Volume 2, Issue 3, 2023, Page 472-478

International Journal of Pharma Research and Technology

# A Critical Review on Flavonoids Used in Treatment of Various Cancers

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## Abstract

Flavonoids are natural phenol compounds that form a large group of secondary plant metabolites with interesting biological activities they are found in fruits, vegetables, grains, bark, roots, stems, flowers, tea and wine. These natural products are well known for their beneficial effects on health and efforts are being made to isolate the ingredients so called flavonoid. Flavonoids are of particular interest as they have significant effects on human health. Flavonoids possess anti-cancer properties and they exert their curative effect by modulating different cell. Flavonoids have gained Importance as anti-cancer agents and have shown great potential as cytotoxic anti-cancer agents Promoting apoptosis in cancer cells. Increasing evidence shows that flavonoids can inhibit carcinogenesis via suppressing ROS Levels. Surprisingly, flavonoids can also trigger excessive oxidative stress, but this can also induce death of malignant cells. High dietary flavonoid intake has strongly been suggested to reduce the risk of numerous cancer entities in a large body of epidemiological studies. . In this review, a summary of flavonoids and their effectiveness in cancer treatment targeting apoptosis has been discussed.

**Key Words:** Flavonoids, Cancer, Anti -Cancer Effects, Natural Polyphenols, Medicinal Herbs, Plant Compounds

## Introduction

Cancer is a diverse illness brought on by irreversible dysfunction and disruption of cellular homeostasis. Uncontrolled cell proliferation, differentiation, and loss of apoptotic capabilities all contribute to the progression of cancer. Which results in a significant increase in the population of neoplastic cells [1]. Internal Causes of cancer include genetic mutations, oxidative stress, and a lack of apoptotic activity and hypoxia, whereas excessive exposure to UV radiation may be connected to extrinsic causes of cancer, Smoking, stress, pollution, and radiation [2]. Because of research and prevention efforts, the mortality rate from cancer has decreased over time, but its incidence rate has grown. Numerous studies have emphasized the value of a plant-based diet in preventing illnesses linked to the development of tumours [3]. Vegetables

include a variety of bioactive substances, including phenolic compounds, carotenoids, and notably flavonoids, which may contribute to the health advantages of a plant-based diet. The second are regarded as essential and present in numerous nutraceutical, cosmetic, and pharmaceutical products. Uses in call, pharmaceutical, and cosmetic fields. These applications have spurred flavonoid research, has significantly grown in recent years. There are various subclasses of flavonoids, including flavones, isoflavones, flavanones, flavanols, catching-like flavonoids, anthocyanins and chalcones [4]. Due to the quantitative and qualitative variety of flavonoids in vegetables and fruits, it is exceedingly challenging to quantify dietary intake. This makes it difficult to establish epidemiologic connections about the effects of flavonoids on human health and disease. There have been several researches on absorption and bioavailability in the literature review by several writers. The bioavailability of flavonoids can be influenced by a number of factors, including some uncertainty due to factors including molecular weights, glycosylation, and esterification [5]. These studies suggest that flavonoids inhibit proliferation of various pancreatic cancer cell lines through induction of apoptosis and inhibition of cell growth [6]. A compelling argument for a lack of association between dietary flavonoids and lignans and pancreatic cancer risk is that fruits, their main food source, do not appear to play a role in the aetiology of this cancer. However, given their diabetes-prevention effects, an association between flavonoids and lignans and pancreatic cancer risk is probable [7]. The purpose of this work is to review and analyzing the potential of flavonoids as natural therapeutics with cancer. We thereby focus our research on their role as antioxidants How different subfamilies affect tumour incidence and survival Regulation of cellular ROS.

**Role of flavonoids in plant**

The conservation of genes involved in flavonoid metabolism over the evolution of terrestrial plants is a convincing evidence of their vital importance in plant physiology [8]. Flavonoids are involved in flower colour and fragrance, involved in reproductive strategiesand protects cells from harmful UV rays (life of terrestrial plants), disease resistance and symbiosis by participating in stress response; it protects plants from harsh environmental conditions [9].

**Some plants can be used for cancer treatment**

**1. Chamomile Anticancer Activity: -**

Glioma is one of the most common intracranial malignancies with high incidence, rapidgrowth, high recurrence rate, high mortality and poor prognosis In vitro studies confirmed theanti-proliferative effect of this plant on cervical cancer cells [10]. In vitro studies confirmed the anti-proliferative effect of this plant on cervical cancer cells [11].

**2. Capsaicin**

**Anticancer effect**

Tumour development is a multistep process and usually occurs over a long period of time. Cancer cells acquire unique abilities that most healthy cells do not have Cancer arises and progresses through multiple genetic alterations and defective signalling pathways [12]. Identification of molecular targets involved in stages of tumorigenesis offers an opportunity to establish promising anticancer strategies [13]. Capsaicin's proposed anticancer mechanisms include cell cycle arrest and increased apoptosis [14].

### 3. Ginko biloba

**Anticancer effects**

Plants have provided a rich source of therapeutic agents and bases for synthetic drugs. G. biloba is dioecious. Male ginkgo biloba release pollen in spring to fertilize the female ginkgo biloba,which produces a large amount of ginkgo drop-like seeds in fall [15]. The anticancer effect of Ginkgo Folium was studied extensively in recent years. The tumour inhibition effect of Ginkgo Folium was demonstrated in mouse S180 mouse sarcoma, which might be due to the elevation on free radical scavenger enzymes [16]

### 4. Vinca rosea

**Anticancer activity**

Belonging to the genus vinca and oleander it has for a very long time been an important medicinal plant of great concern. In a study on human skin cancer cell line A431, the methanol extract of the plant had a positive effect on reducing the proliferation in this category [17]. The effects of this plant's alkaloids on cancer cells of breast, prostate, were studied, indicating that these alkaloids' tubular protein links changed its structure by blocking the division of cancerous cells; these compounds with antioxidant properties will prevent cancer cells fromprogression [18].

### 5. Thymus vulgar Aris

**Anticancer activity**

This plant has a variety of compounds, including flavonoids. Thymol and carvacrol are the most important plant phenol compounds that are useful in the treatment of breast cancer and colorectal cancer [19]. A study proved that thyme inhibits proliferation of human colorectal cancer cell migration and [20]. In another study, the effect of inhibiting growth was proved in human breast and colorectal cancer [21].

### 6. Curcuma longa

**Anti-cancer activity**

The study of cytotoxic properties of turmeric on liver cancer cells (Hep-2) showed that the cytotoxicity mediated by curcumin in a dose-dependent manner leads to apoptosis of cancer cells through mitochondrial pathway [22]. In another study, it was found that turmeric imposesits cytotoxic effects on lung cancer cells through inhibition of telomerase activity in a dose- dependent manner [23]. Curcumin, as an important ingredient of turmeric, plays a significant role in the prevention and treatment of primary ovarian cancer, and multiple clinical studies have proven its effectiveness [24].The anticancer potential of curcumin against cancers, including leukaemia, lymphoma, digestive, urinary, reproductive, breast, uterus, ovary, lung, melanoma, colon cancers, and brain tumours have been shown [25].

### Chemical composition of Flavonoids

**Flavanols (E.g. -Epigallocatechin gallate (EGCG))**

EGCG is one of the extensively studied flavonoids due to its characterization as the main constituent of green tea, an herb that is associated with several health benefits [26]. As previously mentioned, flavonoids mitigate free radical production via the Fenton reaction by binding iron. However, EGCG green tea elicits protective capacity against cardiovascular diseases, cancer, obesity, neurodegenerative disorders, diabetes, and several other pathologies
[27]. EGCG also exerts anti-promotion and anti-progression effects in several cancer types. Forinstance, EGCG protects against 2-amino-1- methyl-6-phenylimidazo [4, 5-b] pyridine (PhIP) - induced malignant

transformation of breast cancer cells [28].

**Flavones (E.g.-Luteolin)**

Luteolin is abundant in certain vegetables and herbs such as bell Peppers, parsley, celery, and carrots [29]. This agent displays prominent anticancer effects in cell cycle arrest and apoptosis [30]. In lung carcinoma mediated by attenuation of oxidative stress. In bladder cancer cell line T24, luteolin induces a drop in ROS levels and a subset quant inactivation of mTOR signalling resulting, luteolin elicits pro-apoptotic effects by virtue of its antioxidant capacity [31]. Additionally, luteolin increases the generation of ROS, which makes NSCLC more susceptible to radiotherapy-induced cell death [32] it's unknown how this characteristic is controlled. It's vital to note that luteolin appears to have selective prooxidative effects. Cancerous cells while sparing healthy cells [33].

**Flavan-3-ols**

Apples, grapes, wine, chocolate, and tea are a few examples of foods that are rich in flavan-3- ols [34] Next to water, tea is the beverage that is consumed most frequently worldwide [35]. The most common teas are green, black, and oolong, which vary in their levels of fermentation. Tea leaves are green Oolong tea is simply dried and roasted and partially fermented and heavily fermented black tea [36]. Further research revealed that DNMT activity was directly inhibited by EGCG, resulting in lower cellular amounts of 5-methylcytosine, although Stresemann and colleagues reported that EGCG had no impact on DNMT activity (2- ).50 mol/L) on cancer cells following a 3-day course of therapy [37]

**Isoflavones**

Isoflavonoids are a large and very distinctive subgroup of flavonoids. Isoflavonoids enjoy only a limited distribution in the Plant kingdom and are predominantly found in soya beans and other leguminous plants. Some isoflavonoids have also been reported to be present in microbes[38] They are also play an important role as precursors for the development of phytoalexins during plant microbe interactions [39]. High consumption of isoflavonoids was correlated with decreased risk of estrogen Related Cancers [40].

**Flavanones**

Flavanones are another important class which is generally pre-Sent in all citrus fruits such as oranges, lemons and grapes.Flavonones are associated with A number of health benefits because of their free radical-Scavenging properties [41]. Flavanones, also known as di-hydroflavones, are characterized by a saturated, oxidized C ring. Hesperetin and Naringenin are two main flavanone compounds [42].

**Functions of foods and their role in cancer treatment**

Nutrition and foods are related to about 30% of all the cancers cases. There are numerous studies showing relation between functional foods and reduce in cancer [43]. Cancer biologists have concerned in the application of natural products to improve the survival rate of cancer patients. Americans, Japanese, and Europeans are turning to the use of dietary vegetables, medicinal herbs, and their extracts or components to prevent or treat cancer. Newly, food

Producers have embarked on a health criterion in the development of "functional foods", the latter being defined as food products that have an added positive health benefit [44]. Functional foods are foods and food components that supply health benefits beyond basic nutrition. These foods are

similar in appearance to conventional foods; functional foods consumed as part of the normal diet. Functional food supplies the body with the needed number of vitamins, fats, proteins, carbohydrates, etc., required for its healthy survival [45]. A number of compounds naturally occurring in foods, particularly anti-oxidative compounds in plants or their extracts and essential oils, have shown promise as potential chemo preventive factors [46].

**Direct intake fruits and vegetables for cancer treatment.**

One of the most important messages of modern nutrition research is that a diet rich in fruits and vegetables protects against cancer. (The greatest message is that this same diet protects against almost all other diseases, too, including cardiovascular disease and diabetes) [47]. For most cancers, people in the lower quartile (1/4 of the population) who ate the least number of fruits and vegetables had about twice the risk of cancer compared to those who in the upper quartile who ate the most fruits and vegetables. Steinmetz and Potter reviewed the relationship between fruits, vegetables, and cancer in 206 human epidemiologic studies and 22 animal studies. They found "the evidence for a protective effect of greater vegetable and fruit consumption is consistent for cancers of the stomach, esophagus, lung, oral cavity and pharynx, endometrium, pancreas, and colon." Allium vegetables, carrots, green vegetables, cruciferous vegetables, a significant correlation between saturated fat intake and breast cancer, but using a FFQ there was no significant correlation [48].

**Conclusions and Future Perspectives**

Over the past ten years, flavonoids have attracted a lot of interest in the literature, and a number of potential positive benefits have been clarified. Numerous reports have emphasized the need for molecular docking studies to find new flavonoid compounds for use in treating a range of illnesses in the human health system. Therefore, more research is required to increase the value of flavonoids in the diet and promote human health Future study should focus on how flavonoids interact with receptor molecules to treat both acute and chronic diseases.

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