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# A Review On : Cancer preventive effects of flavonoids

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## Abstract:

A cancer protective effect from plant-derived foods has been found with uncommon consistency in epidemiologic studies. However, it Has been difficult to identify specific components responsible for this effect.

Many phytochemicals have been shown to be biologically active And they may interact to protect against cancer. In recent years, experimental studies have provided growing evidence for the beneficial Action of flavonoids on multiple cancer-related biological pathways (carcinogen bioactivation, cell-signaling, cell cycle regulation Angiogenesis, oxidative stress, inflammation). Although the epidemiologic data on flavonoids and cancer are still limited and conflicting, Some protective associations have been suggested for flavonoid-rich foods (soy and premenopausal breast cancer; green tea and stomach Cancer; onion and lung cancer). This review focuses on the biological effects of the main flavonoids, as well as the epidemiologic evidence That support their potential cancer protective properties. 

**Keywords**: Flavonoids, Anti-cancer, Breast cancer, Therapeutic potential, Health benefits,Dietary flavonoids

## 1.Introduction

The scientific evidence that plant-based diets, in particular those rich in vegetables and fruits, protect against Cancers of various sites has been found to be strong and Consistent by a recent expert panel. This effects may result from the low energy content of these diets and/or from Their specific constituents. Although plant-derived foods .Vary in their nutritional composition profiles, they generally are good sources of important nutrients (i.e., fiber, carotenoids, vitamin C, folate, minerals) and of many less Well-characterized bioactive compounds (phytochemicals).

Accordingly, public health authorities have uniformly emphasized the potential benefits of fruits and vegetables in Their recommendations to the public. Moreover, the identification of the specific constituents of these foods that are Protective may lead to additional means of prevention, success the fortification of the food supply (e.g., folate), the use Of chemo preventive agents in high risk individuals and the Engineering of "designer foods" enriched in protective Compounds.

## 1.Clasiification of flavonoids and their sources

| Subclass | Flavonoids | Sources |
|---|---|---|
| Flavones | Apigenin, luteolin | Apple skin, celery |
| Flavonols | Quercetin, kaempferol, myricetin Flavan-3- ols: catechin, gallocatechin, catechin-3-gallate, epicaechin, epigallocatechin | Onions, apples, tea Chocolate, green and black tea, beans, cherry, strawberries, cocoa, apple |
| Flavonols | Catechin, epicatechin, epigallocatechin gallate | Tea |
| Flavanones | Hesperitin,naringenin | Citrus fruits,grapefruit |
| Anthocyanins | Cyanidin | Berries |
| Isoflavones | Genistein, daidzein | Soy |
| | | |

## 2 . Flavonoids in the diet

Flavonoids are the most common and widely distributed group of plant phenolics.Over 5000 different flavonoids have been described to date and they are classified into at least 10 chemical groups.Among them, flavones,flavonols, flavanols, flavanones, anthocyanins and isoflavones are particularly common in the diet. The most-studied members of these groups are included in Table 1, along with some of their food sources. Flavonols are the most abundant flavonoids in foods, with quercetin, kaempferol and myricetin being the three most common Flavonols.

Flavanones are mainly found in citrus fruit and flavones in celery. Catechins are present in large amounts in green and black tea and in red wine, where as anthocyanins are found in strawberries and other berries. Isoflavones are almost exclusively found in soy foods. Flavonoids are heat stable, and losses due to cooking and frying are relatively low. It is usually thought thatflavonoids are absorbed by passive diffusion after glycosylated flavonoids are converted to theirglycines.

## 3. Effects of flavonoids on cancer-related biological Pathways

A number of flavonoids have been shown to suppress carcinogenesis in various animal models. There is currently considerable interest in these compounds as they appear to exert a beneficial effect on several key mechanisms involved in the pathogenesis of cancer. The antioxidant property of flavonoids was the first mechanism of action studied, in particular with regard to their protective effect against cardiovascular diseases. Flavonoids have been shown to be highly effective scavengers of most types of oxidizing molecules, including singlet oxygen and various free radicals, which are possibly involved in DNA damage and tumor promotion. Flavonoids may also have a beneficial effect through their impact on the bioactivation of carcinogens. Most chemical carcinogens require transformation by phase I metabolizing enzymes into a more reactive form able to bind to DNA. If the resulting mutation is not repaired, it may initiate or promote the carcinogenesis process. The reactive chemical group introduced by phase I enzymes (or the original carcinogen) can be detoxified through conjugation by phase II metabolizing enzymes into a water-soluble compound which can then be eliminated from the body. The flavonols quercetin, kaempferol and galangin, and the flavone apigenin have been shown to inhibit cytochrome P450 enzymes of the CYP1A family. These enzymes play a major role in the activation of a number of suspected human carcinogens, such as polycyclic hydrocarbons and heterocyclic amines. Quercetin and naringin have also been shown to inhibit CYP3A4 and to contribute to the suppressive effect of grapefruit juice on this enzyme.

## 4. Tea and cancer

Tea is an important source of flavanols and flavonols. A large number of experimental studies suggest an anti-neoplastic effect for tea polyphenols several epide-miological studies conducted inAsia have also shown a

protective effect of green tea on stomach cancer, although a number of other studies have found no association. None of the most carefully conducted studies to date, Yu et al.

Assessed the type of tea, age when tea drinking started, frequency of new batches of tea leaves per day, number of Cups from each batch, duration per batch, and strength and Temperature of the tea. Risk of stomach cancer in this Chinese study decreased with increasing number of batches of greentea prepared per day.

## Flavonoid as anti-cancer agents Epidemiological studies

A huge number of epidemiological studies have been conducted to prove the protective effect of flavonoids against cancer. Increased consumption of liganans and greater plasma concentrations of their metabolites have been linked with reduced incidence of estrogen-related cancers in some and a prospective study was equivocal .It has been suggested that this inconsistency might have a genetic basis .Increased consumption of isoflavones has also been associated with decreased risk of estrogen-related cancers and vascular diseases. Data from four cohort studies and six case– control studies, which have examined associations of flavonoid intake with cancer risk revealed that flavonoids, especially quercetin, may reduce the risk of lung cancer in two studies but a non-significant increased risk in a third study. High versus low quercetin and kaempferol intakes were associated with 40 and 50 % reduction in risk, respectively, for stomach cancer.

## In vitro studies

Isoflavonoids have biphasic effects on the proliferation of breast cancer cells in culture; at concentrations >5 mM, genistein exhibits a concentration-dependent ability to inhibit both growth factor-stimulated and estrogen-

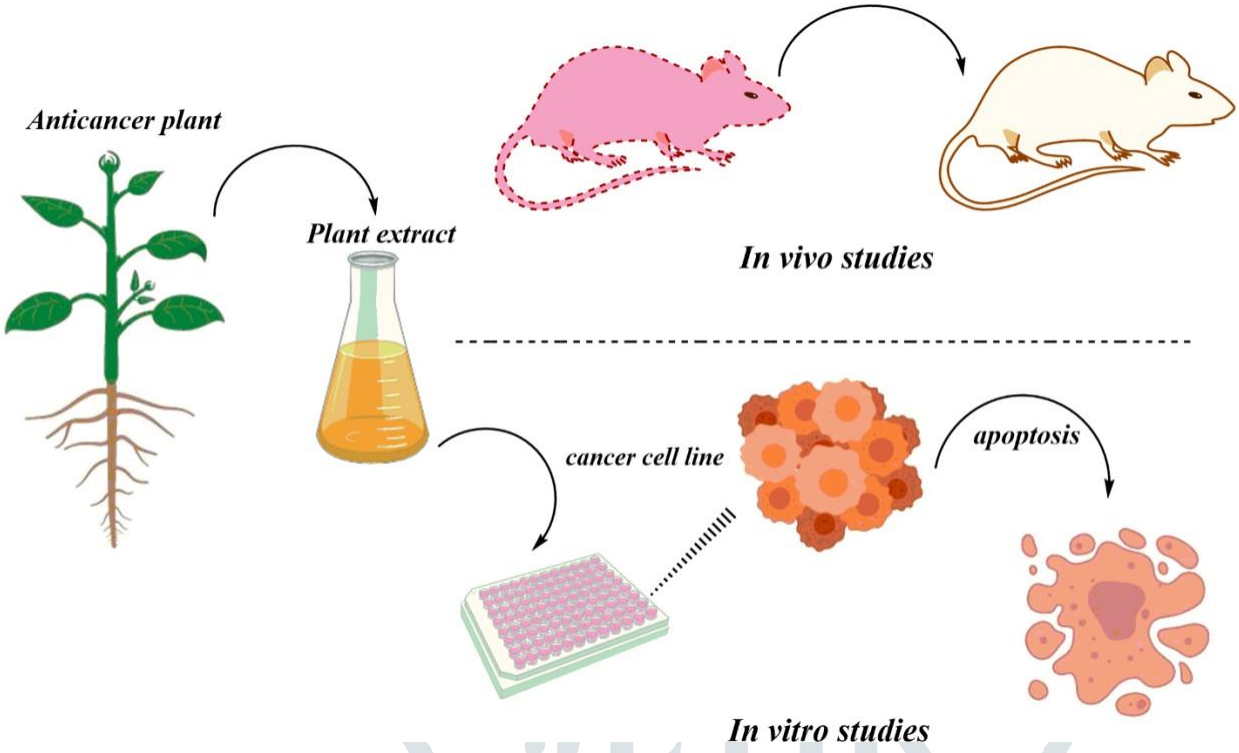
stimulated (reversed by 17b-estradiol) cell proliferation. Although genistein is a much better ligand for ERb than for the ERa (20-fold higher binding affinity) ,it can also act as an estrogen agonist via both ERa and ERb in some test systems.

Furthermore, although genistein binds to the ligand-binding domain of ERb in a manner similar to that observed for 17β-estradiol, in the ERb–genistein complex the AF-2 helix (H12) does not adopt the normal agonist type position, but instead takes up a similar orientation to that inducedby ER antagonists such as raloxifene

Anti-cancer activity of methanolic flower extract of *Tecoma stans* (METS) was evaluated by both in vitro (Vero and Hep 2 cell lines) and in vivo (using Ehrlich ascites carcinoma tumor model) methods and compared with 5-flurouracil. A significant dose-dependent anti-tumor activity was indicated. In vitro and in vivo studies on anti-cancer activity of flavonoids isolated from a herbal formulation revealed IC 50 of 24.948, 31.569 and 6.923 µg/ml, respectively, on three cancer cell lines MCF-7, Hep G-2 and ES-2 with dose-dependent inhibitory effect on hepatocellular carcinoma in mice. Broccolini leaf flavonoids (BLF) possess a dose-dependent anti-proliferative effects on four human cancer cell lines (SW480, HepG2, Hela, and A549) and apoptosis induction activity on SW480 cell line. Thus, the hybrid species Broccolini could be considered as a functional vegetable with potential in assisting for the treatment of four human cancers examined.

## In vivo studies

In vivo studies using animal models have suggested the protective effect of flavonoids against initiation as well as tumor progression. Animal model studies have provided the initial experimental evidence that soy can prevent breast cancer. Fermented soy milk (rich in genistein and daidzein), given to rats at 7 weeks of age, inhibited mammary tumor genesis induced by PhIP (2-amino-1-methyl-6-phenylimidazo pyridine .In syngenetic mice, i.p. administration of quercetin and apigenin inhibited growth and metastatic potential of melanoma cell (B16-BL6) along with significant decrease in their invasion in vitro. A polymethoxy flavonoid, nobiletin, inhibited the tumor-invasive activity of human fibrosarcoma HT-1080 cells in the Matrigel model through suppressing the expression of metalloproteases and augmenting of production of tissue inhibitors of metalloproteinases in tumor cells Flavonoids greatly influence the cascade of immunological events associated with the development and progression of cancer. One has to understand the mechanism how these flavonoids get accumulated in cellular organelles and tissues once they enter inside. Flavonoids have the potential of modulating many biological events in cancer such as apoptosis, vascularization, cell differentiation, cell proliferation, etc. A strong correlation persists between flavonoid-induced modulation of kinases with apoptosis, cell proliferation and tumor cell invasive behavior in vitro. Also, some of the dietary flavonoids have been known to display in vivo anti-tumor activity and repress in vivo angiogenesis. The cross talk between flavonoids and the key enzymes related to neoplastic cells and metastasis has to be understood in vitro and in vivo as well, providing new insights for fighting against cancer.




## Conclusion

The experimental data accumulated,particularly in the past three year, have demonstrated a wide variety of biological actions for flavonides which may be benefical against cancer. However,it not clear whether these effects would also be present at physiological concentration and for the metabolites that are likely to be most relevant to humans . studies of humans that would particularly be useful include prospective studies testing the association of flavonoid intake with cancer incidence, as well as biomarker studies testing the effect of specific flavonoid rich foods on relevant biological pathways , such as biotransformation's of carcinogens DNA damage, cell proliferation, apoptosis and inflammation.

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