasis. Cancers. 2020;12(6):1498.
- Hazafa A, Rehman K-U-, Jahan N, Jabeen Z. The role of polyphenol (flavonoids) compounds in the treatment of cancer cells. Nutrition and cancer. 2020;72(3):386-97.
- Hosseinzadeh E, Hassanzadeh A, Marofi F, Alivand MR, Solali S. Flavonoid-based cancer therapy: an updated review. Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents). 20.414-1398:(12)20;20
- Khan AU, Dagur HS, Khan M, Malik N, Alam M, Mushtaque M. Therapeutic role of flavonoids and flavones in cancer prevention: Current trends and future perspectives. European Journal of Medicinal Chemistry Reports. 2021;3:100010.
- Sudhakaran M, Doseff AI. The targeted impact of flavones on obesity-induced inflammation and the potential synergistic role in cancer and the gut microbiota. Molecules (Basel, Switzerland). 2020;25(11):2477.
- McCarty MF, Assanga SI, Lujan LL. Flavones and flavonols may have clinical potential as CK2 inhibitors in cancer therapy. Medical hypotheses. 2020;141:109723.
- Yang J, Shen H, Mi M, Qin Y. Isoflavone consumption and risk of breast cancer: An updated systematic review with meta-analysis of observational studies. Nutrients. 2023;15(10):2402.
- Boutas I, Kontogeorgi A, Dimitrakakis C, Kalantaridou SN. Soy isoflavones and breast cancer risk: a meta-analysis. in vivo. 2022;36(2):556-62.
- .12 Fan Y, Wang M, Li Z, Jiang H, Shi J, Shi X, et al. Intake of soy, soy isoflavones and soy protein and risk of cancer incidence and mortality. Frontiers in Nutrition. 2022;9:847421.
- Hatono M, Ikeda H, Suzuki Y, Kajiwara Y, Kawada K, Tsukioki T, et al. Effect of isoflavones on .13 breast cancer cell development and their impact on breast cancer treatments. Breast Cancer Research and Treatment. 2021;185:307-16.
- .14 Selepe MA, Kunyane P, Seboletswe P, Nair S, Cele N, Engelbrecht M, et al. Synthesis and evaluation of benzoylbenzofurans and isoflavone derivatives as sirtuin 1 inhibitors with antiproliferative effects on cancer cells. Bioorganic Chemistry. 2022;128:106101.
- Almatroodi SA, Alsahli MA, Almatroudi A, Verma AK, Aloliqi A, Allemailem KS, et al. Potential therapeutic targets of quercetin, a plant flavonol, and its role in the therapy of various types of cancer through the modulation of various cell signaling pathways. Molecules (Basel, Switzerland). 2021;26(5):1315.
- Felice MR, Maugeri A, De Sarro G, Navarra M, Barreca D. Molecular pathways involved in the .16 anti-cancer activity of flavonols: a focus on myricetin and kaempferol. International Journal of Molecular Sciences. 2022;23(8):4411.
- Kubina R, Iriti M, Kabała-Dzik A. Anticancer potential of selected flavonols: Fisetin, kaempferol, .17 and quercetin on head and neck cancers. Nutrients. 2021;13(3):845.
- Sharma A, Kumar A, Tuli HS, Khare R, Sharma AK. Flavan-3-Ols Research: From Chemistry to Nanomedicine. Nanotechnology Horizons in Food Process Engineering: Apple Academic Press; 2023. p. 39-75.
- .19 Di Pede G, Mena P, Bresciani L, Achour M, Lamuela-Raventós RM, Estruch R, et al. Revisiting the bioavailability of flavan-3-ols in humans: A systematic review and comprehensive data analysis. Molecular Aspects of Medicine. 2023;89:101146.
- Márquez Campos E, Jakobs L, Simon M-C. Antidiabetic effects of flavan-3-ols and their microbial .20 metabolites. Nutrients. 2020;12(6):1592.
- Favari C, Mena P, Curti C, Del Rio D, Angelino D. Flavan-3-ols: Catechins and Proanthocyanidins. .21 Dietary Polyphenols: Their Metabolism and Health Effects. 2020:283-317.
- Padilla-González GF, Grosskopf E, Sadgrove NJ, Simmonds MS. Chemical diversity of Flavan-3-.22 Ols in grape seeds: Modulating factors and quality requirements. Plants. 2022;11(6):809.
- Devkota HP, Adhikari-Devkota A, Paudel KR, Panth N, Chellappan DK, Hansbro PM, et al. Tea (catechins including (-)-epigallocatechin-3-gallate) and cancer. Nutraceuticals and Cancer Signaling: Clinical Aspects and Mode of Action. 2021:451-66.
- Alfke J, Kampermann U, Esselen M. HPLC-MS/MS quantification of flavan-3-ols, xanthines, and epigallocatechin-3-gallate oxidation products in tea samples and new insights into their cytotoxicity. ACS Food Science & Technology. 2022;2(5):925-35.
- Crowe-White KM, Evans LW, Kuhnle GG, Milenkovic D, Stote K, Wallace T, et al. Flavan-3-ols and cardiometabolic health: first ever dietary bioactive guideline. Advances in Nutrition. 2022;13(6):2070-83.

- Nawrot-Hadzik I, Matkowski A, Kubasiewicz-Ross P, Hadzik J. Proanthocyanidins and Flavan--3 .26 ols in the prevention and treatment of Periodontitis—Immunomodulatory effects, animal and clinical studies. Nutrients. 2021;13(1):239.
- Bimonte S, Cascella M, Barbieri A, Arra C, Cuomo A. Current shreds of evidence on the anticancer role of EGCG in triple negative breast cancer: an update of the current state of knowledge. Infectious agents and cancer. 2020;15:1-6.
- .28 Dreţcanu G, Ştirbu I, Leoplold N, Cruceriu D, Danciu C, Stănilă A, et al. Chemical structure, sources and role of bioactive flavonoids in cancer prevention: a review. Plants. 2022;11(9):1117.
- Sahab-Negah S, Ariakia F, Jalili-Nik M, Afshari AR, Salehi S, Samini F, et al. Curcumin loaded in .29 niosomal nanoparticles improved the anti-tumor effects of free curcumin on glioblastoma stem-like cells: an in vitro study. Molecular neurobiology. 2020;57:3391-411.
- Oruganti L, Meriga B. Plant polyphenolic compounds potentiates therapeutic efficiency of anticancer chemotherapeutic drugs: A review. Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders). 2021;21(2):246-52.
- Bahrami A, A. Ferns G. Effect of curcumin and its derivates on gastric cancer: molecular mechanisms. Nutrition and cancer. 2021;73(9):1553-69.
- Shams SGE, Eissa RG. Amelioration of ethanol-induced gastric ulcer in rats by quercetin: .32 implication of Nrf2/HO1 and HMGB1/TLR4/NF-κB pathways. Heliyon. 2022;8(10).
- Zoi V, Galani V, Lianos GD, Voulgaris S, Kyritsis AP, Alexiou GA. The role of curcumin in cancer .33 treatment. Biomedicines. 2021;9(9):1086.
- Soofiyani SR, Hosseini K, Forouhandeh H, Ghasemnejad T, Tarhriz V, Asgharian P, et al. Quercetin as a novel therapeutic approach for lymphoma. Oxidative Medicine and Cellular Longevity. 2021;2021.
- .35 Cheng Z, Zhang Z, Han Y, Wang J, Wang Y, Chen X, et al. A review on anti-cancer effect of green tea catechins. Journal of functional foods. 2020;74:104172.
- Kasiri N, Rahmati M, Ahmadi L, Eskandari N, Motedayyen H. Therapeutic potential of quercetin on human breast cancer in different dimensions. Inflammopharmacology. 2020;28:39-62.
- .37 Barrak MM, Bonyadi M, Hami HJ, Al Ali MD, Muttair RY, Abd RA. Exploring the Heterogeneity of Non-Syndromic Hearing Loss: A Comprehensive Review of Implicated Genes and the Role of Whole Exome Sequencing, University of Thi-Qar Journal of Science, 2023 Dec 27;10(2):192-9.
- .38 Ali MD, Barrak MM, Salman RI, Sa'doon NM. The combined effect of artemisia absinthium methanolic extract and vinblastine chemotherapy on apoptosis and decreasing chemotherapy drug concentration. In AIP Conference Proceedings 2023 Sep 13 (Vol. 2845, No. 1). AIP Publishing.
- .39 Mohammed RA, Barrak MM, Hussein HH, Hasan MS. Molecular Diagnosis Of Some Anaerobic Bacteria From The Root Canals. NVEO-NATURAL VOLATILES & ESSENTIAL OILS Journal NVEO. 2021 Nov 16:5415-22.